NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
REVISED COMPREHENSIVE STRATEGIC PLAN AND BUDGET TO REDUCE AND ULTIMATELY ELIMINATE HEALTH DISPARITIES
FISCAL YEAR 2002-2006

MISSION

The mission of the National Institute of Allergy and Infectious Diseases (NIAID) is to conduct and support research that strives to understand, treat, and ultimately prevent the multitude of infectious, immunologic, and allergic diseases that endanger the lives of millions of people nationally and globally.

OVERVIEW

A central feature of contemporary human societies is their increasing diversity. Differences in socioeconomic status, racial and ethnic background, education level, and occupation all intersect in complex ways to create disparities in health status. These disparities may stem from many factors, including accessibility of health care, increased risk of disease from occupational exposure, and increased risk of disease from underlying genetic, ethnic, or familial factors.

The NIAID has long recognized the importance of differential risks among populations for infectious and immunologic diseases. It is commonplace in the field of infectious diseases to identify subgroups within a population who are at higher risk for infection and disease because of identifiable factors, such as advanced age, which increases susceptibility to serious influenza virus infections.

NIAID also recognizes that racial and ethnic differences affect susceptibility to infection and disease. African-American individuals with chronic hepatitis C virus infection do not respond as well to antiviral therapy as do members of other groups. Pneumococcal infections are much more serious in children who have sickle cell disease. African American women experience a higher rate of autoimmune diseases than do white women. Native American populations have higher rates of meningitis and invasive bacterial disease from *Haemophilus influenzae* type B (Hib) than do other groups. It is important to study differential disease susceptibilities because of the pragmatic benefit of research products, such as improved therapies, vaccines, or other interventions. This research also reveals critical information about the disease process, which in turn yields more opportunities for prevention or treatment.

This plan is based on over 50 years of progress in the understanding, treatment, and prevention of infectious and immunologic diseases. Many of NIAID's advances have helped to eliminate or mitigate health disparities. Development of effective glyco-conjugate vaccines to prevent Hib infections, for example, has almost eliminated Hib-related diseases in the Native-American population. Development of effective therapies for hepatitis B, education and interventions to

improve asthma control in inner-city populations, and development of better therapies for HIV infection are all NIAID-supported research advances that have reduced health disparities. However, not all citizens reap the full benefits of our increased knowledge. Although health disparities affect numerous segments of the U.S. population, medically underserved populations bear a disproportionate share of the burden. NIAID maintains its commitment to improve minority health and attract capable minority scientists to infectious and immunologic disease research. Recognizing that we can achieve our mission only through the interaction and participation of the minority scientific community throughout the United States, NIAID is committed to an extensive campaign that involves colleges and universities, medical centers, other professional organizations, minority communities, and groups that assist underserved populations.

NIAID's Health Disparities Strategic Plan focuses on those disease entities within our research portfolio that disproportionately affect underserved minority and socio-economic populations. The objectives articulated in the plan embody our aim of eliminating health disparities and are designed to strengthen our research, research training and career development, and education and outreach programs.

I. RESEARCH

The research facet of NIAID's Health Disparities Strategic Plan focuses on the Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome (HIV/AIDS), transplantation, autoimmune diseases, asthma, tuberculosis (TB), hepatitis C virus (HCV), and sexually transmitted diseases (STDs). NIAID did not receive public comments on these research areas when its' first health disparities strategic plan was issued in the Spring of 2000. However, the NIAID has received confirmation from advisory groups, community organizations as well as professional societies and advocacy groups that those are important foci for our health disparities research agenda. Given the devastating public health impact of HIV/AIDS, preventing this disease and making its' treatment affordable and practical is NIAID's highest priority. Nonetheless, the public health needs for each of the foci in the research section of our health disparities strategic plan also are critical, too critical to be subject to prioritization based on that criteria alone. Thus, scientific opportunity and the feasibility and potential impact of those opportunities will drive our priorities. Because the emergence of scientific opportunity is unpredictable, priorities inevitably will shift over the course of the next five years.

The research section of the plan addresses both NIAID's extramural and intramural research programs. The extramural program supports individual investigators, groups, and centers outside the NIAID to conduct research. Such investigator initiated research sometimes is in response to a specific initiative and always undergoes a competitive review process. The intramural program conducts research. Because of these different foci, the action plans articulated for the extramural program tend to be more programatic while the plans for the intramural program tend to be more explicitly research oriented.

Area of Emphasis: I.A. HIV/AIDS

Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome (HIV/AIDS) have had a direct impact on the lives of 36.1 million people worldwide (2.7 million in North America). In 2000, there were a total of 774,467 cases reported in the U.S. Of the total U.S. cases, 38 percent were among African Americans and 18 percent among Hispanics – rates very disparate from the representation of these groups in the U.S. population.

Transmission due to substance abuse continues to be a significant factor in contributing to the spread of HIV/AIDS in minority communities. As a result, a large proportion of minority women have become infected during sex with an injection drug user. African American and Hispanic women comprise 78 percent of all reported cases among HIV-infected women in this country with most of them infected through heterosexual sex. As a consequence, the majority of HIV-infected children in this country are African American or Hispanic.

NIAID supports a comprehensive portfolio of biomedical and behavioral research aimed at preventing and treating HIV/AIDS disease in minority communities. The Institute has taken strong steps to ensure minority participation in clinical trials, natural history studies, and in prevention studies to assure that enrollment is reflective of the national epidemic.

NIAID has and continues to increase its enrollment of minority participants in all of its clinical studies. Through this effort, in FY 2000, a total of 6,886 participants were enrolled in our Pediatric AIDS Clinical Trials Group, of which 46 percent of the enrollees were African Americans and 23 percent Hispanic. Of the 7,158 patients enrolled in the Adult AIDS Clinical Trials Group during FY 2000, 27 percent were African American, 17 percent Hispanic, 2 percent Asian/Pacific Islander, and 1 percent American/ Alaskan Native. These and numerous other trials are meeting the challenge of increased enrollment of underserved populations in HIV/AIDS research. NIAID will continue to support research in therapy, vaccine development, and prevention of HIV/AIDS.

Objective: I.A.1 Support research on vaccines that would help to reduce disparities in the incidence and prevalence of HIV/AIDS.

A vaccine that effectively prevents infection with multiple strains of HIV/AIDS will be key to reducing disparities in the incidence and prevalence of this still fatal disease. While such a vaccine remains the ultimate HIV/AIDS vaccine objective, vaccines that provide immunity to one or more strains and vaccines that slow disease progression so that the immunized person is healthier and less contagious also are important objectives.

Action Plan

Steps

1. Support and conduct research to discover, design, and develop HIV/AIDS vaccine candidates.

2. Study the scope and relationship of viral and human genetic variation in the context of vaccine development.
3. Support and conduct clinical trials to determine the safety and efficacy of vaccine candidates.

Timeline

FY 2002

- Fund initiatives to:
  - Renew the **Innovation Grant Program (IGP)**. This program fosters exploratory investigator-initiated AIDS vaccine research at the earliest stages of concept development.
  - Establish **Vaccine Design and Development Teams,** which support consortia of scientists who have identified particularly promising vaccine concepts for targeted accelerated product development.
  - Expand the **HIV Vaccine Research and Design** program. This program advances concepts identified in the IGP (above) through support of basic HIV/AIDS vaccine research and design including concept testing in animal models, development of potential vaccine candidates, evaluation of their mechanism of action, development of animal models, and studies of immune correlates.
  - Renew the **Integrated Preclinical/Clinical AIDS Vaccine Development Program.** IPCAVD pursues the development, evaluation, and refinement of vaccine concepts through early clinical trials.
  - Renew the **HIV Vaccine Development Resources.** These contracts support vaccine development through the manufacture of pilot lots of vaccine for testing, preclinical testing of vaccine candidates, and preparation of FDA submissions.
- Fund applications addressing on-going initiatives (initiatives launched in earlier years, such as the **Simian Vaccine Evaluation Units**).
- Fund related investigator-initiated research.
- In 2001 NIAID's Vaccine Research Center received regulatory approval to move forward with its first clinical trial; **"Evaluation of an HIV-1 DNA Vaccine Encoding a Modified Gag-Pol Protein in Uninfected Adult Volunteers."** This is a phase I study of a genetic vaccine, VRC 4302, in HIV-negative volunteers that will evaluate the safety, tolerance and immune response of three dose levels. Genetic vaccines contain genes that direct production of specific proteins of the HIV virus. In FY 2002 this and other VRC clinical trials will enroll participants in phase I studies. The VRC will produce and initiate preclinical testing of multivalent vaccines. The multivalent vaccine products will eventually be evaluated in phase I trials with the goal of advancement into Phase II and Phase III trials, if the results are promising.

FY 2003

- Fund initiatives to:
  - Renew the **Basic HIV Vaccine Research Program (the IGP and HIV Research and Development program).** Both described above.
  - Expand the **HIV Vaccine Design and Development Teams** (see above)

- Expand **HIV Vaccine Trials Network.** HVTN carries out a comprehensive clinical research program (human testing) to identify safe and effective HIV/AIDS vaccines.
- Expand **HLA Typing and Epitope Mapping Relative to HIV Vaccine Design.** This program supports the characterization of viral (HIV) and human genetic variation in the context of vaccine development.
- Expand the **New Technologies for HIV** and **HIV Vaccine Related Research.** These programs stimulate the application of new technologies to development of assays needed in clinical HIV vaccine studies
- Expand **Vaccine Preclinical Resources**. This program ensures that preclinical vaccine development (vaccine candidate production, testing, generation of reagents and technologies, database management) proceeds expeditiously.

- Fund applications addressing on-going initiatives
- Fund related investigator-initiated research.
- Study immune reconstitution to understand the mechanisms by which recovery from HIV disease can be enhanced.
- Develop manufacturing processes and release tests that provide material for Phase I/II clinical trials, with particular emphasis on techniques suitable for eventual large-scale manufacture of vaccines.
- Study viral immunity and develop animal models of viral immunopathogenesis.
- Perform Phase I trials of candidate HIV vaccines developed by the VRC. This will involve community education on HIV prevention, recruitment of healthy adults into clinical trials, study design and analysis, and maintenance of regulatory standards.
- Investigate novel aspects of the cellular immune response to pathogens in support of the rational development of a vaccine against HIV.
- Develop, validate, and perform assays of the immune response to HIV and other pathogens on clinical samples derived from recipients of candidate vaccines.
- Apply the tools of atomic resolution structural analysis, primarily X-ray crystallography, to the design of an effective HIV vaccine.
- Produce and characterize viral stocks of SIV and HIV, including diverse viral strains representing multiple genetic subtypes.
- Utilize genetic mutations and immunologic assessment in order to develop immunogens that elicit broadly neutralizing antibodies to HIV with the goal of developing safe and effective AIDS vaccines.
- Design CTL-based HIV vaccine candidates by preparing gene-based immunogens. HIV cDNAs will be inserted into relevant plasmids in order to produce effective immunogens that induce CTL.
- Define the functional roles of uniquely identifiable leukocyte subsets in the healthy immune system to understand how perturbations in the balance of these subsets lead to disease.
- Develop new flow cytometry-based assays and technologies.
- Develop understanding of the cellular and molecular mechanisms by which various cytokines and co-stimulatory molecules regulate cellular immunity *in vivo*.
- Utilize virological, immunological, structural, and biophysical information on HIV-1 envelope glycoproteins to rationally design subunit vaccine candidates.

FY 2004 – FY 2006:

- Release new, expansion, and renewal initiatives as appropriate.
- Fund meritorious applications addressing on-going initiatives related to AIDS vaccine development.
- Fund related investigator-initiated research.
- Continue on-going and initiate new activities at the VRC.

Performance Measures

- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Funding of awards.
- Initiation of clinical trials.

Outcome Measures

- Availability of new and improved vaccine candidates for testing.
- Publication of scientific advances relevant to HIV/AIDS vaccines in refereed scientific journals.
- Interest of industry and governments in the production of HIV/AIDS vaccines.

Objective I.A.2. Support research on topical microbicides in order to reduce health disparities related to AIDS and sexually transmitted diseases.

Efficacy trials for topical microbicides are planned through the HIV Prevention Trials Network. This research will directly benefit minority women because microbicides are expected to reduce the risk of sexually transmitted HIV. In addition, studies to design and develop new microbicides will continue.

Action Plan

Steps

Develop a topical microbicide that

A. Prevents infection and/or viral replication by both cell-free infectious HIV particles and cell-associated infectious particles;
B. Is safe and non-inflammatory (causes no irritation to the vaginal/cervical/urethral/rectal epithelium); and
C. Reduces infectivity of other sexually transmitted infectious agents.

2. Support research and development of safe and effective formulations and delivery methods.
3. Support preclinical to clinical translational research for topical microbicides.
4. Conduct clinical trials to determine safety, acceptability, efficacy and effectiveness of potential topical microbicides.
5. Continue to promote NIAID programs to domestic and international researchers to ensure that researchers worldwide pursue the best approaches.

Timeline

FY 2002

- Fund initiatives to:
  - Renew the **Microbicide Preclinical Development Program,** cosponsored with NICHD, to expand the range of microbicide candidates, with and without contraceptive activity, through support of discovery and preclinical development of novel or under-explored microbicides.
  - Fund the **Integrated Preclinical/Clinical Program for HIV Topical Microbicides** to target research on novel topical microbicides at the preclinical/clinical interface of the research pipeline.

FY 2003

- Fund initiatives to:
  - Renew the **Integrated Preclinical/Clinical Program for HIV Topical Microbicides** to target research on novel topical microbicides at the preclinical/clinical interface of the research pipeline
  - Establish **Microbicide Design and Development Teams** to advance microbicide candidates into Phase I safety trials.
  - Expand the **HIV Prevention Trials Network's (HPTN)** clinical and laboratory capacity for topical microbicide trials.

FY 2004 – FY 2006:

- Release new, expansion, and renewal initiatives as appropriate.
- Fund meritorious applications addressing on-going initiatives.
- Fund related investigator-initiated research.

Performance Measures:
- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Funding of awards.
- Initiation of clinical trials.

Outcome Measures:
- Availability of new and improved topical microbicide candidates for testing.
- Publication of scientific advances relevant to HIV/AIDS topical microbicides in refereed scientific journals.
- Interest of industry and governments in the production of topical microbicides to prevent HIV/AIDS.

Objective I.A.3. Support research to prevent perinatal transmission of HIV

Prevention of perinatal transmission of HIV from mothers to their children is of vital importance and a high priority on the NIAID research agenda. Almost three million children have died of AIDS with perinatally acquired HIV-1 infection. Ninety percent of pediatric HIV-infection is acquired by mother-to-child-transmission and 90 percent of these infected children live in the developing world. It is estimated that 1,600 infants are infected daily, which amounts to 600,000 annually.

Opportunities exist to intervene successfully in the antepartum, intrapartum, and postpartum periods to prevent transmission from an HIV infected woman to her infant. Safe, simple, inexpensive interventions that could be widely applicable, particularly in the developing world, are of highest importance.

Action Plan:

<u>Steps</u>
- Further develop and test strategies to prevent mother to infant HIV infection through clinical trials in the U.S. and international settings.
- Define the mechanisms and risk factors for HIV transmission to children and adolescents as well as risks for disease progression within the framework of clinical studies and trials.
- Identify, develop and test treatments of HIV disease to improve the survival and quality of life of HIV-infected infants, children and adolescents in the U.S. and international settings.
- Develop optimal use of treatment management strategies for HIV-infected infants, children and adolescents from acute/early infection through advanced disease that are appropriate domestically as well as in resource-constrained communities.

<u>Timeline</u>

FY 2002
- Fund initiatives to:

- Continue the **Women's and Infants Transmission Study (WITS)** to study the impact of HIV infection on HIV infected women and their infants.
- Continue the **HPTN** to study methods of preventing perinatal transmission of HIV.
- Renew the **Pediatrics AIDS Clinical Trials Group (PACTG)** to evaluate treatments for HIV-infected children and adolescents, and for developing new approaches for the interruption of mother-to-infant transmission.

FY 2003
- Fund initiatives to:
  - Continue the PACTG.
  - Continue the WITS.
  - Continue the HPTN.

FY 2004 – FY 2006:
- Release new, expansion, and renewal initiatives as appropriate.
- Fund applications pursuant to on-going initiatives.
- Fund related investigator-initiated research.

Performance Measures:
- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Funding of awards.
- Initiation of clinical trials.

Outcome Measures:
- Publication of scientific advances relevant to perinatal transmission of HIV/AIDS.
- Availability of new and improved antiretroviral treatments for testing
- Interest of industry and governments in the production of HIV/AIDS therapeutics.

Area of Emphasis: I.B. Organ Transplantation

Illnesses such as kidney failure, diabetes, leukemia, coronary disease, and liver disease affect millions of Americans. For many of these patients, organ, tissue, or cell transplantation would prevent, and in some cases reverse, the severe outcomes of these diseases. Between 1990 and 1999, the number of transplants increased by 59 percent. Today, transplantation procedures are performed using more than 25 different organs and tissues, with first-year graft survival rates often exceeding 80 percent. Despite these successes, two major impediments remain: the critical shortage of donor organs (over 75,000 patients are on organ waiting lists) and immune-mediated graft rejection.

Organ transplantation represents a key health disparity for African Americans. It has been shown that African Americans are less likely to be identified as candidates for renal transplantation or to find a suitable donor, and tend to remain longer on transplant waiting lists. There is a lower organ donation rate among African Americans, compared with other racial

groups, although African Americans comprise approximately 35 percent of patients on the renal transplant waiting list.

Successful transplantation depends on the availability of donated organs and accurate methods to match donor and recipient HLA types. Recognizing that knowledge of the relevant HLA types in minority populations is incomplete, the NIAID supports efforts to improve the definition of ethnically restricted HLA genes. The NIAID also supports a national program to identify HLA genes in African American, Native American, and Hispanic populations. This program has led to the development of specific DNA reagents to further enhance HLA typing in minority populations and the definition of 13 new HLA genes in African Americans and 3 new HLA genes in Native Alaskan Yupiks. These efforts have contributed to reducing incomplete tissue matching for transplant recipients.

Objective: I.B.1. Support programs that would help reduce disparities by improving donor matching for organ transplantation through discovery of immune response gene variants in minority populations and development and application of advanced technologies for rapid donor-recipient matching.

Action Plan:

Steps:

1. Support research to identify and catalog new HLA genes in minority populations.
2. Encourage the development and application of DNA-based technologies to rapidly type HLA genes.

Timeline

FY2002

- Support the **13th International Histocompatibility Working Group (IHWG)** to standardize and improve histocompatibility testing worldwide through the discovery, development, and distribution of information and new tissue typing reagents. The IHWG is a network of more than 200 laboratories in over 70 countries that collect and share data on genes of the human leukocyte antigen complex.
- Support the IHWG project to identify single nucleotide polymorphisms in immune response genes, which will increase our ability to accurately predict, diagnose, and ultimately treat immune-mediated diseases.
- Continue to support **SBIR grants** for the development and application of DNA-based technologies to rapidly type HLA genes.
- Continue support for ongoing investigator-initiated research related to organ transplantation.
- Fund meritorious new investigator-initiated research related to organ transplantation.

FY 2003

- Continue to support the IHWG.

- Continue to support SBIR grants for the development and application of DNA-based technologies to rapidly type HLA genes
- Continue support for ongoing investigator-initiated research related to organ transplantation.
- Fund meritorious new investigator-initiated research related to organ transplantation.

FY 2004 – 2006
- Continue to support the IHWG.
- Continue to support SBIR grants for the development of DNA-based technologies to rapidly type HLA genes
- Continue support for ongoing investigator-initiated research related to organ transplantation.
- Fund meritorious new investigator-initiated research related to organ transplantation.

Performance Measures
- Publication of initiatives in the NIH Guide and the Commerce Business Daily.
- Funding of meritorious awards related to organ transplantation.

Outcome Measures
- Presentation of significant findings at scientific meetings.
- Deposition of new allele sequence data in the WHO database and GenBank.
- Publication of new HLA alleles that appear at a high frequency in minority populations.
- Prototyping of new, high-throughput methods to type HLA genes in donors and recipients.

Objective: I.B.2. Support clinical studies on the immunological mechanisms of graft acceptance and rejection in order to address health disparities in minority populations.

The development of new immunosuppressive medications has improved graft survival such that the one-year graft survival rates for some organs approach 90 percent. In addition, preliminary data indicate that dietary supplementation with omega-3 fatty acids may have a beneficial effect on kidney graft survival in African-Americans. However there are still significant differences in acute rejection among ethnic and racial groups. African Americans mount more vigorous immune responses against transplanted organs than do other racial groups.

Action Plan:

Steps
1. Support research to identify differences in immune response genes in African Americans.
2. Support clinical research on the immunological mechanisms of acute and chronic graft rejection.
3. Conduct clinical trials of novel therapies to prevent acute and chronic graft rejection.

Timeline

FY2002

- Initiate a clinical trial to evaluate the effect of dietary omega-3 fatty acids in kidney transplant recipients. In 1999, a three-year clinical study by an NIAID-supported investigator indicated that canola oil (a source of omega-3 fatty acids) and arginine in addition to immunosuppressive therapy resulted in fewer graft rejection episodes and fewer re-hospitalizations in kidney transplant recipients, especially among African American patients.
- Initiate clinical trials through the **Cooperative Clinical Trials in Adult Kidney Transplantation** to:
    - Determine the ability of intravenous immunoglobulin to lower allosensitization in patients with high titers of anti-HLA antibodies. A preliminary study has shown that treatment with intravenous immunoglobulin (IVIG) can lower a patient's PRA titer, suggesting that IVIG may allow these patients to be more suitable candidates for organ transplantation. PRA, or panel reactive antibodies, are antibodies against potential donor HLA molecules. African Americans have high titers of PRA.
    - Evaluate the safety and efficacy of kidney transplantation in HIV+ patients with end-stage renal disease and the interactions between the anti-rejection and the anti-viral therapies.

FY 2003

- Renew the **Cooperative Clinical Trials in Pediatric Kidney Transplantation.** This program examines the causes of decreased patient and graft survival rates in children versus adults and the effects of immunosuppressive therapy on growth retardation.
- Continue to solicit, review, and fund applications for novel tolerance induction regimens in kidney and islet transplantation through the **Immune Tolerance Network (ITN)**. The ITN is an international consortium of over 70 basic scientists and clinical investigators in 9 countries established to test promising tolerogenic treatment regimens in islet transplantation, kidney transplantation, autoimmune diseases, and asthma and allergic diseases. The ITN is co-sponsored by NIDDK and the Juvenile Diabetes Research Foundation International.

FY 2004-2006

- Release new, expansion, and renewal initiatives as appropriate.
- Continue support for ongoing initiatives.
- Continue support for ongoing investigator-initiated research related to organ transplantation.
- Fund meritorious new investigator-initiated research related to organ transplantation.

Performance Measures:

- Publication of initiatives in the NIH Guide and the Commerce Business Daily.
- Funding of awards.
- Initiation of clinical trials.

Outcome Measures:

- Publication advances regarding the development of non-invasive methods to detect organ graft rejection

- Publication of results from assessment of outcomes in kidney transplant recipients receiving IVIG
- Publication of results from analysis of therapeutic interventions for organ graft rejection in African Americans.
- Publication of findings on the effect of dietary modifications on organ graft survival in African Americans.
- Publication of analysis of patient and graft survival rates in children.

Area of Emphasis: I. C. Autoimmune Diseases

Autoimmune diseases are those in which the immune system mistakenly attacks the body's own cells, tissues, and organs. Collectively, autoimmune diseases afflict more than 5 percent of the U.S. population. Several of these diseases, such as systemic lupus erythematosus (SLE) and scleroderma, disproportionately affect minority populations, particularly African American women. Reports also indicate an increased prevalence of SLE and rheumatoid arthritis among many Native American tribes.

Systemic lupus erythematosus is a chronic, inflammatory, multisystem disorder of the immune system in which antibodies develop that react against a person's own tissue. SLE varies greatly in severity, from mild cases requiring minimal intervention to those in which significant and potentially fatal damage occurs to vital organs such as the lungs, heart, kidneys, and brain. SLE occurs in 1 out of 2,000 Americans and is more common and more severe in African American women, occurring in as many as 1 in 250 young African American women. SLE is two-fold more prevalent among African American men than among Caucasian men.

Scleroderma is an autoimmune disease that involves the abnormal growth of connective tissue, which supports the skin and internal organs. Localized scleroderma affects the skin and musculoskeletal system; systemic sclerosis may affect blood vessels and damage the heart, lungs, and kidneys. The number of Americans affected by scleroderma is estimated to range from 40,000 to 165,000. Systemic scleroderma affects more African American women than women of European descent.

The NIAID supports a broad portfolio of basic, pre-clinical, and clinical research aimed at understanding the pathogenesis of autoimmune diseases, investigating new ways to modify the immune system, and applying this knowledge to the identification and evaluation of promising approaches to treat and prevent these diseases.

Objective: I.C.1. Support research on the causes, treatment, and prevention of autoimmune diseases to help reduce disparities in the incidence and prevalence of these diseases that disproportionately affect minorities.

Basic and clinical research that advance our understanding of the underlying immune mechanisms of autoimmune diseases is important in reducing disparities in the incidence and prevalence of these diseases. This research will provide insight into the mechanisms of tolerance

induction and lead to the development and evaluation of new immune modulation interventions to treat and prevent autoimmune diseases. Central to the success of translating basic research findings to clinical applications are the close, cross-disciplinary interactions between basic and clinical researchers.

Action Plan:

Steps

1. Establish and support a collaborative approach to basic research and clinical trials among multiple institutions in various geographic areas, and enhance the exchange of information between basic scientists and clinicians involved in the study and treatment of autoimmune diseases.
2. Support the design, conduct, and analysis of clinical trials to determine the safety and efficacy of hematopoietic stem cell transplantation as a treatment for multiple autoimmune diseases, including SLE and systemic scleroderma.
3. Support a broad range of investigator-initiated research to elucidate and understand the factors relevant to initiation, maintenance, diagnosis, prevention, and treatment of systemic autoimmune disease.

Timeline

FY 2002

- Support clinical trials and clinical studies of new immunomodulatory and tolerogenic approaches to prevent or treat autoimmune diseases, including integrated basic research studies to understand disease mechanisms, knowledge that can be applied to the development of therapeutic and preventive approaches.
    - Continue support for the **Autoimmunity Centers of Excellence (ACEs)** clinical trials to evaluate immunotherapies for SLE and scleroderma. The ACEs support integrated basic, pre-clinical, and clinical research focused on tolerance induction and immune modulation to treat and prevent autoimmune diseases. The ACEs are co-sponsored by the NIDDK, NIAMS, and ORWH.
    - Initiate clinical trials of tolerogenic approaches through the **Immune Tolerance Network (ITN)** for autoimmune diseases, including those that disproportionately affect minority populations. The ITN is an international consortium of over 70 basic scientists and clinical investigators in nine countries, established to test promising tolerogenic treatment regimens in islet transplantation, kidney transplantation, autoimmune diseases, and asthma and allergic diseases. The ITN is co-sponsored by NIDDK and the Juvenile Diabetes Research Foundation International.
- Continue support for multi-site clinical trials for evaluation of hematopoietic stem cell transplantation as a treatment for systemic autoimmune diseases, including those affecting minority populations. The **Clinical Trials in Stem Cell Transplantation for the Treatment of Autoimmune Diseases** support the development of effective approaches for the treatment and prevention of autoimmune diseases. This program is co-sponsored by the NHLBI, NIDDK, NIDCR, NICHD, and ORWH.

- Fund the clinical coordinating center to support the ACEs and the Clinical Trials in Stem Cell Transplantation for the Treatment of Autoimmune Diseases.
- Continue support for ongoing investigator-initiated research on all aspects of autoimmune diseases.
- Fund meritorious new investigator-initiated research on all aspects of autoimmune diseases.

FY 2003
- Issue an initiative to renew the ACEs, including the clinical trials component testing immunotherapies for SLE and scleroderma.
- Continue support for Clinical Trials in Stem Cell Transplantation for Treatment of Autoimmune Diseases.
- Continue support for the clinical coordinating center to support the ACEs and the Clinical Trials in Stem Cell Transplantation for Treatment of Autoimmune Diseases.
- Continue support for ongoing investigator-initiated research on all aspects of autoimmune diseases.
- Fund meritorious new investigator-initiated research on all aspects of autoimmune diseases.

FY 2004 – FY 2006
- Support new and renewal initiatives, as appropriate.
- Continue support for ongoing clinical trials.
- Continue support for ongoing investigator-initiated research on all aspects of autoimmune diseases.
- Fund meritorious new investigator-initiated research on all aspects of autoimmune diseases.

Performance Measures:
- Presentation of significant findings and report on progress at biennial meeting of the ACEs and at national scientific meetings.
- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Initiation of clinical studies and trials.

Outcome Measures:
- Publication of scientific advances (in peer-reviewed scientific journals) relevant to understanding mechanisms of induction, maintenance, prevention, and treatment of autoimmune diseases.
- Publication of the identification and evaluation of new approaches for the treatment and prevention of autoimmune diseases.
- Availability of applications of clinical trial results to the diagnosis, treatment, and prevention of autoimmune diseases.

Area of Emphasis: I.D. Asthma

Over the past few years, attention has focused on the disproportionate burden of asthma on minorities, particularly African American and Hispanic children residing in the inner city. Data

on overall asthma prevalence and severity, and on the impact of asthma on minority populations, highlight the extreme burden of this disease in medical, economic, and social costs.

Asthma affects more than 14 million Americans, or approximately 6 percent of the population, resulting in over 130 million days of restricted activity and nearly 500,000 hospitalizations annually. Poorly controlled asthma is the leading cause of school absenteeism and hospital admissions among children. Recent studies estimate that in certain urban areas between 20 and 25 percent of school children suffer from asthma. African Americans are hospitalized for asthma three times more often than other Americans, and African Americans and Hispanic Americans living in inner cities are two to six times more likely to die from asthma. It is particularly disturbing that, from 1980 to 1993, the death rate from asthma doubled for children 5 to 14 years of age. Over this same period, the disparity between the burden of asthma on African American and white populations remained unchanged, or actually worsened, as was the case for emergency room visits. Furthermore, the costs associated with asthma are substantial. A rigorous economic study estimated 1990 costs at $6.2 billion; more recent analyses estimate over $11 billion in asthma-associated costs.

Disadvantaged populations have not benefited fully from the scientific advances that have improved asthma treatment and management for middle and upper income populations. In order to address this disparity, in 1991 the NIAID established the **National Cooperative Inner City Asthma Study (NCICAS)**, which demonstrated the efficacy of a multifaceted asthma educational intervention in reducing asthma severity among inner-city children. The Centers for Disease Control and Prevention is implementing this educational and behavioral intervention at 23 community-based health organizations nationwide in a four-year, $12 million program launched in FY 2001. Building on the success of NCICAS, in 1996 the NIAID and the National Institute of Environmental Health Sciences established the **Inner City Asthma Study (ICAS)** to evaluate the effectiveness of physician education and an extensive environmental intervention on asthma severity. Data collection for these studies was completed in September 2001 and analysis is currently underway.

Objective I.D.1: Support research on the causes, treatment, and prevention of asthma to help reduce disparities in the incidence and prevalence of this disease.

Over the past two decades, our understanding of the pathophysiology and management of asthma has improved significantly, yet the prevalence of this disease has increased by more than 80% in all age and ethnic groups. The increasing prevalence and high morbidity from asthma among inner-city children demonstrates the need for developing new therapies to both reduce asthma severity and prevent disease onset. Recent studies suggest that the stage is set for the development of asthma during the first several months of gestation. These and other findings offer promising new opportunities to initiate basic and clinical research aimed at clearly defining the early-life perturbations of the immune system that lead to the development of asthma.

Action Plan:

Steps

1. Design and conduct clinical trials of immune-based therapies in inner-city children with asthma, carry out research to study and understand the mechanisms of action of these therapies and their effect on disease, and conduct basic research studies on the immunopathogenesis of asthma in inner-city children.
2. Support basic and clinical research on the pathobiology of asthma that will lead to a better understanding of the role immune dysfunction plays in the early life origins of asthma in humans.
3. Support research that will explore the potential benefits of tolerogenic approaches to asthma prevention and treatment.
4. Continue to support investigator-initiated research projects that address important scientific questions relevant to the pathogenesis, diagnosis, treatment, and prevention of asthma in inner-city children.

Timeline

FY 2002

- Fund the **Inner-City Asthma Consortium: Immunologic Approaches to Reduce Asthma** and the **Statistical and Clinical Coordinating Center for the Inner-City Asthma Consortium.**
    - The Consortium will support a network of basic scientists and clinical investigators to evaluate the safety and efficacy of promising immune-based therapies to reduce asthma severity and prevent disease onset in minority children residing in inner cities.
    - The Consortium will conduct research to delineate the mechanisms underlying immune-based therapies and develop and validate surrogate biomarkers to measure disease stage, progression, and therapeutic effect. Other studies will involve immunologic pathogenesis and population-specific aberrations in response to drug dosing or drug selection for optimal disease control.
- Continue support for the **Asthma and Allergic Diseases Research Centers (AADRCs).**
    - The AADRCs are one cornerstone of the pathobiology component of the NIAID asthma and allergy research program, and support basic and clinical research on the mechanisms, diagnosis, treatment, and prevention of these diseases. Renewal of the AADRCs will emphasize clinical studies of the immunobiology of asthma, a focus that has great potential to benefit minority populations.
- Fund proposals for **Phase I and II trials** of tolerance induction for allergic diseases; these trials will be conducted through the **Immune Tolerance Network (ITN)**. The ITN is an international consortium of over 70 basic scientists and clinical investigators in 9 countries established to test promising tolerogenic treatment regimens in islet transplantation, kidney transplantation, autoimmune diseases, and asthma and allergic diseases. The ITN is co-sponsored by NIDDK and the Juvenile Diabetes Research Foundation International.
- Continue support for ongoing investigator-initiated research related to asthma.
- Fund meritorious new investigator-initiated research related to asthma.

FY 2003

- Continue support for the Inner-City Asthma Consortium and the Statistical and Clinical Coordinating Center.
- Issue initiative to renew the AADRC program, with increased emphasis on clinical research and developmental immunobiology as it pertains to the early life origins of asthma in humans.
- Continue support for the AADRCs.
- Fund proposals for Phase I and II trials of tolerance induction to allergens relevant to asthma.
- Continue support for ongoing investigator-initiated research related to asthma.
- Fund meritorious new investigator-initiated research related to asthma.

FY 2004 - 2006

- Continue support for the Inner-City Asthma Consortium and the Statistical and Clinical Coordinating Center.
- Continue support for AADRCs.
- Issue initiative to renew nine AADRCs.
- Fund proposals for Phase I and II trials of tolerance induction to allergens relevant to asthma.
- Continue support for ongoing investigator-initiated research related to asthma.
- Fund meritorious new investigator-initiated research related to asthma.

Performance Measures:

- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Funding of awards.
- Initiation of clinical studies and trials.

Outcome Measures:

- Presentation of significant findings at scientific meetings.
- Presentation and publication of results of clinical trials.
- Presentation and publication of scientific advances in basic and clinical research studies.
- Identification and evaluation of new approaches for the treatment and prevention of asthma.
- Applications of clinical trial results to the diagnosis, treatment, and prevention of asthma in underserved populations.

Area of Emphasis I.E.: Tuberculosis (TB)

A number of factors have combined to cause a disproportionate impact of *Mycobacterium tuberculosis* (TB) among minorities and low socioeconomic populations in the U.S. Foreign-born minorities, who have emigrated from TB endemic countries, may harbor TB infection or active TB disease. In addition, the problems of urban poverty, high HIV infection rates, and the effects of household crowding may converge to increase the incidence of TB disease in this population. During 1999, approximately 76 percent of active TB cases were reported among racial and ethnic minorities. Worldwide TB is the leading cause of death for those persons infected with HIV and 15 percent of HIV+ individuals die of TB, according to the World Health Organization.

NIAID supports an extensive portfolio of TB research aimed at improving diagnosis, prevention and treatment of TB in minority populations. NIAID's **Tuberculosis Research Unit (TBRU)** encompasses an international, multidisciplinary team of collaborators who translate TB basic research findings into improved clinical tools and strategies. TBRU-initiated studies develop or evaluate a variety of new assays, markers, prevention strategies, and therapeutics. A new drug that needs to be taken less often, now under study, would help solve compliance problems that currently exist within minority populations. A shortened therapeutic regimen is also being tested for efficacy in a clinical trial. In addition, NIAID supports epidemiological studies to better understand the genetic and environmental factors that contribute to TB disease susceptibility and transmission.

Objective I.E.1. Support research on vaccines that would help reduce disparities in the incidence and prevalence of TB

A widely delivered vaccine that effectively prevents adult, pulmonary TB would dramatically reduce the burden of this disease in minority populations and the health disparities associated with tuberculosis. Effective immunotherapeutic agents that prevent those with latent TB infection from developing active disease or that would be given to TB patients in addition to standard TB therapy to speed and improve cure rates would also be important advances that would help reduce health disparities.

Action Plan:

Steps

1. Support preclinical and clinical research to develop TB vaccine candidates.
2. Support studies of host and pathogen genetic contributions to TB susceptibility and resistance and epidemiologic studies of transmission, incidence and prevalence within high burden populations.
3. Conduct clinical trials of safety, immunogenicity and efficacy of TB vaccine and immunotherapeutic candidates.

Timeline

FY 2002

- Continue to support the **NIAID Tuberculosis Research Unit (TBRU)** and expand the **TB Research Materials and Vaccine Testing** contracts to increase conduct of vaccine research and development and related genetic and epidemiologic studies.
- Fund new initiatives to:
  - Support development of novel TB vaccine candidates **(Millennium Vaccine Initiative)**
  - Elucidate the mechanisms underlying TB latency and reactivation disease so that novel vaccine candidates can target the large number of minorities already infected with *M. tuberculosis* and at risk for developing active disease **(Response to the Presidential Vaccine Initiative – Overcoming the TB Latency Challenge)**
- Fund applications pursuant to on-going related initiatives, such as the Challenge Grant, "Development of a Recombinant Tuberculosis Vaccine" and "A Non-human Primate Model of TB and AIDS".
- Fund related investigator-initiated research.

FY 2003

- Fund an initiative to support development of new animal models for TB vaccine development.
- Continue to support the TBRU and expanded TB Research Materials and Vaccine Testing contracts.
- Fund applications pursuant to on-going initiatives.
- Fund related investigator-initiated research.

FY 2004 – FY 2006
- Release new, expansion and renewal initiatives as appropriate.
- Fund applications pursuant to on-going initiatives.
- Fund related investigator-initiated research.

Performance Measures:
- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Funding of awards.
- Initiation of clinical trials.

Outcome Measures:
- Availability of new and improved vaccine candidates for testing.
- Publication of scientific advances related to TB vaccines.
- Interest of private and public sector partners in development of TB vaccines.

Objective I.E.2. Support research on improved therapeutic and diagnostic strategies that would reduce disparities in the incidence and prevalence of TB.

Current recommended therapy for tuberculosis requires patients to adhere to long and complicated regimens (4 drugs over 6-9 months). Development of new drugs that would simplify and shorten these regimens, provide effective treatments for drug-resistant TB, and shorten effective prophylactic courses for treatment of latent TB infection (which has relatively high prevalence in minority populations), would make major contributions to reducing health disparities in treatment and cure of TB.

Action Plan

Steps
1. Support research to discover, design and develop novel TB therapies.
2. Support research to develop inexpensive, robust, sensitive and specific diagnostics of TB infection and disease, especially for immunocompromised (e.g., HIV+) individuals, in whom current diagnostics are inadequate.
3. Conduct clinical trials to determine safety and efficacy of novel therapeutic strategies.

Timeline

FY 2002

- Continue to support the NIAID **Tuberculosis Research Unit (TBRU)** and the **TB Research Materials and Vaccine Testing** contracts to increase the conduct of drug and diagnostics research and development.
- Support clinical trials of shortened regimens and novel therapeutic candidates under the TBRU.
- Fund an initiative to encourage **Partnerships for Novel Therapeutics and Vector Control Strategies in Infectious Diseases.**
- Fund applications pursuant to on-going related initiatives, such as the **Challenge Grants** for TB drug development.
- Continue to support the **TB Structural Genomics** initiative to determine the 3-dimensional structure of 400 TB proteins, leading to discovery of novel drug targets.
- Fund drug and diagnostics related investigator-initiated research.
- Continue to conduct a tuberculosis telemedicine program through the intramural research program. The TB telemedicine program is a collaboration with physicians at South Texas Hospital. The majority of the patients in this program are impoverished Mexican Americans from rural South Texas who receive state-of-the-art TB treatment from an NIAID TB expert and collaborators in Texas. Telemedicine technology allows the South Texas Hospital physicians and NIAID investigators to simultaneously interview and examine patients and study patient x-rays, pathology, and laboratories tests. This program allows patients who normally would not have access to experimental therapies and clinical trials to benefit from the expertise and innovative approaches available at the NIH.

FY 2003

- Fund a new initiative to support development of new animal models for TB drug development.
- Continue to support the TB Structural Genomics initiative to determine the 3-dimensional structure of 400 TB proteins, leading to discovery of novel drug targets.
- Continue to support drug-screening contracts. Southern Research Institute in Birmingham, Alabama has established a **Tuberculosis Antimicrobial Acquisition and Coordinating Facility** (TAACF) to acquire compounds for screening against Mtb, maintain a computerized chemical database of compound structures, coordinate and distribute compounds for evaluation *in vitro* and in an animal model, and report data back to suppliers.
- Continue to monitor progress under the **Challenge Grants** for TB drug development.
- Fund drug and diagnostics related investigator-initiated research.

FY 2004 – FY 2006

- Release new, expansion and renewal initiatives as appropriate.
- Fund applications pursuant to on-going initiatives.
- Fund drug and diagnostics related investigator-initiated research.

Performance Measures:
- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Funding of awards.
- Initiation of clinical trials.

Outcome Measures:
- Publication of scientific advances related to TB therapeutics and diagnostics.
- Availability of new and improved therapeutic candidates for testing.
- Interest of private and public sector partners in development of TB drugs and diagnostics.
- Identification of active anti-TB compounds in vitro.
- Evaluation of active compounds in pre-clinical and then clinical studies.

Objective I.E.3: Conduct tuberculosis epidemiology studies in an area with a high concentration of racial and ethnic minorities.

The objective of this program is to study all aspects of the genetic and social epidemiology of tuberculosis in Harris County, Texas, a metropolitan area with more than 500 new TB cases per year, over 75 percent of which occur among African Americans and Latinos. This study will identify traditional risk factors among patients with tuberculosis, such as HIV infection, injection drug use, homelessness, and history of incarceration. In addition, the analysis of genetic polymorphisms among TB strains will allow investigators to more exactly characterize TB transmission in this defined geographic area. Molecular subtyping of the TB organism can uncover previously unrecognized outbreaks and will lead to greater understanding of transmission dynamics among this population.

Action Plan:

Steps:
1. Maintain facility to enroll 500 tuberculosis patients, including at least 25 pediatric patients and 250 control patients per year for a longitudinal, population-based, active surveillance and molecular epidemiologic study of tuberculosis cases.
2. Interview patients using a standardized questionnaire designed to gather basic demographic and socioeconomic data and to identify tuberculosis risk factors.
3. Acquire *M. tuberculosis* isolates from all available culture-positive patients for genetic characterization by molecular subtyping methods.
4. Use information from questionnaires and data from molecular analysis of TB isolates to characterize the epidemiology of TB in this area.

Timeline:

This program began in FY 2000.

FY2002

- Maintain appropriate community liaisons to facilitate patient ability to participate in NIAID DIR programs related to *M. tuberculosis*. Facilitate patient participation by providing transportation of patients from their homes or workplaces to the study facility, and identification of incentives for study participation such as meals and/or reimbursement for time.
- Collect clinical material from a minimum of 500 tuberculosis patients and 250 control subjects. Interview patients using a standardized questionnaire designed to gather basic demographic and socioeconomic data and to identify tuberculosis risk factors.

FYs 2003-2006

- Each year of the project, collect clinical material and epidemiologic data from a minimum of 500 tuberculosis patients and 250 control subjects.
- Conduct molecular characterization of *M. tuberculosis* strains from a minimum of 750 patients per year.
- Compile results and delineate molecular epidemiology and risk factors associated with TB transmission in this geographic area.

Performance Measures:

- Number of subjects enrolled in the trial
- Percentage of subjects that remain enrolled through trail completion
- Completion of the trial

Outcome Measures:

- Publication of scientific advances regarding risk factors and transmission dynamics associated with TB in the population.

Area of Emphasis I.F: Hepatitis C

Hepatitis C virus (HCV) is a blood-borne pathogen that infects the cells in the liver called hepatocytes and causes liver damage. Populations at highest risk for this infectious disease are injection and cocaine drug users and individuals who received blood or blood products before 1992. Transmission more rarely occurs via sexual, body piercing/tattooing and unknown routes. Approximately 3.9 million Americans show evidence of infection, with 74 percent being active carriers of the virus. United States population-based surveys indicate that HCV more heavily affects minority populations and persons living in poverty. NIAID has calculated that 44.3 percent of HCV infected individuals are minorities. In addition to bearing a higher prevalence burden, because African-Americans have a uniquely poor response to HCV therapies, the racial disparity is compounded.

Viral genotyping and inherent genetic differences between Caucasians and African Americans are coming to light to begin explaining these differences, but further investigation as part of the health disparities research plan is strongly warranted.

Five years ago, NIAID took the lead and developed a **Hepatitis C Framework for Progress** that outlined the important research questions from the standpoint of its mission. In addition, a timeline was developed for provision of key resources and initiation of research in specific areas. Two years ago, multiple NIH institutes and centers broadened this Framework incorporating their individual mission and mission specific objectives.

Objective I.F.1. Support research on vaccines and related areas that would help reduce the disparities in the incidence and prevalence of hepatitis C.

NIAID has two distinct, but coordinated, on-going efforts in hepatitis C vaccine development: the first is **extramural**, and the second one is **intramural**. They are presented separately in this document.

I.F.1a. Extramural Program in Hepatitis C Vaccine Development

Vaccine development for HCV is primarily in a research and development phase. Extramural investigators are working to identify what composes the protective immune response. Focus areas include: defining early natural history, investigating mechanisms and correlates of recovery, persistence and resistance, and identifying mechanisms of immune evasion. Investigators are employing several novel approaches to the development of vaccine candidates. Extramural investigators were the first to develop infectious clones an advance that has significantly expanded the field. Investigators are working to develop key missing resources such as cell culture and small animal models. NIAID is supporting extramural investigators' work in chimpanzees. In terms of clinical research, the study of newly infected individuals and natural history is an emphasis area. NIAID is funding research on acquisition of HCV in an injection drug use study initiated by NIDA over a decade ago to study HIV infection. This group is 85 percent African American. These investigators have successfully taken a multi-disciplinary approach to understanding infection, natural history and disease. Last year they published the finding that African-Americans are more likely to acquire HCV infection but that the disease progresses more slowly in this population. A similar approach is being taken to study acquisition of HCV in health care workers via needlestick exposures. Such studies are critical for understanding the immune response in its natural host.

Action Plan

The extramural action plan is guided by the Hepatitis C Framework for Progress.

Steps

1. Support development of animal models and other systems.
2. Support pre-clinical and clinical research to develop HCV vaccine candidates.
3. Support host and pathogen genetic contributions to HCV infection and disease progression outcomes.
4. Support both prophylactic and therapeutic clinical trials of safety, immunogenicity, and efficacy of HCV vaccine candidates.

Timeline

FY 2002

- Continue ongoing support to develop infection and disease preclinical models including cell culture, mouse, tamarin and chimpanzee systems.
- Continue to fund research designed to understand host and viral components of recovery and persistence outcomes, resistance to infection and mechanisms of protective immunity to HCV infections in animal models and humans.
- Continue to support preclinical vaccine efforts, including new construct development.
- Continue to collaborate with NIDA on international efforts focused on acquisition of HCV in sex workers.
- Continue application of advanced technologies such as genomics, proteomics, and the use of overlapping peptides for vaccine development and host immune response studies.
- Begin to support the acquisition, production and provision of research and reference reagents for the research community.
- Begin Phase 1 evaluation of a hepatitis C immunoglobulin for prevention of reinfection of transplanted livers via the **Collaborative Antiviral Studies Group (CASG)**.
- Begin Phase 1 evaluation of hepatitis C vaccine candidates in normal volunteers via the **Vaccine and Treatment Evaluation Units (VTEUs).**
- Plan Phase 1 evaluation of vaccine candidates in HCV chronic carriers.
- Fund new initiative for cell and animal model development for hepatitis C.
- Fund re-competition of VTEUs .

FY 2003

- Continue above initiatives.
- Fund related investigator-initiated research.
- Expand the acquisition, production and provision of research and reference reagents.
- Partner with industry involved in HIV vaccine research and development to apply the same novel technologies such as CTL epitope strategies and vector development to HCV.
- Expand activities to understand mechanisms of recovery, persistence, and resistance to HCV infection as well as disease progression.

- Begin Phase 1 evaluation of HCV vaccine candidates for treatment of chronic carriers.

FY 2004-2006
- Continue above
- Fund related investigator initiated research
- Release and fund new, expansion and renewal initiatives as appropriate

Objective 1.F.1b. Intramural Program in Hepatitis C Vaccine Development

A better understanding of the molecular biology of hepatitis C virus and the immune response to hepatitis C infection are critical to the development of a safe and effective hepatitis C vaccine. The action plan for hepatitis vaccine development is based on the NIAID's **"Hepatitis C Framework for Progress"**, developed by a panel of expert scientists, including representatives who are implementing this plan in the NIAID's intramural laboratories.

Action plan:

Steps:
1. Define mechanisms of protective immunity to hepatitis C.
2. Define neutralizing antibodies to hepatitis C antigens.
3. Define natural mechanisms and correlates of recovery and persistence.
4. Distinguish protective from injury-invoking role of cell-mediated immunity responses.
5. Define immunological mechanisms associated with, and identify alterations in response to, repeated infections and co-infections.

Timeline:

FY 2002
- *Develop capabilities for studies and evaluation in human acute infection cohorts and include specimen collection and repository capabilities*. Continue examination of the genetic heterogeneity of HCV isolates and the implications of that heterogeneity on disease outcomes by launching studies to delineate the immunological mechanisms behind genetically-based differences in disease outcome.
- *Take advantage of infectious cDNA clones and viral pools.* The availability of chimpanzees and titered challenge pools of polyclonal and monoclonal HCV has permitted us to dissect the immune response to HCV infection. These ongoing studies are yielding important information about the role of humoral and cellular immunity, cytokines and other biologically active substances in the control of HCV infections.
- *Develop and make available a standardized set of viral reagents for use in evaluation of human immune responses to include HCV antibodies, cDNA clones and confirmation of sequences in databases.* Prototype strains of the various genotypes of HCV, including some of those discovered in NIAID's Laboratory of Infectious Diseases, have been biologically amplified in chimpanzees, packaged and distributed for use as challenge inocula in various studies, including studies of passive and active immunoprophylaxis. This work is ongoing.

FY 2003-2006

- *Continue to use infectious cDNA clones and viral pools and to develop and make available a standardized set of viral reagents for use in evaluation of human immune responses to include HCV antibodies, cDNA clones and confirmation of sequences in databases.*
- *Characterize immune response in the chimpanzee – the only existing model.* Full-length cDNA clones of HCV (genotypes 1a, 1b and 2a) have been constructed and transcribed RNA used to transmit hepatitis C to chimpanzees by in vivo hepatic transfection. Chimpanzees, transfected with infectious cDNA clones of HCV, are being followed to determine the natural history of infection.
- *Develop, characterize, and comparatively evaluate model systems of infection, both tissue culture and small animal models. Exploit appropriate models for immune response research and vaccine evaluation.* NIAID investigators have constructed an infectious cDNA clone of GB virus-B (GBV-B), a monkey virus that is the closest relative to HCV. In addition, we have prepared challenge pools of GBV-B and have determined the infectivity titer of these in tamarins. We will continue to use the GBV-B tamarin system to study characteristics of the virus that it shares with HCV.
- *Provide for detailed, multiple, and iterative vaccine approaches and detailed immune response studies.* Challenge pools of polyclonal virus, representing each of the major genotypes, will be employed in vaccine evaluation studies in the NIAID's intramural program and will be supplied to extramural laboratories as a service to the scientific community.
- *Use basic and clinical research results to devise ever more rational vaccination strategies.*
- *Promote development of better methods to study the immune response*.

Performance Measures:
- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Addition of research and reference reagents.
- Funding of awards.
- Distribution and availability of reagents necessary to conduct hepatitis vaccine research.
- Initiation of trials in animals.
- Initiation of clinical trials of candidate hepatitis C vaccine

Outcome Measures:
- Publication of scientific advances.
- Application of new technologies.
- Availability of new candidate vaccines for testing.
- FDA licensure of effective hepatitis vaccine.

Objective 1.F.2. Support research on improved therapeutic strategies for hepatitis C and related areas that would reduce disparities in treatment outcomes

NIAID's "bench-to-bedside" focus supports a wide range of research, development and evaluation activities. Based on NIAID's Hepatitis C Framework for Progress there is special emphasis on understanding viral replication and discovery of new therapeutic targets, availability

of both preclinical and clinical resources to accurately evaluate the safety and effectiveness of candidate drugs, and understanding the mechanisms of viral clearance. Two of the nine **Hepatitis C Cooperative Research Centers** have disease progression and therapy clinical projects specifically focused on minority populations. One center is looking at long-term natural history and disease progression in a well-defined Alaskan Native cohort. A second center, new from the latest recompetition, is performing a clinical trial in HCV chronic carriers using pegylated Interferon and ribavirin. They are over-sampling African Americans seeking to enroll 75 African Americans and 50 Caucasians. The trial is powered to provide more definitive evidence related to response rate differences. In addition to clinical outcome, a multi-disciplinary group of investigators will investigate virological and host differences (e.g., immunological and genetic) between the two groups. Finally, a third center plans an early phase clinical trial to evaluate a novel immunomodulatory adjunct to improve standard therapy. In addition, NIAID is providing funding for NIDDK's HALT-C trial. These efforts are focused on understanding the virological and immunological responses and their association with recovery and disease progression. If more successful therapeutic modalities can be identified, the prevalence of hepatitis C will decrease.

Action Plan

Steps

1. Support model system development.
2. Support understanding of viral replication.
3. Support development of new therapeutic modalities.
4. Perform preclinical evaluation of candidate antivirals.
5. Support research focused on host and pathogen genetic contributions to and mechanisms involved in sustained elimination of HCV in response to therapy.
6. Support research on early predictors of both disease progression and sustained response to therapy.
7. Support clinical trials of new antivirals, immunomodulators, and therapeutic vaccines.

Timeline

FY 2002

- Continue to support ongoing development of infection and disease preclinical models including cell culture, mouse, tamarin and chimpanzee systems.
- Fund new initiative for cell and animal model development for hepatitis C.
- Promote and fund evaluation of candidate therapies in preclinical models.
- Continue to fund research on viral replication.
- Continue to fund research on mechanisms involved in determining response vs non-response to therapy.
- Continue to support preclinical development of new therapeutic strategies.
- Continue to apply advanced technologies such as genomics, proteomics and the use of overlapping peptides for therapeutics development and host immune response studies.
- Initiate novel combination treatment trial.

- Begin to support the acquisition, production and provision of research and reference reagents for the research community.
- Continue evaluation of therapies in HIV/HCV co-infections.
- Plan Phase 1 evaluation of a vaccine as a therapeutic strategy.
- Re-compete and expand the **Collaborative Antiviral Testing Groups** to include HCV.
- Re-compete the **Collaborative Antiviral Studies Group.**

FY 2003
- Continue initiatives above.
- Fund related investigator-initiated research.
- Expand the acquisition, production and provision of research and reference reagents.
- Begin Phase 1 evaluation of HCV vaccine candidates for treatment of chronic carriers.
- Fund the **Collaborative Antiviral Testing Group** and the **Collaborative Antiviral Studies Group.**

FY 2004-2006
- Release and fund new, expansion and renewal initiatives as appropriate.
- Fund related investigator-initiated research.

Performance Measures:
- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Addition of research and reference reagents.
- Funding of awards.
- Initiation of clinical trials.

Outcome Measures:
- Publication of scientific advances related to HCV replication and therapeutics including development and use of model systems for preclinical antiviral development and increased understanding of the host and viral parameters involved in sustained response to therapy.
- Availability of new technologies for application
- Availability of new candidate therapies for testing.

Area of Emphasis: I.G. Sexually Transmitted Diseases (STDs)

The current sexually transmitted disease (STD) epidemic in the United States disproportionately affects minority populations. Recent studies indicate that the more prevalent non-ulcerative STDs (such as chlamydia, gonorrhea, and trichomoniasis) as well as ulcerative diseases (genital herpes, syphilis, and chancroid) increase the risk of HIV transmission by at least three-to fivefold. Although STDS like chlamydia, HPV, and herpes are widespread across racial and ethnic groups, STD rates tend to be higher among African-Americans than whites. For herpes, one study determined that African Americans accounted for 60 percent of herpes cases in STD clinics. Reported rates for gonorrhea and syphilis have been shown to be as much as 30 times higher for African Americans than for whites. Based on data for 1999, when all reportable STDs are combined, African Americans and Latinos account for 45 percent of all STDs.

The long-term consequences, as well as the incidence of STDs, are higher among nonwhites than among whites. For example, although black and Hispanic women comprise only 17 percent of the total female population of the United States, they make up a disproportionate share (33 percent) of the reported clinic visits for pelvic inflammatory disease (PID) a disease of the upper reproductive tract, PID, is primarily caused by sexually transmitted bacterial infections. Moreover, women in these populations suffer more often from cervical cancer, a sequelae of the human papilloma virus infection.

Among all populations, adolescents bear an enormous burden of STDs. In 1998, 64 percent of the 14 million new STD cases occurred in young people under age 24, with more than 3 million cases occurring in teenagers

Objective I.G.1 Support research on therapeutics that would help reduce disparities in the incidence and prevalence of syphilis.

In 1999, syphilis rates among blacks were more than 30 times greater than the rate infection among non-Hispanics whites, which was 0.5 per 100,000. Based on 1999 data, minorities account for approximately 75 percent of all reported cases of syphilis. This makes syphilis a serious health concern in this population. [NOTE: CDC's STD Surveillance 1999 Report notes that its surveillance data are based on cases of STDs reported to state and local health departments. In many areas, reporting from public sources, e.g., STD clinics, is more complete than reporting from private sources. Since minority populations may utilize public clinics more than whites, the differences in rates between minorities and whites are potentially misleading.]

Action Plan

Steps

1. Intensify efforts to assess new, easy-to-administer treatments for syphilis and gonorrhea such as, a single-dose oral therapy that will increase compliance among affected populations for that disease.
2. Collaborate with CDC on research activities related to the **Syphilis Elimination Plan**.

Timeline

FY 2002
- Support a large efficacy study examining azithromycin for the treatment of syphilis.
- Support research on cutaneous immune response in early syphilis.
- Support relevant investigator-initiated research.

FY 2003
- Continue efficacy study for treatment of syphilis.
- Support additional relevant investigator-initiated research.

FY 2004-FY 2006
- Completion of azithromycin efficacy trial for syphilis and analysis of data.
- Recompetition of STD Clinical Trials Unit.
- Continue support of relevant investigator-initiated research.

Performance Measures:
- Identification and testing of new treatment modalities for syphilis and gonorrhea.
- Additional awards for research and clinical programs in syphilis and gonorrhea.

Outcome Measures:
- Availability of new treatment modalities for syphilis and gonorrhea.
- Publication of scientific advances relevant to syphilis and gonorrhea.

Objective I.G.2 Support research on vaccines that would help reduce disparities in the incidence and prevalence of STDs.

A widely delivered vaccine that effectively prevents STDs would dramatically reduce the burden of these diseases in minority populations and the health disparities associated with them.

Action Plan

Steps
1. Stimulate syphilis vaccine development by analyzing the newly sequenced genome of *Treponema pallidum.*
2. Stimulate development of vaccines against Herpes, gonorrhea, and chlamydia.

Timeline

FY 2002
- Continue support of grants for the development of vaccines to prevent chlamydial infections and gonorrhea.
- Support an efficacy trial of a herpes vaccine.
- Support relevant additional investigator-initiated research.

FY 2003
- Continue support of grants on development of vaccines for STDs.
- Continue efficacy trial of herpes vaccine.
- Continue to support relevant investigator-initiated research.

FY 2004-FY 2006
- Re-competition of the STD Cooperative Research Centers grant program.
- Continue to support relevant investigator-initiated research.

Performance Measures:
- Publication of initiatives in the NIH Guide and Commerce Business Dailey
- Funding of awards for vaccine research in STDs
- Initiation of clinical trials

Outcome Measures:
- Availability of new STD vaccine candidates for testing.
- Publication of scientific advances relevant to STDs.

Objective I.G.3. Support intervention/prevention/behavior studies to help reduce disparities in the incidence and prevalence of STDs.

Intervention/prevention/behavior research is a high priority for NIAID. The spiraling acute and chronic morbidity of STDs, particularly amongst minority populations, provide a clear rationale for the development of better, more effective strategies to prevent these diseases.

Action Plan

Steps
1. Develop studies to examine strategies for intervening and preventing STDS. These include exploring the impact of restoring normal vaginal flora on frequency of STDs and evaluating douching as a risk factor for PID in African-American women.
2. Expand the understanding of factors that contribute to high-risk sexual behavior in African-American and Latina women.
3. Evaluate behavioral approaches to STD prevention and control in inner-city high schools.
4. Conduct clinical studies of African-American adolescents that will identify behavioral and cultural risk factors for acquiring STDs.

Timeline

FY 2002
- Continue to support the STD Cooperative Research Center focused on the prevention of STDs. Through this center, two studies examining strategies for preventing bacterial vaginosis, herpes, and chlamydia infections will be conducted.
- Continue support of the STD Cooperative Research Center that is focused on multidisciplinary research on sexual behavior, clinical epidemiology, immunobiology, and pathogenesis of gonococcal and chlamydial infections.
- Continue to support the STD Cooperative Research Center program with emphasis on research into more effective interventions for preventing STD morbidity in adolescents.
- Continue to support a longitudinal study to examine social and sexual networks of Latino/a adolescents in San Francisco.
- Continue support of research on STD risks associated with adolescent sexual networks.
- Continue to support additional relevant investigator-initiated research.

FY 2003
- Complete a longitudinal study to examine social and sexual networks of Latino/a adolescents in San Francisco.
- Continue to support additional relevant investigator-initiated research.

FY 2004 – FY 2006
- Re-competition of the STD Cooperative Research Centers grants program.
- Continuation of support of relevant investigator-initiated research.

Performance Measures
- Publication of initiatives in the NIH Guide and Commerce Business Daily.
- Funding of awards.
- Initiation of clinical trials and evaluations of behavioral interventions

Outcome Measures:
- Publication of scientific advances related to STD therapeutics, vaccines, diagnostics, and behavioral interventions
- Availability of new and improved therapeutic candidates for testing.
- Interest of private and public sector partners in development of STD drugs, diagnostics, and behavioral interventions.

II. RESEARCH INFRASTRUCTURE AND TRAINING

Intellectual talent propels the research enterprise. As long as some minorities are underrepresented among immunology and infectious disease researchers, training and developing the careers of members of those communities will be an NIAID priority. NIAID supports a comprehensive portfolio of biomedical and behavioral research aimed at addressing health

disparities through capacity building. These activities include (1) fostering infrastructure development, (2) promoting the training and career development of minority investigators, and (3) stimulating interest in the biomedical sciences among young minority students.

Area of Emphasis II.A. Research infrastructure of minority institutions and research careers of minority investigators

NIAID is strongly committed to increasing the number of minority researchers in all areas of science within its mission. This commitment arises from the realization that scientists from *all* segments of our society can and should contribute to eliminate the health disparities that exist in our country. As a result, NIAID supports a wide spectrum of activities dealing with the development of infrastructure at minority institutions, as well as fostering the careers of minority investigators in order to increase their competitiveness within the research community. These programs are designed to insure that an increasing number of qualified minority researchers become productive and remain in the fields of biomedical research funded by NIAID.

Objective II.A.1. Through the Research Centers in Minority Institutions program, support AIDS research infrastructure development of minority colleges and universities

The ability of our nation to address health disparities is directly related to the capacity of minority institutions to conduct biomedical and behavioral research. The Research Centers in Minority Institutions (RCMI) program, has been administered by NIH's National Center for Research Resources since 1990. The program supports predominantly minority health professional schools and graduate institutions in the health professions and health-related sciences. Under the RCMI program, NIAID funds the AIDS Infrastructure initiative, which seeks to expand physical facilities and faculty competence in virology, immunology, molecular biology and neurobiology. The purpose of NIAID support is to enable minority institutions to join mainstream AIDS research at the national and international level. NIAID funding of RCMIs is particularly timely because the institutions we support are located in communities in which the AIDS epidemic has hit particularly hard.

Action Plan:

Steps
1. Support funding of infrastructure capacity building in minority institutions that conduct biomedical and behavioral research.

Timeline

FY 2002
- Continue to provide support for AIDS studies in at least 6 minority institutions, 3 of which are Historically Black Colleges.

FY 2003-2006
- Increase the number of minority institutions participating in the NIAID RCMI program.

Performance Measures:
- Number of RCMIs supported
- Number of researchers supported under this mechanism.

Outcome Measures:
- Number of research grants awarded to minority researchers in AIDS research.
- Collaborative partnerships between junior minority researchers and NIAID-supported researchers to foster mentoring relationships and transference of scientific expertise.

Objective II.A.2. Support early career development of minority scientists through the Enhancement Awards for Underrepresented Minorities.

NIAID supports a number of programs to foster the career development of minority scientists and increase their competitiveness within the research community. These programs are designed to insure that qualified minority researchers become productive and remain in fields of biomedical research funded by NIAID. However, NIAID aims to increase its commitment in this area by initiating a new award.

Action Plan:

Steps
1. Initiate and fund a new enhancement award for Underrepresented Minority Scientists.
2. Broadly advertise new initiative to generate enough applications to insure the success of the initiative.
3. Target advertising to minority investigators to encourage their participation in our scientific agenda.

Timeline

FY 2002
- Issue Program Announcement for Underrepresented Minority Scientists Enhancement Award.

FY 2003-2006
- Make awards from applicant pool. Funding of four, 4-year awards anticipated.

Performance Measures:
- Funding of four awards in FY 2003.

Outcome Measures:
- Monitor progress of grantees by established methods such as quarterly performance reports.
- Success of award recipients in securing a NIH research grant support in FY 2007.

Objective II.A.3. Support career development of minority scientists by means of the Research Supplements for Underrepresented Minorities (RSUM) program.

This program supports minority students and scientists who work with independent researchers supported by NIAID-funded research project grants. NIAID will closely monitor this cadre of young investigators to insure that they continue to progress in their chosen areas of research.

Action Plan:

Steps
1. Continue advertising the RSUM mechanism at scientific conferences attended by minority students and professionals as well as on the NIAID website.
2. Establish a database to record and track the RSUM awardees funded by NIAID for success in receiving NIH Independent Researchers Award (R01).

Timeline

FY 2002
- Continue to fund and support 80% of applications received for this mechanism, with the expectation that a larger number will be funded because of a larger applicant pool.

FY 2003-2006
- Continue to fund and support 80% of applications received for this mechanism, with the expectation that a larger number will be funded because of a larger applicant pool.

Performance Measures:
- Number of RSUMs supported in FY 2003.
- Number of researchers supported under this mechanism.
- RSUM Tracking Database operational by end of FY 2003

Outcome Measures:

- Progress of grantees as documented by established methods such as quarterly performance reports.
- Success of award recipients in securing a NIH research grants support at the conclusion of their supplemental award.

Objective II.A. 4. Foster the career development of minority graduate students and postdoctoral trainees through the Bridging the Career Gap program.

In 1993, NIAID launched the Bridging the Career Gap program, with the goal of providing young minority investigators with the tools and information needed to carve out successful careers in biomedical research. This biennial program brings young minority scientists supported by NIAID to NIH for a two-day program that addresses career choices, networking, the importance of selecting the right mentor, and an overview of NIH's grant system and its components. NIAID is extremely proud of this model and its staff works very closely with many of these students throughout the various phases of their careers. This program celebrated its fifth anniversary in FY 2002 and will be repeated in FY 2004 and FY 2006.

Action Plan:

Steps

1. Actively encourage young minority scientists receiving NIAID support to attend the NIAID Bridge Seminar.
2. Provide funding for attendant travel expenses of participants.

Timeline

FY 2002:
- Bridge Seminar held on October 4-5, 2001. Feedback from session validates our continuance of this initiative in FY 2004.

FY 2003-2006
- Encourage young minority scientists receiving NIAID support to attend the Bridge Programs in FY 2004 and FY 2006, in an effort to increase attendance.

Performance Measures:
- Attendance numbers

Outcome Measures:
- Views and opinions of attendees gathered at the conclusion of each Bridging the Career Gap Workshop.
- Success rate of attendees in later securing NIH research grants.

Objective II.A.5. Ensure that the development of young, independent minority investigators is fostered through the use of regular research award mechanisms.

NIAID will increase funding of minority scientists applying for research grants by utilizing grant mechanisms currently in place. The amount of funding dedicated specifically to this purpose varies according to the meritorious applicants in the pool. NIAID has taken strong measures to insure that funding for minority scientists is increasing. This has been incorporated into the spending plans of NIAID's FY 2002-2006 appropriations.

Action Plan:

Steps
1. Advertise Program Announcements, Requests for Applications, and Requests for Proposals through various media and conferences to insure wider audience of minority scientist's circulation.
2. Adapt award mechanisms to foster support of minority researchers , i.e. **Research Scholar Development Award (K22)**. The K22 program supports postdoctoral trainees as they make the transition to assistant professor positions in an academic institution. This mechanism's eligibility criteria have been modified to include minority postdoctoral trainees supported on RSUMs.

Timeline

FY 2002-2006
- Increase advertising of the program via the NIH/NIAID websites and professional journals and promotions at scientific meetings.

- Continue utilization of existing mechanisms to fund minority investigators

Performance Measures:
- Number of new placements of advertisements of research initiatives that target minority investigators.

Outcome Measures:
- Number of awards to underrepresented minorities.

Area of Emphasis: II.B. Training for Minority Scientists

NIH and NIAID's training programs are designed to guarantee the pool of qualified researchers that this country needs to remain at the forefront of scientific discovery. A well trained cadre of minority researchers who bring a special blend of cultural knowledge and intellectual interest is required to address and resolve health disparities issues. NIAID hopes that an increase in the number of minority investigators participating in our scientific agenda will provide the level of minority presence needed to ensure that the agenda appropriately targets minority concerns and that clinical research is designed to be responsive to the needs and concerns of the minority community, which, in turn, would increase the benefits of our research efforts to that community. Training efforts focus on both NIAID's intramural and extramural programs.

Objective II.B.1 : Provide training opportunities for minority scientists in NIAID intramural programs.

NIAID will continue and expand its highly successful mechanism of recruiting minority pre- and postdoctoral scientists into its intramural research laboratories. Special seminars and events are planned for trainees in our minority programs to enrich their research experience and their professional development

Action Plan:

Steps:
1. Develop office infrastructure to support outreach, recruitment, and program management.
2. Develop national recruitment contacts.
3. Enrich NIAID training experience for minority scientists.
4. Increase the number of sponsored minority post-baccalaureate and post-doctoral Intramural Research Training Awards (ITRAs)
5. Track graduates of minority training programs for program evaluation, networking, and recruitment contacts.
6. Inform scientists about NIAID diversity issues and progress.

Timeline:
FY 2002
- Expand office staff to include program assistant and program analyst.

- Develop and test data management system. Enter information for minority trainees and summer interns (approximately 200 records).
- Develop a national database of recruitment contacts.
- Develop relationships with universities serving minorities to inform of NIAID programs and to identify students interested in NIAID's programs.
- Create Office of Special Emphasis webpage with key links.
- Initiate annual reports to Lab Chiefs re: NIAID DIR diversity issues and progress.
- Increase the number of sponsored minority post-baccalaureate IRTAs from 5 to 7
- Plan 4-6 seminars for minority trainees. Videoconference to include RML.
- Plan and conduct a one-day retreat for minority trainees focusing on NIAID's scientific challenges. RML minority trainees to attend.
- Write report based on the initial tracking information, including results and recommendations for NIAID DIR minority programs.

FY 2003

- Expand office staff to include program assistant for the Graduate Partnership Program. Role will include recruiting minorities to NIAID-university doctoral programs.
- Revise data management system and enter information for all DIR trainees, including pre- and postdocs (approximately 600 records).
- Expand national recruitment contact database.
- Visit selected universities to meet with science professors and minority students to inform about NIAID programs. Include current trainees in visits. NIAID minority trainees to be included in visits.
- Focus recruitment activities on increasing diversity at RML in Hamilton, MT.
- Revise recruitment video and brochures.
- Increase the number of sponsored minority post-baccalaureate IRTAs from 7 to 9
- Plan 4-6 seminars for minority trainees. Videoconference to include RML.
- Develop newsletter for current and past NIAID minority trainees.
- Update tracking information.
- Hold diversity trainee program for DIR scientists.

FY 2004-2006

- Increase the number of sponsored minority post-baccalaureate IRTAs from 9 to 10
- Increase the number of sponsored minority post-doctoral IRTAs from 5 to 7
- Plan 4-6 seminars for minority trainees. Videoconference to include RML.
- Update tracking information.
- Organize NIH workshop: Strategies for Increasing Diversity at NIH, using NIAID as the model.
- Hold retreat for all past and current NIAID minority trainees (from 1996 to present).

Performance Measures:

- The computerized data management system: stores data on all DIR trainees; provides search-sort-report abilities; interfaces with other NIH databases; maintains contact with all DIR minority trainees (past and present) for newsletters, and announcements; tracks career paths of minority program participants; maintains national recruitment database and tracks recruitment contacts.
- National recruitment database used by DIR for minority trainee and tenure track recruitment efforts.
- Minority trainees participate in seminars, workshops, and retreats.
- Tracking report assists office in program planning for minority trainees.
- Office of Special Emphasis visibility increased among DIR scientists and NIH community.

Outcome Measures:

- Post-baccalaureate and postdoctoral minority programs expand significantly.
- Network of NIAID minority trainees established.
- Tenure track job postings yield qualified minority candidates.
- Publish article on increasing diversity in the scientific community, what works!

Objective II.B.2. Support the training of young minority scientists in the field of AIDS by means of the Minority AIDS Clinical Training Program.

NIAID will continue to provide training opportunities through our Minority AIDS Clinical Training Program within the Adult AIDS Clinical Trials Network. This program, to be funded through FY 2006, will recruit and train minority health professionals by providing fellowships for four minority clinical researchers each year

Action Plan:

Steps

1. Provide up to 4 fellowships per year to minority clinical researchers in the area of HIV/AIDS research.

Timeline

FY 2002-2006

- Continue to offer up to 4 fellowships per year to minority clinical researchers

Performance Measures:

- The progress of grantees as documented by established methods such as quarterly performance reports.

Outcome Measures:

- Number of minorities participating in infectious diseases research, specifically in the area of HIV/AIDS

Objective II. B.3. Support the beginning research careers of minority medical students by the use of Short Term Research Training Grants.

NIAID will continue funding the Short-Term Research Training Grant in STD Research at Howard University School of Medicine. This program works in partnership with the Sexually Transmitted Disease Cooperative Research Centers (STD-CRCs) and funds minority medical students' summer research activities at STD-CRC sites. NIAID will use this model to establish similar programs in its other disease areas with institutions that focus on serving minority students by FY 2003.

Action Plan:

Steps

1. Initiate new Short Term Training Grants in division of AIDS and Allergy Immunology and Transplantation for minority medical and graduate students.
2. Link training grants to majority Centers for Excellence established with NIAID to minority institutions.

Timeline

FY 2002

- Planning and development of new Short Term Training grants in AIDS and Allergy Immunology and Transplantation.

FY 2003-2006

- Implementation and awarding of new Short Term Training grants in AIDS and Allergy Immunology and Transplantation.

Performance Measures:

- Number of Short Term Research Training Grants awarded to minority institutions.
- Number of minority medical students exposed to areas within NIAID's scientific programs, through Short Term Research Training Grants.

Outcome Measures:

- Number Short Term Research Training Grant participants who eventually participate in biomedical research.

Area of Emphasis II.C. Stimulating interest in the biomedical sciences and biomedical research careers among minority students.

NIAID has long recognized that increasing the participation of minorities in science requires attention to the pipeline of students who have not yet made career decisions. NIAID has supported programs that address several "segments" of the pipeline from undergraduates on the cusp of career decisions to students in pre-college programs. These efforts aim to stimulate the entry of minority students into training for research careers.

Objective II.C.1. Support the Introduction to Biomedical Research Program (IBRP) in order to stimulate minority student interest in research careers.

Our Nation's biomedical research agenda requires that we utilize every segment of our diverse population. Yet, the pipeline of minority scientists in the United States is so meager that it results in under-representation of minorities. This is quite notable within the ranks of NIH biomedical researchers where the representation of minority scientists is extremely low.

In FY 2002, NIAID's Introduction to Biomedical Research Program will have been in existence for 24 years. The program brings outstanding minority undergraduate and first year graduate/medical students to the NIH campus for a week long program of mentoring, advice, and scientific talks. NIAID staff work very closely with many of these students throughout the various phases of their careers. We are extremely proud of this program.

Action Plan

Steps

1. Continue to support our long-standing and highly successful IBRP program. Current plans provide for its continuance at least through FY 2006.

Timeline

FY 2002

- NIAID had intended to bring 60 academically outstanding underrepresented minority students to NIH/NIAID for a week of scientific seminars and exposure to biomedical research laboratories. However, due to concern about the safety of air travel in the wake of tragic national events, IBRP will have a smaller number of participants this year, about 20 or 25.

FY 2003-2006

- Continue support the IBRP program by bringing 60 Underrepresented minority students to the NIH/NIAID for a week of scientific seminars and exposure to biomedical research training.

Performance Measures:

- Number of applicants
- Number of attendees

Outcome Measures:

- Number of IBRP participants accepted into the NIAID Division of Intramural Research (or other ICs Intramural Programs) via the NIH Pre-Intramural Research Training Initiative Program.
- Number of IBRP students accepted into the NIH/NIAID Intramural Summer Internship Program.
- Number of IBRP students accepted to graduate school in the biomedical sciences.

Objective II.C. 2. Support the development of novel educational materials to stimulate high school student interest in science and research careers.

NIAID will expand its efforts with the Office of Science Education (OSE) to reach high school students through the issuance of its scientific curriculum supplement, "Emerging Diseases". NIAID staff are members of the Office of Science Education Resource Group and will continue to participate fully in their on-going activities.

In addition, NIAID will develop additional educational/outreach materials in Spanish, both in print and on our website.

Action Plan:

Steps

1. Work with the Office of Science Education in broadcasting existing NIAID curriculum on the Internet via an Open Classroom concept with Public Broadcasting System.
2. Disseminate instructional materials to science teachers through the Office of Education's website that was establish for this purpose.

Timeline

FY2002

- Begin discussions with OE/PBS on establishing an Open Classroom concept with NIH/NIAID as the focus.

- Continue to support Office's effort in the dissemination of NIAID's Curriculum Supplement as well as those of the other five participating institutes.

FY 2003-2006

- Launch Open Classroom initiative with OSE in FY 2004, when all nine of the curricula are completed.

Performance Measures:

- Establishment of an Open Classroom on PBS by 2004.
- Number of NIAID curricula (printed and/or electronic) distributed to national high schools.

Outcome Measures:

- Number of viewers/participants of the NIAID segment of Open Classroom
- Number of classes/teachers/students using the NIAID high school curricula

Area of Emphasis III.A. Outreach and transfer of health information to minority communities.

In its effort to reduce the incidence, prevalence, and severity of health problems that are particularly critical for some populations, NIAID must continue to reach out to the affected communities seeking input from diverse groups to guide priority setting. Through such outreach NIAID learns about the extent and impact of disparities, has a window on health issues that may be addressed by further research, and finds out what features clinical trial protocols must include to facilitate participation by the affected community.

Reducing health disparities also requires that the affected communities and their health care providers understand and be aware of health-related information that will reduce or eliminate risks for immunologic and infectious diseases and improve their options to treat those diseases when they do occur. This is a complex activity that requires the development and dissemination of consistent and credible messages on health risks and health care, as well as information about

ongoing research activities and developments. Often these messages must be tailored to the communities at highest risk for the adverse consequences of the health disparity in question.

NIAID's efforts to date have been strong and include pioneering the concept of community advisory boards for clinical trial networks, producing and disseminating print and audiovisual materials, exhibiting at professional and community meetings, sponsoring workshops and conferences for community health care providers and the public, and supporting demonstration and education research projects. Also, the NIAID website is heavily utilized as a reliable source of health information. However, strengthening and expanding our efforts is needed in order to produce health information that is culturally appropriate and to ensure that the information is disseminated to the appropriate communities. Developing methods to assess the effectiveness of these outreach and communication efforts is also critical.

Objective III.A.1. Support the National HIV Vaccine Trial Outreach as part of our interactions with minority populations.

NIAID will continue to implement a national HIV vaccine trial communication effort to increase public understanding of HIV vaccine research and to facilitate recruitment and retention of volunteers in vaccine trials. This effort is critically important to ensure that the participants in NIAID clinical trials programs represent the affected racial/ethnic populations.

Action Plan:

Steps:

1. Develop a broad-based, national, research-driven communications campaign with Ogilvy PR Worldwide
2. Develop messages through research, focus groups and national surveys
3. Build national community partnerships
4. Launch national education campaign
5. Collaborate closely with the HVTN and the NIAID National HIV Vaccine Communications Steering Group
6. Provide issues management support

Timeline:

FY 2002-2003
- Continue the contract with Ogilvy Public Relations Worldwide

FY 2004-2006
- Release new or expansion HIV vaccine outreach initiatives, as appropriate

Performance Measures:
- Completion of research component of communications campaign
- Launch of public awareness campaign

Outcome Measures:
- Increased support for HIV vaccine research in "at risk" communities
- Successful recruitment and retention of vaccine study volunteers

Objective III.A.2. Support programs that will help reduce disparities by improving donor matching for organ transplantation through donor outreach programs.

Outreach is an essential complement to biomedical research in the effort to improve matching of donated organs with patients who need them. NIAID continues to support demonstration and education research projects to increase minority involvement in organ donor registries. In Louisiana, the Legacy Donor Registry continues its efforts to increase organ donation by: expanding the range of the current registry with new and non-traditional approaches to increasing organ donor recruitment; improving the consent process to enhance organ donations; and facilitating the medical community's access to donor registry information. The Legacy Donor Registry began its Corporate Donor Program in 2000 and has conducted organ donation awareness events that reach major corporations and employers in Louisiana.

The NIAID also continues to support the demonstration and education research project at the Hope Heart Institute to evaluate the effectiveness of a unique community-based outreach network to increase organ donation among minority populations in Seattle and Tacoma, Washington. This project involves: (1) the development and distribution of educational materials in local neighborhoods and churches, using the services of VISTA volunteers recruited from targeted African American and Asian communities; (2) the production of an educational video for local communities and schools; (3) public service announcements at Department of Motor Vehicles offices; and (4) the development of a computerized database of community residents to record donation preferences, educational levels, and medical histories.

A second research project of the Hope Heart Institute aims to increase organ donation among rural Alaskan Natives. Culturally sensitive educational materials and community health education programs are being developed on transplant options, and living and cadaveric organ donation for this population, including: an educational video featuring Alaskan Native transplant recipients and donor families; an attitudinal survey; and regional training for Native Corporation local health educators, community health aides, local school teachers, and regional hospital staff.

Action Plan:

Steps:
1. Support donor registries to increase awareness of organ donation among minority groups.

Timeline:

FY 2002
- Support **demonstration and education research projects** to increase minority involvement in organ donor registries.
  - **Legacy Donor Registry** project, in Louisiana, increases minority involvement in organ donor registries by using new and non-traditional approaches for organ donor recruitment.
  - **Hope Heart Institute** projects:
    - Evaluate a unique community-based outreach network to increase organ donation among minority populations in Seattle and Tacoma, Washington.
    - Evaluate the effectiveness of culturally sensitive educational materials and community health education programs to increase organ donation among rural Alaskan Natives.

FY 2003
- Continue to support the Legacy Donor Registry project.
- Disseminate findings from evaluation of the Hope Heart Institute projects.

FY2004-2006
- Continue to support the Legacy Donor Registry project.

Performance Measures
- Increases in minority organ donation (Legacy Donor Registry)
- Development of educational materials to increase organ donation awareness among minority populations (Hope Heart Institute projects)

Outcome Measures
- Publication of findings on effective means to increase organ donation in minority populations
- Dissemination of education materials that build on lessons learned in by the Legacy Donor Registry and the Hope Heart projects

***Objective III.A.*3.: Improve the access of racial and ethnic minorities to tuberculosis clinical trials.**

The objective of this program is to establish relationships with community-based, public health, and hospital-based clinics in the Washington, D.C., metropolitan area that are treating patients with tuberculosis to facilitate participation of these clinics in future NIAID Division of Intramural Research basic studies and clinical trials.

Action Plan:

Steps

1. Maintain liaison with community-based, public health, and hospital-based clinics.
2. Collect prospective data from these facilities on a yearly basis from available records to better characterize the ongoing epidemic of TB in the locality of these facilities and the greater metropolitan area.
3. Assess the needs of these clinics and hospitals to determine what resources are needed to enable these facilities to participate in this project and provide a plan to overcome any barriers to participation.
4. Develop informational materials to assist in recruiting.
5. Recruit patients into TB clinical trials.

Timeline

This program began in 1999 and is slated to run through 2005.

FY2002

- Maintain liaisons in 1-6 hospital or public health department-based clinics that are diagnosing and treating at least 3 new cases of TB per month and 1-3 community based clinics that are diagnosing and treating at least 1 new case of TB per month. These facilities must be willing to participate in DIR investigation of TB.
- Collect prospective data from these facilities on a yearly basis from available records to better characterize the ongoing epidemic of TB in the locality of these facilities and the greater metropolitan area. Include reporting of TB incidence in the catchment area; factors associated with successful and unsuccessful TB treatment in these facilities; and factors associated with the development and diagnosis of multi-drug resistant TB in these facilities.
- Develop informational brochures appropriate for patient and physicians populations at the participating facilities.

FY2003-2005

- Maintain liaisons in hospitals, public health department-based clinics, and community-based clinics.
- Continue collecting prospective data from these facilities on a yearly basis.
- Facilitate patient recruitment for clinical studies conducted by DIR and provide clinical material, clinical data, and epidemiologic data for both basic and clinical research studies.
- Arrange periodic meetings (approximately one every three months) with key staff of participating facilities to discuss program progress and any specific areas needing direction or attention.
- Maintain social work and community outreach programs to facilitate patients' ability to participate in NIAID DIR programs. Services must include collecting clinical and research specimens in the field and the ability to monitor and report on directly observed therapy. Programs may include transportation of patients from their homes to NIH and identification of incentives for study participants, such as daycare provision and provision of meals.
- Provide laboratory and diagnostic tools for the identification of *Mycobacterium tuberculosis* from clinical specimens.

- Convene an annual one-day meeting of program contractor, participating clinics and hospitals, participating NIH intramural scientists and other key personnel for discussion and sharing of the progress and intended direction of the program.

Performance Measures:
- Number of sites participating in program.
- Establishment of patient services to promote patient participation.
- Number of brochures distributed.

Outcome Measures:
- Increased enrollment of ethnic and racial minorities in DIR TB clinical trials using 1999 as the base year.

Objective III.A.4. Support new and maintain established partnerships with agencies, organizations, and advocacy groups that have minority health agendas, in order to maximize the impact of NIAID activities to address health disparities.

NIAID frequently partners with other NIH institutes and centers, sister HHS agencies, non-governmental organizations (NGOs), and industry in order to coordinate research and outreach activities and to amplify the potential impact of NIAID efforts. The following examples from just two disease areas, asthma and tuberculosis, illustrate NIAID's use of partnerships.

NIAID's Inner City Asthma Study was co-funded by the National Institute of Environmental Health Sciences and the Environmental Protection Agency jointly funded a sub-study under that initiative. Also in the area of asthma, NIAID collaborated with NHLBI, Synermed Communications, the American Lung Association, and the American Academy of Family Practice (AAFP), to develop continuing medical education (CME) materials for primary care physicians on topics including asthma, sinusitis, otitis media, and allergic rhinitis.

The activities of the NIAID support Tuberculosis Research Unit (TBRU) at Case Western Reserve University are coordinated with other major organizations involved in TB research, including the CDC, USAID, FDA, WHO, Global Alliance for TB Drug Development and International Union Against Tuberculosis and Lung Disease, and with interested industrial partners. Also the NIAID Program Announcement "Collaborations for Advanced Strategies in Complications of HIV Infection" is co-sponsored with four other NIH institutes -- the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Drug Abuse, the National Institute of Alcohol Abuse and Alcoholism, and the National Institute of Mental Health.

Action Plan:

<u>Steps</u>
1. Invite other NIH institutes and centers or scientific organizations with similar research agendas to participate in the IBRP via guest lecturers and extending student one-on-one sessions with members of their scientific staff.
2. Seek input from program staff to identify appropriated organizations and societies.

3. Maintain existing partnerships

Timeline

FY 2002
- Enter discussions with at least one institute or scientific organization, i.e. American Chemistry Association, to establish a scientific guest lecturer as part of our IBRP seminar sessions and one-on-one sessions with scientific staff.
- Maintain existing partnerships

FY 2003-2006
- Expand the IBRP one-on-one sessions to include one or two other NIH institutes/centers.
- Continue with an institute/center or scientific organization guest lecturer in the seminar sessions.
- Maintain existing partnerships

Performance Measures:
- Scientific guest lecturer incorporated into IBRP seminar segment.
- One-on-one interface sessions with other institutes and/or scientific organizations.
- Co-sponsorship of initiatives, meetings, and workshops

Outcome Measures:
- Views and opinions of IBRP participants regarding the quality of the IBRP experience.
- Complementarity of activities across NIH, DHHS, and the Federal government
- Complementarity of activities among the Government, NGOs, and industry

Objective III.A.5. NIAID will continue to seek input and participation from diverse groups on its National Advisory Allergy and Infectious Diseases Council (NAAIDC), as well as ad hoc Community Advisory Boards, Blue Ribbon Panels, and scientific workshops, in order to maximize and improve it's health disparity agenda.

Action Plan:

Steps

1. Seek input from NAAIDC regarding NIAID plans to address health disparities.
2. Seek input from NIAID standing review committees and other *ad hoc* groups regarding NIAID plans to address health disparities.

Timeline

FY 2002

- Present NAAIDC with NIAID's Comprehensive Strategic Plan on Health Disparities and seek comments.
- Present NIAID standing review committees and other *ad hoc* groups with NIAID's Comprehensive Strategic Plan on Health Disparities and seek comments.

FY 2003-2006

- Utilize input and comments from NAAIDC, NIAID standing review committees, and *ad hoc* groups to improve NIAID's Comprehensive Strategic Plan on Health Disparities.
- Continue to seek input from NAAIDC, NIAID standing review committees, and *ad hoc* groups on matters pertaining to health disparities.

Performance Measures:

- Substantive input, comments, and recommendations from NAAIDC, NIAID standing review committees, and *ad hoc* groups, on NIAID's Comprehensive Strategic Plan on Health Disparities.

Outcome Measures:

- Revisions to the NIAID Health Disparities Strategic Plan and implementation of initiatives based on revisions to the Plan.

Objective III.A.6 Support participation of NIAID scientists in the presentation of information to audiences in minority communities and expand the translation and dissemination of health information materials to high-risk populations, as part of our institute's efforts to reach minority populations.

In 1998, NIAID Intramural Staff located in our Rocky Mountain Laboratories (RML) in Montana began on outreach program for local public schools. In 2000, RML expanded the program to schools located in Native-American communities. The Biomedical Research After School Scholars (BRASS) is designed to communicate the nature of scientific research and to stimulate interest in science careers among students in junior high and middle schools. The typical BRASS course runs for 5 weeks and consists of lab sessions covering topics such as blood, genetics, cancer, AIDS, infectious diseases and animal research.

For about a decade, NIAID has written and published biennial pamphlets on minority health research (A Partnership for Health) and women's health research (Women's Health in the U.S.). This pair of pamphlets sets forth the latest statistics on health disparities related to immunology and infectious diseases, highlights recent scientific findings of particular concern to minorities and women, and articulates research plans and priorities. These documents are key tools in NIAID's effort to reach out to minority communities with information on biomedical research that is of special interest to those populations. Both are distributed to outside organizations, at scientific meetings, and the general public.

The NIAID National Cooperative Inner City Asthma Study (NCICAS, 1991-96) developed a highly successful asthma intervention. This educational and behavioral intervention is delivered by an asthma counselor and has been shown to reduce symptoms and hospitalizations in inner-city children with moderate to severe asthma. Recently, NIAID collaborated with the CDC to launch a program to disseminate and implement the intervention. NIAID-funded scientists translated the complex NCICAS research intervention into a form that can be efficiently utilized in a variety of health care delivery settings, including health maintenance organizations (HMOs), health departments, and community clinics. Now, NIAID is working with CDC to disseminate the Asthma Treatment Guidelines. The 4-year program targets children with moderate to severe asthma living in inner cities and is being implemented through 23 inner-city health care organizations throughout the U.S. More than 6,000 inner-city children with asthma will benefit from the effort.

Action Plan:

Steps

1. Expand outreach by NIAID Intramural Staff located in our Rocky Mountain Laboratories in Montana to public schools located in Native-American communities.
2. Continue to publish and disseminate NIAID's minority and women's health pamphlets.
3. Collaborate with CDC to disseminate the asthma intervention guidelines developed and tested by the Inner-City Asthma Study.

Timeline

FY 2002

- Conduct of "introduction to science sessions" in Montana public schools.
- Update and published the Partner for Health and Women's Health in the U.S. pamphlets. Incorporate requirements of Section 508 of the Rehabilitation Act into the web-based display of these documents.
- Support dissemination of the asthma intervention guidelines.

FY 2003-2006

- Continue the outreach to Montana Public schools by RML scientists.
- Continue to update pamphlets on a bi-annual basis, FY 2004 and FY 2006.
- Continue outreach efforts to Native American students in the Montana public school system.

Performance Measures:

- Publication of updated versions of the pamphlets "Partnership for Health" and "Women's Health in the U.S.," as well as provision of Section 508 compliant versions of the pamphlets on the NIAID website.
  - Number of copies of each pamphlet distributed.
  - Range of venues in which the pamphlets are distributed.
- Number of outreach sessions targeted to Native Americans in Montana Public Schools by RML staff.
- Number of copies of the Asthma Treatment Guidelines disseminated..

Objective III.A.7. NIAID will continue to support internet-based methods of communication and audiovisual materials to disseminate health information to persons subject to health disparities..

NIAID's web site provides a wealth of health information useful to persons subject to health disparities. Equally important, the site includes research plans and links for people seeking to participate in clinical trials.

Action Plan:

Steps

1. Establish a standards committee to formulate the re-design of the NIAID website and establish standards for publication in both print and electronic media .
2. Regularly review the content of the NIAID website for opportunities to enrich and supplement content.
3. Incorporate requirements of Section 508 of the Rehabilitation Act into the web-based display of NIAID publications.

Timeline

FY 2002
- Develop a more subject-oriented and user-friendly website
- Develop a publication standards guide to be used in the development of Institute printed and film media.
- Explore software to make the NIAID website to become Section 508 compliant.

FY 2003-2006
- Begin the re-design of the NIAID website based on new standards.
- Develop a publication standards guide to be used in the development of Institute printed and film media.
- Make the NIAID website Section 508 compliant.

Performance Measures:
- Completion of NIAID website re-design
- Compliance with Section 508.
- Prominence of Minority and Women's health issues on website.
- Completion of Publications and Media Standards Guide
- Dissemination of the Publications and Media Standards Guide

Outcome Measures:
- Number of hits on NIAID website locations pertinent to health disparities
- Compliance of website and printed materials with Standards Guide

NIAID Health Disparities Budget
(Dollars in Millions)

Institute / Center	FY 2002			FY 2003		
	Research	Infrastructure	Outreach	Research	Infrastructure	Outreach
NIAID	$534.20	$19.80	$105.50	$602.40	$22.40	$119.10