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National Institute of Allergy and Infectious Diseases

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NIAID RESEARCH ON AIDS

The National Institute of Allergy and Infectious Diseases (NIAID) is the principal agency of the U.S. Public Health Service responsible for conducting basic and clinical research on acquired immunodeficiency syndrome (AIDS), and the human immunodeficiency virus (HIV).

NIAID's efforts cover five broad scientific areas: (1) HIV pathogenesis research, (2) epidemiology and natural history, (3) vaccine research and development, (4) treatment research and development, and (5) HIV disease in children.

NIAID sponsors investigations through research project grants, contracts and cooperative agreements. Several major contracts provide critical resources to NIAID and to researchers nationally. These contracts include the AIDS Research and Reference Reagent Program, which makes substances available to laboratory scientists, and the AIDS Clinical Trials Information Service, whose staff provides telephone callers with information about specific clinical trials of AIDS therapies.

Investigators in NIAID's intramural laboratories conduct basic research in such areas as molecular biology, virology, microbiology and immunology. In addition, NIAID scientists carry out clinical research --investigating promising new therapies and testing potential vaccines.

HIV Pathogenesis Research

Pathogenesis research and basic research in a range of fields has laid the foundation for the many rapid advances that have contributed to our knowledge of HIV and AIDS. Multidisciplinary studies increase our understanding of the biology of HIV, including the life cycle of the virus and its effects on the host. Knowledge gained from these studies enhances the ability of researchers to create new drugs and vaccines to combat HIV infection.

NIAID scientists have undertaken landmark studies in this area, resulting in findings such as the discovery of lymphoid tissue as a major reservoir for HIV, and the demonstration that so-called clinical latency is, in fact, a period of active viral replication.

The Centers for AIDS Research, which NIAID established at U.S. research institutions and universities, provide critical resources and enhance collaboration in AIDS-related basic research.

Epidemiology and Natural History

NIAID-sponsored epidemiologic studies characterize and provide data on the clinical history of HIV infection and related diseases and develop the knowledge base for vaccine and treatment interventions. Several large, multicenter epidemiologic research projects are under way. These

studies document the changing natural history and spectrum of complications of HIV disease in different populations.

Vaccine Research and Development

Development of a safe and effective vaccine for AIDS is a public health priority. NIAID-supported basic research studies add knowledge about the mechanisms of immunity to HIV and provide information on the most promising candidate vaccines. The National Cooperative Vaccine Development Groups are developing and testing novel experimental HIV vaccine concepts. NIAID-supported animal studies examine the effects of potential vaccines in several retroviral models. Other studies focus on identifying vaccine adjuvants, compounds that enhance the immune responses to the vaccine.

In the United States, several candidate vaccines currently are being evaluated in people for safety and the ability to stimulate the immune system. The NIAID Division of Intramural Research and six NIAID-supported AIDS Vaccine Evaluation Units, located at universities throughout the United States, are conducting clinical vaccine trials. NIAID is also laying the foundation for prevention research and the conduct of efficacy trials when suitable vaccine products become available.

Treatment Research and Development

NIAID's goal is to foster the discovery and development of interventions that will improve the quality and duration of life of HIV-infected individuals. Basic research is the foundation of this effort, underpinning programs of targeted drug discovery to combat HIV and opportunistic infections.

NIAID has four diverse networks that conduct clinical trials to evaluate promising therapies for HIV infection and associated opportunistic infections and cancers. The AIDS Clinical Trials Group (ACTG), the Terry Bein Community Programs for Clinical Research on AIDS (CPCRA), the Division of AIDS Treatment Research Initiative (DATRI) and intramural facilities in the NIH Clinical Center in Bethesda.

Pediatric HIV Disease

NIAID's pediatric AIDS research program focuses on identifying and supporting the development of improved ways to prevent and treat HIV infection in infants, children and adolescents. Besides conducting treatment research, NIAID-supported investigators are looking for ways to prevent perinatal transmission and to identify early HIV-infected infants.

NIAID, a component of the National Institutes of Health, supports research on AIDS, tuberculosis and other infectious diseases as well as allergies and immunology. NIH is an agency of the U.S. Public Health Service, U.S. Department of Health and Human Services.

Prepared by:
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National Institute of Allergy and Infectious Diseases

Clinical Trials for AIDS Therapies

The National Institute of Allergy and Infectious Diseases (NIAID) has the lead responsibility within the National Institutes of Health for research on therapies for HIV disease and associated opportunistic infections and cancers.

In keeping with NIAID's mission to foster the discovery and development of interventions that improve the quality and duration of life for HIV-infected individuals, the institute supports four diverse clinical trials programs: the AIDS Clinical Trials Group (ACTG), the Terry Bein Community Programs for Clinical Research on AIDS (CPCRA), the Division of AIDS Treatment Research Initiative (DATRI) and the Division of Intramural Research (DIR) clinical trials effort. NIAID's Division of AIDS (DAIDS) coordinates the first three of these programs.

The programs investigate therapeutic agents and novel treatment approaches including studies and trials of safety, dose, activity, efficacy and optimal use. Together, the programs represent the largest AIDS therapy research initiative in the United States, if not the world.

AIDS Clinical Trials Group

With a large patient capacity, clinical expertise and sophisticated laboratory capabilities, the ACTG conducts trials ranging from early safety studies to large-scale, multi-center efficacy trials that evaluate therapies for all aspects of HIV disease.

As a result, ACTG trials have yielded an unprecedented amount of information on the safest and most effective ways to treat people with HIV infection and related diseases.

For example, as a result of ACTG studies, the U.S. Food and Drug Administration (FDA) approved the use of antiviral therapy using zidovudine (AZT), didanosine (ddI), zalcitabine (ddC) and stavudine (d4T). These four drugs inhibit HIV's ability to replicate by interfering with the reverse transcriptase enzyme. In February 1994 an interim review of a study (ACTG 076) conducted by the Pediatric ACTG found that AZT therapy reduced the risk of viral transmission from HIV-infected pregnant women to their babies by two-thirds and led to the FDA approval of AZT for this purpose.

The ACTG has made tremendous contributions and defined the standards of care for the treatment and prevention of several opportunistic infections (OIs). ACTG studies found that the oral drug trimethoprim-sulfamethoxazole (TMP/SMX) is better than aerosolized pentamidine for preventing a second episode of *Pneumocystis carinii* pneumonia (PCP) in people with AIDS who tolerate both drugs.

ACTG research also has defined the standard treatment for other OIs, for example: fluconazole as treatment and maintenance therapy for patients with cryptococcal

meningitis, itraconazole as treatment and maintenance therapy for those with disseminated histoplasmosis, clarithromycin for the treatment of patients with disseminated *Mycobacterium avium* complex (MAC) and foscarnet for the management of patients with cytomegalovirus (CMV) retinitis and acyclovir-resistant herpes simplex. Currently, more than 30 drugs and drug combinations remain under investigation by ACTG scientists for use against HIV-related OIs and cancers.

The ACTG grew from NIAID's first comprehensive AIDS clinical trials effort, which began in June 1986 with 14 sites that evaluated potential therapies in HIV-infected adults. By December 1987 NIAID had established the ACTG as a network of more than 20 medical centers across the country. This expansion reflected NIAID's goal of promoting greater collaboration among investigators by sponsoring multicenter studies of anti-HIV agents, drugs for treatment and prevention of OIs, and immune-based therapies.

Today, the ACTG includes 57 AIDS Clinical Trials Units (ACTUs) at universities and medical centers located in 20 states, the District of Columbia and Puerto Rico. Of the units, 35 conduct clinical trials in adults, while 22 units comprise the Pediatric ACTG, which conducts trials in children, adolescents and pregnant women. In addition, the National Hemophilia Foundation participates in the ACTG through its Hemophilia Treatment Centers.

Four of the adult clinical trials sites are at minority institutions: Howard University in Washington, D.C., Meharry Medical College in Nashville, Tenn., University of Hawaii in Manoa and the University of Puerto Rico in San Juan.

The ACTG Operations Office provides technical and logistical support, and the ACTG Statistical and Data Analysis Center collects and analyzes the data for both the pediatric and adult sites.

To improve the efficiency and productivity of the ACTG, a comprehensive assessment was conducted in 1993. This effort included an independent scientific review of the group's accomplishments and future research plans, as well as an evaluation by DAIDS staff of the group's mission, organization and management. As a result, several changes occurred. Most notably is the administrative and scientific separation of the adult and pediatric components of the ACTG. Other organizational changes will be implemented over the next two years, particularly during the next regular competitive renewal of funding for the Adult ACTG in early 1996 and the Pediatric ACTG in early 1997.

Terry Bein Community Programs for Clinical Research on AIDS

NIAID established the Community Programs for Clinical Research on AIDS (CPCRA) in 1989, renamed in 1991 by an act of Congress in memory of Terry Bein, a health policy consultant to Sen. Edward M. Kennedy and a manager at the American Foundation for AIDS Research.

The CPCRA builds on the expertise of primary care providers, involving them in the design and conduct of scientifically sound, community-based clinical trials.

In the CPCRA, community-based physicians work with DAIDS staff to set research priorities, design and conduct clinical research projects, develop new methods for conducting clinical trials and

incorporate existing research methods into community-based settings. The majority of CPCRA studies focus on optimizing use and determining the long-term, clinical consequences of different, commercially available treatments.

For example, a CPCRA study (CP 002) found that ddC is at least as effective as ddI for people with late stage HIV disease who fail or cannot tolerate AZT. Another CPCRA study (CP 001) found that the use of pyrimethamine as a primary preventive treatment for toxoplasmosis adversely influenced survival.

At present, the prevention and treatment of OIs associated with HIV infection are of highest scientific priority in the CPCRA. Specific priorities include: simpler therapeutic strategies for simultaneous prevention of diseases caused by multiple opportunistic pathogens, prevention and treatment of *Mycobacterium tuberculosis*, new regimens for preventing PCP, prevention of fungal infections in HIV-infected women, the prevention and treatment of MAC and oral prevention treatment against CMV. The CPCRA also has a strong interest in identifying better antiretroviral treatment strategies and is studying various combination therapies.

NIAID recomputed the CPCRA in September 1994, and now includes 16 units with more than 100 affiliated sites in 15 U.S. cities. As part of the CPCRA network, a Statistical Center manages research design and data analysis and an Operations Center provides necessary administrative, technical and educational services.

Division of AIDS Treatment Research Initiative

The Division of AIDS Treatment Research Initiative (DATRI), established in 1991, is a small, highly flexible, contract-supported effort that conducts unusual or intensive studies of high priority to the NIAID that are not easily performed within the other clinical trials networks.

Currently, DATRI includes 50 sites with clinical trials capabilities. The program will be expanded in the future to include special preclinical studies, allowing for an integrated preclinical/clinical approach to studying drugs and drug combinations.

Most of DATRI's Phase I and Phase I/II studies are performed at university-based medical centers that have the facilities, personnel and experience to conduct highly technical in-patient and out-patient research. For some Phase II studies, a mix of university and community-based sites may be used to recruit, manage, follow and evaluate volunteers.

Several Phase I DATRI trials, designed to examine the safety and biologic activity of a new treatment in small numbers of participants, have had significant findings. One such trial demonstrated a potentially harmful interaction between clarithromycin and rifabutin, finding that the rifabutin concentration in plasma increased 75 percent in the presence of clarithromycin. Another study demonstrated that AZT therapy had no detectable effect on the amount of HIV in lymphoid tissue or in peripheral blood mononuclear cells of patients with early HIV disease. This study also found that antiretroviral therapy during early HIV disease does not affect HIV replication in such cells.

NIAID Intramural AIDS Research

NIAID's Division of Intramural Research (DIR) investigates the response of the human immune system to invasion by HIV, and evaluates drugs to fight the infection and candidate vaccines designed to prevent disease.

Using the knowledge gained in the laboratory, scientists at DIR and the NIH Clinical Center examine agents that may interrupt viral replication, study potential therapies to stop OIs and explore ways to reconstitute the damaged immune systems of people with AIDS.

DIR investigators have shown that the drug atovaquone, formerly called 566C80, is safe and effective for treating patients with mild to moderate PCP, making it a possible alternative to the standard therapies pentamidine and TMP/SMX. In addition, the investigators demonstrated that this agent has the potential for wide-reaching clinical use because it effectively treated patients with cerebral toxoplasmosis who did not respond to conventional therapy.

Preliminary DIR studies have shown that intermittent therapy with interleukin-2 can lead to sustained increases in numbers and percent of CD4+ T cells in HIV-infected patients. Controlled trials are underway to evaluate this treatment further. Another DIR study, a controlled trial using foscarnet to treat HIV-infected patients who have CMV retinitis, showed clear-cut benefits and provided evidence for the FDA approval of this agent.

For More Information About Clinical Trials

For further information about any of the NIAID-supported clinical trials, call 1-800-TRIALS-A (1-800-243-7012 TTY/TDD) weekdays from 9 a.m. to 5 p.m. Eastern Time. For further information specifically about clinical trials conducted by the NIAID DIR AIDS program, call 1-800-243-7644 weekdays from 9 a.m. to 5 p.m. Eastern Time.

NIAID, a component of the National Institutes of Health, supports research on AIDS, tuberculosis and other infectious diseases as well as allergies and immunology. NIH is an agency of the U.S. Public Health Service, U.S. Department of Health and Human Services.

Prepared by:
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U.S. Department of Health and Human Services
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FACSIMILE COVER SHEET

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COMMENTS:

Jo-
Here's the memo from OAR.

Jane

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NOTE TO JANE SANVILLE:

Attached please find the reformatted NIH portion of the national plan, as requested by your office.

A diskette in Wordperfect 5.1 is also provided; however, we would appreciate knowing if you plan any substantive changes.


Wendy Wertheimer
Senior Advisor

National Institutes of Health

Area Research

Goal 1 Conduct and support research on the natural history and epidemiology of HIV infection and AIDS in all populations

Objectives	Action Steps	Programs				
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement
			FY 1995 (appropri.)	FY 1996 (proposed)		
Natural History and Epidemiology	Develop and assess intervention strategies to reduce or prevent HIV transmission	Support development and evaluation of improved, acceptable, effective physical and non-irritating 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 cesarean sections, vaginal cleansing, and breast-feeding practices that prevent perinatal transmission. These should include randomized trials where possible, cooperation between study groups, and re-analysis of data from existing studies, where appropriate; Assess the efficacy of combined strategies that decrease blood-borne transmission of HIV; for example, evaluating existing needle exchange programs, the use of bleach as a disinfectant, and drug abuse prevention and treatment on reducing HIV transmission and seroincidence;	48,656	48,137	All populations	

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Develop and assess intervention strategies to reduce or prevent HIV transmission (continued)	Develop domestic and international cohort-based infrastructures for testing HIV vaccines and other interventions (e.g., microbicides, behavioral) for preventing HIV transmission; Develop and evaluate interventions related to sexual behavior, including (1) STD treatment and prevention and their effects on HIV transmission, (2) interventions focused on influencing safe sexual behaviors, reproductive decision-making, and contraceptive choices for women, and (3) integration of health care delivery systems such as those that combine reproductive health and STD/HIV prevention and treatment services; Develop methods of outreach that would engage high-risk populations, enroll them in research to identify factors that contribute to high-risk behavior, and increase and maintain compliance with interventions as well as recruit and retain hard-to-reach populations in studies; Incorporate interdisciplinary evaluation research designs of HIV prevention strategies to ensure adequacy of findings regarding outcome, process, and descriptive analysis;					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Develop and assess intervention strategies to reduce or prevent HIV transmission (continued)	Evaluate the social acceptability, the ease of compliance, and barriers to access and use of interventions (e.g., AZT for perinatal transmission, virucides); Develop and evaluate improved procedures for screening, monitoring, and inactivating HIV and other retroviruses in the blood supply; and develop and evaluate alternatives to allogeneic blood transfusion, including artificial blood substitutes and hematopoietic growth factors; and Assess the impact of drug and alcohol abuse on efficacy of behavior modification interventions directed at sexual transmission.					
Natural History and Epidemiology	Characterize the risk factors and mechanisms of HIV transmission in various populations	Evaluate HIV transmission in relationship to: a. viral factors, virus load in the blood and at mucosal sites, characteristics of the HIV virus present (virus subtype and phenotype), and co-infection with other viruses (HTLV and HIV2); b. host factors such as pregnancy, menstrual cycle, hormonal contraceptives, and HLA type;	24,271	26,257	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Characterize the risk factors and mechanisms of HIV transmission in various populations (continued)	c. local factors including intercurrent STDs, oral and anogenital inflammation (ulceration), mucosal immunity, and anatomic factors such as ectopy; and d. behavioral risk factors, such as oral and anal sex; Further differentiate the timing and mechanism of perinatal transmission; Study susceptibility to HIV infection, especially in individuals who are at high risk for repeated exposure to HIV but who remain uninfected, in order to determine factors related to resistance, including mucosal immunity, viral, genetic, and other immunologic factors, endocrinologic factors, and other factors; Determine the role of breast-feeding in the transmission of HIV from infected mother to child; and Examine the extent to which drug use (including alcohol and tobacco) and drug-using behaviors affect susceptibility and/or transmission of HIV.					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Elucidate the progression of HIV-related disease, from early infection through long-term consequences and sequelae, with the goal of understanding, preventing, and treating those factors that may lead to disease	Identify pathogenic mechanisms and cofactors for disease progression and disease-specific outcomes in well-defined subsets of individuals (e.g., high-CD4 long-term survivors, low-CD4 long-term survivors, rapid progressors). Studies should include investigation of behavioral, genetic, virologic, immunologic, and host factors; In diverse populations, describe the full spectrum of HIV-related disease, including OIs, HIV-related malignancies, wasting, and organ-specific complications; evaluate the impact of sociodemographic variables, gender, age, and route of transmission on HIV disease progression, time to AIDS, and specific outcomes; Study the natural history of early HIV infection; Evaluate issues specific to HIV-infected children, including: (1) mechanisms that contribute to impaired growth and neurodevelopment, (2) impact on childhood infectious diseases and the safety and efficacy of immunization, and (3) childhood-specific complications including lymphoid interstitial pneumonitis;	53,565	59,574	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Elucidate the progression of HIV-related disease, from early infection through long-term consequences and sequelae, with the goal of understanding, preventing, and treating those factors that may lead to disease (continued)	Evaluate the interaction of hormonal factors (including pregnancy, contraceptives, and hormonal replacement therapy) and HIV disease progression; Maintain longitudinal cohorts and create linkage with clinical studies (e.g., ACTG, CPCRA) to (1) efficiently examine the full spectrum of disease, (2) assess the impact of therapies on the frequency and severity of HIV-related sequelae, disease progression, and survival, and (3) assess and validate laboratory and behavioral markers; Study the progression of HIV-related disease in adolescents who have acquired their diseases as a result of injecting drug use and/or sexual activity; Study the factors that predict, protect against, contribute to, or limit the progression of HIV infection in the nervous system including early cognitive impairment, dementia, and neuropathy;					

Objectives	Action Steps	Descriptions	Programs				
			Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Elucidate the progression of HIV-related disease, from early infection through long-term consequences and sequelae, with the goal of understanding, preventing, and treating those factors that may lead to disease (continued)	Develop, maintain, and expand national repositories for the collection and banking of blood, other body fluids, and tissue specimens obtained from longitudinal cohort studies and other well-characterized populations of HIV-infected individuals as a resource for studies of HIV-mediated pathogenesis, correlates of immunity to HIV infection, and specific HIV-related outcomes; Study the nutritional and absorption factors that predict, protect against, contribute to, or limit the progression of HIV-related wasting and weight loss; Evaluate strategies of care delivery and case management to determine their impact on HIV disease progression and quality of life; Elucidate the mechanisms of HIV-associated carcinogenesis and improve strategies for early diagnosis and for effectively treating these malignancies; Study oral lesions in HIV disease and progression; and Study the long-term natural history of related retroviruses (e.g., HTLV and HIV-2) to elucidate retroviral pathogenesis and resistance mechanisms.					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Identify, evaluate, and apply innovative laboratory and behavioral strategies to study epidemiologically defined populations with regard to transmission and progression of HIV disease	Apply cutting-edge laboratory approaches and behavioral strategies to assess susceptibility to infection and transmission and monitor disease progression and response to intervention in population studies; Facilitate the transfer of novel laboratory and behavioral strategies from basic research to epidemiologic applications; Promote development and application of laboratory approaches to elucidate mechanisms, cofactors, and timing of maternal-fetal-infant transmission of HIV infection; Assess new virologic parameters (e.g., viral burden, genotype/phenotype) applicable to body fluids that correlate with infectiousness for evaluating interventions (e.g., spermicides/microbicides, vaccines); Identify laboratory parameters associated with HIV-related outcomes, such as intermediate end points preceding HIV-associated infections and malignancies, predictors of long-term survival or rapid progression, and markers of exposure to HIV without infection;	23,074	23,210	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Identify, evaluate, and apply innovative laboratory and behavioral strategies to study epidemiologically defined populations with regard to transmission and progression of HIV disease (continued)	Facilitate, develop, evaluate, and apply assays for assessment of mucosal immunity related to susceptibility to infection and impact of intervention; Identify, characterize, and evaluate reliable diagnostic markers, including markers in saliva, for the purpose of applying rapid and sensitive diagnostic technologies for detecting HIV infection; Promote development and assessment of assays to detect HIV infection in vaccinated populations; and Establish, maintain, and expand national repositories of biologic specimens (e.g., blood, body fluid, and tissue) obtained from well-characterized individuals in longitudinal studies to facilitate rapid evaluation of existing strategies and development of new strategies.					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Perform the epidemiologic studies of HIV infection, related conditions, and risk behaviors in domestic and international populations in which HIV is prevalent, emerging, and/or increasing	Identify emerging high-risk groups in the United States through seroincidence studies and identification of behavior risk factors in the population. Examples of groups that need particular attention and further evaluation include minorities, women, adolescents, children, young gay men, homeless mentally ill, drug users, and the incarcerated; Develop infrastructure to define populations in the United States and throughout the world with high incidence and prevalence suitable for vaccine and other intervention trials; Delineate the epidemiology of behavioral risk factors for HIV in defined population-based studies; Measure the occurrence of other infectious agents, e.g., other viruses (HTLV-1, HSV-2, hepatitis B and C, etc.), sexually transmitted diseases, and mycobacterium (e.g., MTB, <i>M. avium</i>) in populations at risk for HIV; Coordinate with the CDC, WHO, and other institutions to maintain a comprehensive view of the epidemic with as much detailed information about subpopulations as possible;	29,448	31,644	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Natural History and Epidemiology	Perform the epidemiologic studies of HIV infection, related conditions, and risk behaviors in domestic and international populations in which HIV is prevalent, emerging, and/or increasing (continued)	Promote the development of new high-quality biometry programs for AIDS research evaluation, including new methodologies; Define the scope and role of HIV in the etiology of cancer and determine the impact of HIV-related malignancy on total cancer burden in the population; and Cooperate with health services agencies to determine why many individuals and groups continue to underutilize health services related to HIV that are already available (e.g., access to care, perceptions regarding efficacy, etc.).					

Area Research

Goal 2 Conduct and support research on the etiology and pathogenesis of HIV infection to define the mechanism by which the virus causes disease

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Etiology and Pathogenesis	Delineate the cellular and molecular mechanisms associated with the viral immunopathogenesis of HIV-related immune dysfunction	Delineate the direct and indirect mechanisms underlying HIV-induced depletion and dysfunction of target cells/tissues;	201,040	217,368	All populations		
		Define the virologic (load and phenotype), immunologic (specific and nonspecific), genetic, and environmental factors that contribute to disease progression and nonprogression;					
		Delineate the molecular mechanisms by which virus-derived factors regulate HIV replication and pathogenesis, with special emphasis on the use of primary virus isolates and cells;					
		Delineate the role of immune activation and host factors, including cytokines, in HIV replication and pathogenesis;					
		Delineate the role of lymphoid organs, including mucosal-associated lymphoid tissue, in HIV pathogenesis;					
		Further develop and utilize experimental models to examine the pathogenesis of lentiviral infections;					
		Delineate the role of lymphoid and hematopoietic precursor cells and their microenvironment in immune impairment;					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Etiology and Pathogenesis	Delineate the cellular and molecular mechanisms associated with the viral immunopathogenesis of HIV-related immune dysfunction (continued)	Develop new assay systems for effective measurement of changes in viral load and host immune function that are predictive of disease progression; Delineate the range of cell types infected by HIV <i>in vivo</i> and their potential role as viral reservoirs; and Establish and expand collaborative programs to facilitate sharing of key patient samples, animal model resources, and laboratory reagents.					
Etiology and Pathogenesis	Delineate the molecular and cellular mechanisms of transmission and establishment of infection and their impact on disease progression	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 disease; 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 effects of viral genotype and load on transmission of cell-free and cell-associated virus;	28,140	34,233	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Etiology and Pathogenesis	Delineate the molecular and cellular mechanisms of transmission and establishment of infection and their impact on disease progression (continued)	Determine the roles of specific and nonspecific mucosal immunity and host factors that inhibit/enhance HIV transmission; Determine the mechanisms of vertical HIV transmission; and Elucidate unique aspects of HIV transmission and disease progression in underresearched populations.					
Etiology and Pathogenesis	Elucidate the etiologic factors and cofactors in the pathogenesis of HIV-related malignancies	Elucidate the role of HIV infection, immune dysfunction, and interactions with potential cofactors in the development of HIV-associated malignancies; Identify the characteristics of the host that predispose to development of malignant disease, including genetic, hormonal, growth factor, cytokine, and immunologic characteristics; and Identify the molecular correlates of HIV-associated malignancies, including but not limited to oncogenes, tumor suppressor genes, tumor promoters and carcinogens, and viral and microbial genes and proteins.	28,544	28,941	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Etiology and Pathogenesis	Elucidate the pathogenic mechanisms involved in HIV-associated neurological diseases	Investigate the contributions of viral infection and virally induced indirect factors (in neuronal and non-neuronal cells) to nervous system impairment; Delineate how HIV enters and persists in the nervous system and causes functional impairment; Investigate both biological and environmental factors that may affect nervous system function in the context of HIV disease, using neurological and appropriate neuropsychologic assessment tools; Study the effects of neurotrophins and immunoregulatory and proinflammatory cytokines on both host and viral gene expression; Delineate the role of OIs and drug treatment in neurologic complications of AIDS, including peripheral neuropathies, hearing and visual loss, and behavioral changes; Assess neural tissue and organs as virus reservoirs in HIV disease and as sources of specifically neurovirulent/neuroinvasive viral strains; and Develop neuroimaging tools for correlative structural-functional studies of progressive HIV-associated neurological disorders.	38,984	41,067	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Etiology and Pathogenesis	Elucidate the pathogenesis of HIV-related opportunistic infections	Elucidate the mechanisms of immune function that mediate protection against the OIs; Develop <i>in vitro</i> techniques and animal models, where needed, to propagate the opportunistic micro-organisms and conduct studies designed to provide details of the basic biology and pathogenic mechanisms of these micro-organisms; Identify and elucidate the genetic and environmental risk factors associated with susceptibility, development, and progression of opportunistic infections; Develop and validate diagnostic assays for the reliable and rapid identification of HIV-associated opportunistic infections; Study the effects of OIs on immune dysfunction; and Elucidate immunologic markers that are correlative with disease progression for HIV-associated OIs and develop assays to accurately monitor these markers as a function of therapy.	32,222	35,151	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Etiology and Pathogenesis	Elucidate the etiology and pathophysiology of HIV-related wasting, failure to thrive, and growth retardation	Define alterations in body composition, nutritional status, metabolic patterns, energy balance, and growth and development associated with HIV infection; and Elucidate the pathogenesis of HIV-associated wasting and impaired growth and development, including the roles of cytokines, malabsorption, anorexia, opportunistic infections, HIV, and other factors.	2,931	2,918	All populations		
Etiology and Pathogenesis	Elucidate the etiology and pathogenesis of HIV-related organ/tissue-specific disorders, such as HIV-associated renal, gastrointestinal, endocrine, cardiopulmonary, autoimmune, and other diseases	Investigate the etiologic and pathogenic mechanisms of HIV-associated enteropathy, including the role of HIV, opportunistic infections, tumors, and other factors; Identify host, viral, environmental, and other factors responsible for the pathogenesis and progression 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; and Elucidate the etiology and pathogenesis of HIV-related cardiopulmonary disease and other organ/tissue-specific manifestations, including autoimmune disease.	13,802	15,089	All populations		

Area Research

Goal 3 Conduct and support research to develop therapeutics for HIV infection and its sequelae

Objectives	Action Steps	Programs				
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement
			FY 1995 (appropri.)	FY 1996 (proposed)		
Therapeutics	Improve screening, discovery, and preclinical development of therapeutic agents that demonstrate activity against retroviruses, fostering activity by and in collaboration with industry	Identify promising targets for anti-HIV therapy and extend knowledge of their mechanisms of action, develop assays for identifying drugs active against those targets, and develop new compounds active at those targets, with an emphasis placed on identifying agents active at novel targets other than reverse transcriptase inhibitors; Complete preclinical development, in cooperation with industry when appropriate, of promising new compounds and combinations of compounds and novel natural products, including assessment of efficacy, toxicity, teratogenicity, and fertility in animal models;	154,833	162,200	All populations	

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Improve screening, discovery, and preclinical development of therapeutic agents that demonstrate activity against retroviruses, fostering activity by and in collaboration with industry (continued)	Continue and accelerate screening of large numbers of natural and synthesized compounds for anti-HIV activity in the AIDS Drug Screen, with a particular emphasis on the detection of agents that act at unique steps of the HIV life cycle, on an understanding of the molecular basis of bioavailability and pharmacokinetics, and on ability to follow up on lead compounds for the development of analogues; develop and screen combinatorial libraries; emphasize central nervous system penetration; develop formulations that would be suitable for infants and children; Emphasize basic and applied research to advance cross-NIH development of gene therapy; support development of preclinical laboratories to advance gene therapies; 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 approaches for the use of macromolecular structure in designing drugs to combat HIV infection and AIDS; make resolved structures available in publicly accessible data bases;					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Improve screening, discovery, and preclinical development of therapeutic agents that demonstrate activity against retroviruses, fostering activity by and in collaboration with industry (continued)	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; and 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.					
Therapeutics	Perform clinical trials of agents active against HIV based on an understanding of pathogenesis with emphasis on improved design and methodologies, and integrate clinical trials with ongoing natural history studies	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; Increase the understanding of the pathogenesis of HIV disease based on the evaluation of antiretroviral agents in clinical trials;	145,105	151,627	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Perform clinical trials of agents active against HIV based on an understanding of pathogenesis with emphasis on improved design and methodologies, and integrate clinical trials with ongoing natural history studies (continued)	Implement the development and evaluation of virologic, immunologic, and clinical markers to assess drug activity and determine the prognostic value of these 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 the ultimate acceptability of new agents and approaches that translate into clinical use; Improve the utilization of GCRCs for the conduct of single and multi-institutional clinical trials; Establish and expand appropriate career training programs for laboratory investigators, clinical investigators, and translational scientists; 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);					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Perform clinical trials of agents active against HIV based on an understanding of pathogenesis with emphasis on improved design and methodologies, and integrate clinical trials with ongoing natural history studies (continued)	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 followup, enroll patients in sequential randomized trials once they have reached an end point in their initial trial; and Evaluate new and existing compounds capable of inhibiting the sexual transmission of HIV, such as topical microbicides and HIV-specific viricides; nested studies to evaluate the infectivity of body fluids, such as semen and cervical secretions in trials of antiretroviral therapies.					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Extend our understanding of immunopathogenesis through the development and testing of strategies that enhance and/or restore the deficient immune systems of HIV-infected individuals	Evaluate therapeutic approaches that test specific hypotheses of HIV immunopathogenesis; Develop and validate new methods to evaluate immune function in the context of clinical trials; Continue and accelerate the testing of cytokines and modulators of cytokines either alone 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;	18,619	19,349	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Extend our understanding of immunopathogenesis through the development and testing of strategies that enhance and/or restore the deficient immune systems of HIV-infected individuals (continued)	Develop new therapeutic strategies based on gene therapy approaches to protect or potentially reconstitute the immune system; Use structural biologic techniques to determine the structures of various cytokines and cytokine receptors as potential targets for HIV therapies; and Enhance collaboration among ICDs to facilitate the conduct of immune-based therapeutic trials and to enhance pathogenesis-related research in HIV-infected individuals.					
Therapeutics	Target the discovery, development, and evaluation of potential agents for prevention and treatment of HIV-associated OIs and other infections modified by HIV infection, including those specific to women, children, and drug users	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, such as wasting syndrome. 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;	107,915	111,887	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Target the discovery, development, and evaluation of potential agents for prevention and treatment of HIV-associated OIs and other infections modified by HIV infection, including those specific to women, children, and drug users (continued)	Support discovery and preclinical programs to develop therapies especially targeting cryptosporidia, microsporidia, JC virus, CMV, HPV, and azole-resistant fungal organisms, with emphasis on bioavailable agents with favorable pharmacokinetics. Develop <i>in vitro</i> culture systems for OIs such as <i>Pneumocystis carinii</i>. Further conduct clinical trials for the prophylaxis and treatment of HIV-associated OIs in HIV-infected individuals, including pregnant women and children and drug users. Important OIs include <i>Mycobacterium tuberculosis</i> infection (TB), <i>Mycobacterium avium</i> 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;					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Target the discovery, development, and evaluation of potential agents for prevention and treatment of HIV-associated OIs and other infections modified by HIV infection, including those specific to women, children, and drug users (continued)	Determine the optimal strategies and combinations of agents to prevent and treat multiple OIs (i.e., multiple opportunistic pathogen prophylaxis studies [MOPPS]), and their effects in combination with antiretroviral agents. Strategies need to focus on 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 and safety testing of potential agents for OIs, including mutagenicity and teratogenicity; Develop clinically useful assays for the rapid diagnosis, treatment response, and sensitivity testing of OIs, especially TB, MAI, enterics, CMV, HSV, fungi, toxoplasma, and JC virus; Support training of basic investigators, clinical investigators, and translational investigators for OI research; and					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Target the discovery, development, and evaluation of potential agents for prevention and treatment of HIV-associated OIs and other infections modified by HIV infection, including those specific to women, children, and drug users (continued)	Determine the role and capability of preexisting immunity (both induced and natural) to control OI infections and the ability of HIV-infected individuals to respond to vaccination throughout the course of infection and disease.					
Therapeutics	Accelerate the development, evaluation, and implementation of strategies to interrupt vertical transmission of HIV from mother to child	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; Develop strategies and agents to interrupt the vertical transmission of HIV from pregnant women to their offspring, including antiviral agents, anti-HIV immunoglobulin, and monoclonal antibodies, HIV vaccines, adjuvants, virucides, and other intrapartum interventions; explore the potential of combined strategies; evaluate the safety, toxicity, pharmacokinetics, and antiretroviral activity of anti-HIV agents in pregnant women and newborns; Expand the obstetrical and pediatric infrastructure for the conduct of perinatal trials through collaborative efforts, both national and international;	5,690	6,138	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Accelerate the development, evaluation, and implementation of strategies to interrupt vertical transmission of HIV from mother to child (continued)	Support the long-term followup of all women and children who participate in perinatal trials to evaluate potential distant effects of antiretroviral agents and/or biologicals; Investigate the role of the placenta in transmission of anti-HIV drugs from mother to fetus; Develop and improve sensitive and specific diagnostic parameters that are cost-effective to permit early differentiation of HIV-infection status in children born to HIV-infected mothers; Assess the potential efficacy and feasibility of obstetric interventions to prevent vertical transmissions, such as cesarean deliveries and other aspects of intrapartum care; Evaluate the risk of vertical transmission of drug-resistant virus; and Evaluate factors that contribute to or protect against vertical transmission; develop effective strategies that could more easily be afforded globally to help reduce vertical transmission and perhaps decrease transmission via breast milk.					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Target the discovery, development, and clinical evaluation of improved therapeutic strategies for the treatment and prevention of HIV-associated malignancies based on an understanding of pathogenesis	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 cofactors) for treatment and prevention of HIV-associated tumors, including Kaposi's sarcoma, 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 (e.g., oncoprotein of HPV); Encourage the development and coordinate the conduct of clinical trials that concurrently evaluate therapeutic strategies directed against the malignancy with anti-retroviral and anti-OI strategies 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;	16,642	16,939	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Target the discovery, development, and clinical evaluation of improved therapeutic strategies for the treatment and prevention of HIV-associated malignancies based on an understanding of pathogenesis (continued)	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; Support training of basic investigators, clinical investigators, and translational scientists for research of malignancies in HIV-infected patients; Improve diagnostic methods for early diagnosis of malignancies and for early detection of recurrent cancer; Coordinate referral of patients with malignancy end points on other studies to malignancy trials; and					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Target the discovery, development, and clinical evaluation of improved therapeutic strategies for the treatment and prevention of HIV-associated malignancies based on an understanding of pathogenesis (continued)	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.					
Therapeutics	Develop an understanding of the neuropathogenesis of HIV infection and strategies for assessing, preventing, and treating neurologic disease in the course of HIV infection	Develop an improved understanding of the biology and epidemiology of neurologic disease in HIV-infected individuals; 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; Implement clinical trials addressing nervous system complications of HIV infection and incorporate neurologic assessments into other HIV-related clinical trials;	11,614	12,268	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Develop an understanding of the neuropathogenesis of HIV infection and strategies for assessing, preventing, and treating neurologic disease in the course of HIV infection (continued)	Develop therapeutic agents that are capable of crossing the blood-brain barrier and are active against HIV infection in relevant cells in the CNS; develop an understanding of mechanisms involved in penetration of the blood-brain barrier; Better delineate etiologies of peripheral neuropathy in HIV infection, and develop strategies to prevent and treat this complication; Develop and utilize <i>in vitro</i> and animal models of CNS impairment and ADC to further identify agents that can reverse HIV neuropathogenesis; and Implement assessments and approaches for the diagnosis of HIV-related dementia in clinical studies; implement standardized adult 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.					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Therapeutics	Develop therapies for the treatment and prevention of serious HIV-associated complications, including wasting syndrome, growth failure, metabolic disorders, dermatologic disorders, ITP, nephropathy, oral diseases, and other symptoms and serious complications	Support research into the biology of the various clinical sequelae of HIV infection (above); Develop and evaluate therapeutic strategies to ameliorate the various sequelae of HIV infection (above) based on an increased understanding of pathogenesis; Develop and evaluate therapeutic strategies for alleviating the various symptoms of unclear etiology in HIV-infected persons (above) and improving the quality of life; and Develop and validate quality-of-life parameters for the various sequelae of HIV infection (above).	12,844	15,431	All populations		

Area Research

Goal 4 Conduct and support research to develop vaccines for prevention of HIV transmission and infection

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Increase scientific knowledge about host defense mechanisms and protection against HIV infection and disease	Develop nonhuman primate and other animal models for HIV vaccine evaluation; determine immune responses that affect infection and disease course; focus on chronic infection with attenuated virus versus wild-type virus; determine why disease does not occur or is delayed in some models; Determine the correlates of immune protection against, and immunologically mediated control of, HIV; Study acutely infected individuals, exposed/uninfected humans (and other primates), and rapid/nonprogressors to determine viral and host factors that impact clearance 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; Elucidate the three-dimensional structure of viral epitopes and determine the mechanism of escape from antibody-mediated neutralization and recognition by cytotoxic T cells. The identification of epitopes for which escape is not possible should receive more attention;	45,735	47,844	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Increase scientific knowledge about host defense mechanisms and protection against HIV infection and disease (continued)	Define conserved viral epitopes that are potentially relevant to protective immune responses; devise strategies to enhance their immunogenicity; Determine the molecular nature of HIV genetic and antigenic diversity and incorporate the findings into ongoing vaccine development; focus on characterization of HIV at potential efficacy trial sites; Foster multidisciplinary approaches that bridge basic, animal, and clinical approaches; and Develop quantitative measures of HIV concentration in bodily fluids to determine whether there is a relationship between HIV concentration and transmission.					
Vaccines	Apply findings from basic, epidemiologic, and clinical research to the design and evaluation of vaccine strategies in laboratory studies and animal models	Develop further multidisciplinary approaches for the design and development of potential vaccine candidates; expand research on mucosal delivery and stimulation of mucosal immune responses (NIAID);	24,135	25,465	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Apply findings from basic, epidemiologic, and clinical research to the design and evaluation of vaccine strategies in laboratory studies and animal models (continued)	Include research on but not limited to: whole-particle designs such as whole-killed HIV and genetically engineered, noninfectious HIV mutants that lack the viral RNA genome or have a defect in a critical protein but contain a full complement of HIV antigenic proteins; live, recombinant viral and bacterial vectors engineered to express one or more HIV proteins; genetically engineered, live-attenuated strains of HIV; synthetic peptide candidates capable of inducing and boosting both cellular and humoral immunity; DNA candidates as HIV vaccines; combination strategies including priming and boosting;					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Apply findings from basic, epidemiologic, and clinical research to the design and evaluation of vaccine strategies in laboratory studies and animal models (continued)	Evaluate vaccine strategies in AIDS animal models: place additional emphasis on strategies in or about to be in clinical trial, practical immunization schedules, and challenge routes and viral isolates that most closely mimic the human experience; delineate the mechanisms of immune protection; conduct transfer experiments to help dissect immune correlates; determine the impact of dose on the nature and effectiveness of the immune response; examine protection from organ-specific as well as systemic infection; conduct long-term followup of vaccinated animals that become chronically infected to determine the impact of vaccination on disease progression; Encourage development of candidate vaccines suitable for domestic and international use; Conduct research on adjuvants and novel formulations that have a qualitative or quantitative impact on immunologic responses to vaccine candidates;					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Apply findings from basic, epidemiologic, and clinical research to the design and evaluation of vaccine strategies in laboratory studies and animal models (continued)	Evaluate strategies to decrease or eliminate HIV from sexual fluids; Characterize and evaluate the potential negative side effects of candidate vaccines, including production of enhancing antibodies and neurotoxicity; and Develop methodologies for comparative <i>in vitro</i> measure of immune function.					
Vaccines	Identify appropriate domestic and international populations and develop infrastructure, including behavioral research and community education and outreach activities, that is necessary for ensuring adequate performance of Phase III efficacy clinical trials	Prepare for adequate followup of individuals participating in vaccine clinical trials 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; Utilize infrastructures established for the conduct of AIDS vaccine efficacy trials to implement prevention research activities designed to determine the efficacy of other biomedical or behavioral interventions that could prove of benefit in decreasing the incidence of HIV infection in the population; evaluate promising interventions separately and/or as a component of prophylactic vaccine efficacy trials;	19,189	19,912	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Identify appropriate domestic and international populations and develop infrastructure, including behavioral research and community education and outreach activities, that is necessary for ensuring adequate performance of Phase III efficacy clinical trials (continued)	Continue appropriate epidemiologic studies that determine the risk profiles and infection rates of various populations in the United States and internationally in order to identify those groups most likely to be the participants in vaccine trials; Maintain and expand the AIDS Vaccine Clinical Trials Network to include domestic and international sites with access to populations at high risk for acquiring HIV infection and where vaccine or other prevention research activities may be feasible; Maintain the necessary laboratory and epidemiologic research infrastructure at designated sites for conducting domestic and international vaccine efficacy trials; develop optimal assays to distinguish infection from seroconversion to the vaccine; 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;					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Identify appropriate domestic and international populations and develop infrastructure, including behavioral research and community education and outreach activities, that is necessary for ensuring adequate performance of Phase III efficacy clinical trials (continued)	Conduct behavioral research in populations at high risk for HIV infection, particularly those difficult-to-reach populations that have been historically underrepresented in clinical trials; determine optimal education, risk-reduction intervention, recruitment, adherence, and retention approaches and estimate behavior changes and other factors pertinent to the design and execution of a successful efficacy trial; Establish linkages with communities or community organizations where efficacy trials might be conducted to optimize education, recruitment, and followup activities and to help address community concerns related to AIDS vaccine efficacy trials; Link infrastructure development and vaccine research activities in high-risk populations with other prevention and treatment research activities in these populations, including research on TB and STDs; Conduct research to determine optimal methods of achieving truly informed consent; and					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Identify appropriate domestic and international populations and develop infrastructure, including behavioral research and community education and outreach activities, that is necessary for ensuring adequate performance of Phase III efficacy clinical trials (continued)	Conduct research to determine possible adverse social, economic, or legal consequences of participation in clinical trials and develop strategies to mitigate potential harm.					
Vaccines	Identify mechanisms of protective immunity to HIV in newborns and infants and develop a safe and effective immunologic strategy to prevent HIV infection in this population	Evaluate genetic and antigenic variation in viruses transmitted from mothers to infants and in maternal isolates that are not transmitted; Accelerate studies of maternal-infant transmission; Develop and maintain domestic and international infrastructure necessary to enroll mothers and infants in prospective long-term followup vaccine trials; Determine the immunogenicity of various vaccines and adjuvants in newborns and infants; Determine which maternal and infant immune responses are associated with nontransmission of HIV; Identify antibody preparations for use as passive or passive/active HIV prevention; Establish criteria for advancement of candidates in Phase I, Phase II, and Phase III clinical trials; and	3,174	3,501	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Identify mechanisms of protective immunity to HIV in newborns and infants and develop a safe and effective immunologic strategy to prevent HIV infection in this population (continued)	Conduct Phase I, Phase II, and Phase III clinical trials of the most promising candidates that meet established criteria.					
Vaccines	Develop criteria for selection of suitable candidate vaccines, support appropriate infrastructure, and conduct Phase I and Phase II trials	Utilize vaccine selection committees to carefully evaluate promising candidates; emphasize need for thorough consideration of efficacy in animal models; Conduct Phase I and Phase II clinical trials that will determine safety and delineate comparative immunologic analysis of candidates for preventive vaccines; expand immunologic measurements to include a broad range of cell-mediated and mucosal immune responses; Conduct Phase II trials in high-risk individuals of the most promising preventive vaccine candidates or combinations that proved promising in Phase I trials conducted in low-risk individuals and that have genetic or immunologic relatedness to HIV isolates circulating in the proposed trial population; Support and maintain the AIDS Vaccine Evaluation Groups;	19,398	21,177	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Develop criteria for selection of suitable candidate vaccines, support appropriate infrastructure, and conduct Phase I and Phase II trials (continued)	Closely coordinate the evaluation of research findings on prophylactic AIDS vaccines with research on therapeutic AIDS vaccines, e.g., the use of candidate vaccines to ameliorate disease when administration is initiated after establishment of chronic infection; Acquire and analyze HIV isolates from recent seroconverters representative of Phase I and Phase II trial populations so that genetic and antigenic information about viruses circulating in the population can be obtained; and Conduct behavioral research pertinent to preparation for Phase III trials.					
Vaccines	Establish criteria for selection of suitable vaccine candidates and conduct Phase III clinical trials when established criteria are met	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 novel preventive vaccine candidates that have proven promising, safe, and immunogenic in Phase II trials and that meet established criteria; Evaluate HIV vaccine candidate efficacy; Evaluate multiple scientific hypotheses; and	200	229	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Vaccines	Establish criteria for selection of suitable vaccine candidates and conduct Phase III clinical trials when established criteria are met (continued)	Ensure that trials are conducted with the highest regard for social and ethical concerns of the participants.					

Area Research

Goal 5 Conduct and support behavioral and social science research to develop intervention strategies

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Behavioral Research	Prevent new HIV infections through behavior interventions. Translate findings from behavioral and social science research to design, implement, and evaluate interventions in diverse settings and populations	Develop and evaluate demographically and culturally appropriate behavioral and social interventions based on the changing epidemiology of HIV in different populations and on the incidence, frequency, and change in high-risk HIV-related behaviors; international comparisons are essential for identifying effective interventions; Support multidisciplinary research on behavior change strategies that target the sustained adoption and maintenance of HIV preventive behaviors (e.g., increase use of condoms, virucides, spermicides, and sterile injection drug equipment); Support research on increasing the effectiveness of drug abuse, mental health, and alcoholism treatment for reducing HIV risk behavior; Design and test interventions to increase the recruitment, retention, and adherence to protocols for adopting and maintaining low-risk behavior in prevention research, including vaccine studies; and	50,710	51,302	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Behavioral Research	Prevent new HIV infections through behavior interventions. Translate findings from behavioral and social science research to design, implement, and evaluate interventions in diverse settings and populations (continued)	Support research on overcoming barriers associated with the implementation and replication of potentially effective prevention programs.					
Behavioral Research	Strengthen the behavioral science base. Conduct a wide range of studies to expand knowledge of the principles of behavior and behavior change	Support studies to develop models of behavioral, social, cultural, cognitive, and psychological mechanisms and processes that determine the acquisition, maintenance, and change of HIV-related behaviors in individuals and groups in various populations and settings; Identify processes that exacerbate or minimize adverse consequences of HIV infection for the individual, group, and community; Support basic behavioral and social research on factors that shape and change social norms concerning HIV-related behavior and their influence on individual behaviors; Develop and improve methods to obtain and analyze valid and reliable data on HIV-related behaviors; and Study the process of information diffusion; understanding this process is necessary for effective communication of HIV-related knowledge.	79,959	83,149	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Behavioral Research	Preventing the negative consequences of HIV infection. Discover, develop, and evaluate strategies to prevent or minimize the physical, psychological, cognitive, and social consequences of HIV, including strategies to improve adherence to proven therapies and recruitment, retention, and adherence to clinical trial protocols	Identify the behavioral, psychological, cognitive, and social consequences of HIV disease for HIV-seropositive individuals, their support systems, and their communities; develop and evaluate innovative behavioral and social approaches to manage these consequences, including health behavior changes, stress management, and improved access and utilization of care; Discover, implement, and evaluate therapeutic strategies to delay or prevent progression of HIV-associated cognitive dysfunction; Develop and evaluate interventions to increase recruitment, adherence, and retention in HIV treatment studies and clinical trials; Develop and test models of caregiving tailored to the physical, cognitive, and emotional needs of patients with HIV disease, including their significant others, extended family members, and care providers; and Develop and evaluate programs to prevent HIV-related discrimination.	27,293	25,264	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Behavioral Research	Create and test innovative dissemination strategies. Develop, assess, and rapidly disseminate research findings and treatment strategies to give researchers and communities access to state-of-the-art communications	Develop and test innovative dissemination strategies for promoting adoption of successful (empirically tested) behavior change interventions by HIV prevention providers; Develop, test, and rapidly disseminate research findings that have immediate implications for the conduct of HIV prevention and education programs conducted in the community; explore novel mechanisms to disseminate behavioral and social science research findings and model approaches to the prevention field (e.g., consensus conferences, interactive computer bulletin boards, media strategies, and mechanisms to reach providers and community-based organizations); Support and strengthen partnerships between community-based organizations and behavioral and social scientists to encourage bidirectional exchange of information and experience to enhance research and prevention efforts; and Utilize new and innovative techniques (e.g., social marketing) to disseminate research to different populations.	1,364	1,444	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Behavioral Research	Strengthen the behavioral and social science infrastructure. Develop multidisciplinary and interagency collaborative efforts to enhance the AIDS behavioral research effort; enhance the behavioral aspect of research into therapeutics, natural history and epidemiology, and vaccines. Train researchers to conduct basic and applied social science research related to HIV. Provide the state-of-the-art physical facilities and equipment that are necessary to conduct HIV-related behavioral and social science research within relevant settings	Establish multidisciplinary AIDS research consortia to test novel behavioral approaches, replicate psychosocial and behavioral studies, and promote their use in appropriate populations; collaborate with other agencies of the PHS and outside organizations to maximize research resources; Promote HIV-related research in predoctoral and postdoctoral programs; facilitate the development of <i>practica</i> and field placements in HIV treatment, prevention, and research settings; provide research career awards; actively recruit ethnic minorities, women, and those dedicated to community-based programs; expand behavioral and social training and research efforts aimed at limiting infections such as TB and malignancies related to HIV infection; Ensure adequate representation of social and behavioral scientists on IRGs, OAR Advisory Committees, and OAR staff; Support and expand computer networking among behavioral and social science researchers; provide additional laboratory and research facilities for human and animal research for behavioral studies; and	394	436	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Behavioral Research	Strengthen the behavioral and social science infrastructure. Develop multidisciplinary and interagency collaborative efforts to enhance the AIDS behavioral research effort; enhance the behavioral aspect of research into therapeutics, natural history and epidemiology, and vaccines. Train researchers to conduct basic and applied social science research related to HIV. Provide the state-of-the-art physical facilities and equipment that are necessary to conduct HIV-related behavioral and social science research within relevant settings (continued)	Collect, archive, and disseminate existing data for secondary data analysis.					

Area Research

Goal 6 Provide support for training and infrastructure to carry out HIV and AIDS research

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Training and Infrastructure	Provide both domestic and international training in biomedical and behavioral research on HIV	Increase predoctoral and postdoctoral 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 the 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 predoctoral and postdoctoral 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;	33,978	35,486	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Training and Infrastructure	Provide both domestic and international training in biomedical and behavioral research on HIV (continued)	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 leading U.S. AIDS research scientists and institutions with leading AIDS research scientists and institutions in foreign countries; Expand both predoctoral and postdoctoral training in structural biology; and Expand the NIH AIDS Loan Repayment Program to bring scientists and physicians to the NIH to expand the cadre of trained intramural researchers.					
Training and Infrastructure	Establish appropriate infrastructure for the conduct of HIV research domestically and internationally	Provide additional facilities to study animal models of pediatric AIDS; Foster animal models to study HIV-related malignancies; Continue the Research Facilities Infrastructure Program (RFIP) and General Clinical Research Centers (GCRC) Program;	6,858	7,072	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (apppr.)	FY 1996 (proposed)			
Training and Infrastructure	Establish appropriate infrastructure for the conduct of HIV research domestically and internationally (continued)	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., <i>M. nemestrina</i>; 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;					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Training and Infrastructure	Establish appropriate infrastructure for the conduct of HIV research domestically and internationally (continued)	Establish and support repositories of samples obtained from individuals with HIV infection for current and future studies; Increase support for screening for 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; and Provide further support for the development of SPF macaque colonies.					

Area Research

Goal 7 Develop and support appropriate programs for the dissemination of research information to health care providers and affected communities

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Information Dissemination	Expedite the dissemination of the latest information on clinical trials, state-of-the-art therapies, health care, and prevention techniques to domestic as well as international audiences as appropriate	Develop and rapidly disseminate important research findings that have immediate impact on prevention and on health care and treatment of HIV-infected individuals, utilizing all NIH, PHS, and public media communications modes; Provide up-to-date information on eligibility criteria for entry into clinical trials, results of trials, and relevant research findings through the AIDSTRIALS and AIDSDRUGS databases as well as the AIDS Clinical Trials Information Service; Maintain an interface with the Cancer Information System and PDQ to provide information on clinical trials for AIDS-related malignancies; Collaborate with other agencies of the PHS and outside organizations to determine the information needs in the biomedical and behavioral research community and identify appropriate mechanisms for dissemination; Provide online access to the full-text guidelines for state-of-the-art care;	15,400	16,115	All populations		

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Information Dissemination	Expedite the dissemination of the latest information on clinical trials, state-of-the-art therapies, health care, and prevention techniques to domestic as well as international audiences as appropriate (continued)	Continue support of community, regional, national, and international conferences and workshops to facilitate the exchange of scientific information; Provide support for NIH-sponsored annual meetings on pathogenesis, vaccines, and drug development; Collaborate with public and health sciences libraries to facilitate access to needed information by community groups; Disseminate results of behavioral research studies to collaborating centers and service providers for use in planning, designing, and implementing preventive intervention strategies; Continue support for and development of the International Network for AIDS Research and Training; Explore collaborations with the World Health Organization (WHO), the Pan American Health Organization (PAHO), and international AIDS agencies to obtain and disseminate information about international clinical trials;					

Objectives	Action Steps	Programs					
		Descriptions	Resources in Thousands		Populations Served	Constituency Involvement	Unmet Needs
			FY 1995 (appropri.)	FY 1996 (proposed)			
Information Dissemination	Expedite the dissemination of the latest information on clinical trials, state-of-the-art therapies, health care, and prevention techniques to domestic as well as international audiences as appropriate (continued)	Develop and improve user-friendly information systems and services in HIV/AIDS and provide training for them; Provide the full text of abstracts from meetings, where available, online before scientific meetings; Collaborate with the WHO, the PAHO, and the Global Programme on AIDS to develop the Global HIV/AIDS Network, a computerized AIDS information system; and Working with community groups, develop educational materials to foster the dissemination of information about research and the clinical trials process to primary care providers, community-based HIV/AIDS service organizations, and persons with HIV/AIDS.					