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NIAID Global Research:
Improving Health in a Changing World
Foreword

Although infectious diseases have always affected humankind, increasingly we have come to appreciate how infections that emerge even in remote parts of the globe can spread quickly to affect health, security, and economic stability throughout the entire world. While medical science and public health campaigns have greatly reduced or eliminated certain diseases such as polio and smallpox, other diseases such as influenza and emerging forms of drug-resistant tuberculosis remind us that the struggle against infectious diseases continues. In this regard, continuing vigilance and an ongoing commitment to biomedical research is required for the development of appropriate tools for diagnosis, treatment, and prevention of emerging threats.

The recognition of HIV/AIDS approximately 30 years ago signaled the beginning of a new era in global health. Although first diagnosed in the United States, HIV/AIDS soon was found in populations throughout the world—with the highest infection rates in developing countries. Today, an estimated 33 million people are infected with HIV. Of these, more than 90 percent live in low- and middle-income countries.

As governments, nongovernmental organizations, and philanthropic entities have responded to the HIV/AIDS crisis, attention also has begun to focus on many other devastating diseases that afflict people in poorer nations, often in tandem with HIV/AIDS. For example, tuberculosis killed approximately 1.7 million people in 2009, 380,000 of whom also were infected with HIV. An estimated 225 million cases of malaria occurred in 2009, resulting in more than 780,000 deaths. Parasitic diseases such as schistosomiasis, leishmaniasis, trypanosomiasis, and filariasis, while rare or eliminated in many wealthier nations, continue to cause severe illness, disability, and death each year among millions of people worldwide.

Recently, the world again experienced the direct impact of a rapidly spreading, emerging infectious disease when the pandemic 2009 H1N1 influenza virus infected people in more than 214 countries and territories. A concerted global public health response resulted in the development and distribution of safe and effective vaccines that protected millions of people. Furthermore, in the past year, outbreaks of cholera, dengue fever, polio, plague, and meningococcal disease have occurred in many parts of the world, particularly where public health systems do not have adequate resources to deliver preventive and medical services. Finally, the danger of a sustained outbreak of H5N1 influenza (bird flu) among humans still remains.

To meet such challenges, NIAID has for more than six decades supported research to better understand, treat, and prevent infectious diseases of global health importance. We have been privileged to enjoy the generous support of the American people, Congress, and presidential administrations. Of note, President Obama recently launched the Global Health Initiative (GHI), which recognizes that public health is an essential component of international economic and social stability. The GHI gives particular attention to the welfare of women and girls, and its prevention and care strategies rely in part on knowledge derived from research supported by the National Institutes of Health (NIH). Several GHI target areas—HIV/AIDS, tuberculosis, malaria, and neglected tropical diseases—are key foci of the NIAID research program.
Anthony S. Fauci, M.D.

NIAID and our sister agencies at NIH contribute to the GHI through continuing support of research that provides the knowledge and tools needed to make real improvements in disease prevention, control, and treatment. Much has been accomplished in recent months. In one important study, NIAID-supported investigators demonstrated that a daily dose of an oral antiretroviral drug approved to treat HIV infection could reduce the risk of HIV acquisition among men who have sex with men. In other HIV prevention research, scientists sponsored by the U.S. Agency for International Development found that women using a vaginal microbicide gel containing an antiretroviral drug were less likely to become infected with HIV than women receiving a placebo gel. Both of these studies used the extensive research and training infrastructure established by NIAID.

These and similar studies are possible when governments and academic institutions work with research organizations such as NIAID to enhance and sustain local laboratory and clinical research capacity. Many countries now recognize biomedical and infectious disease research as an engine of economic growth and improved public health. Therefore, they are increasingly investing in the hiring and training of local workers and collaborating with NIAID and other scientific organizations.

NIAID remains deeply committed to supporting international research partnerships that are mutually beneficial and scientifically productive. For example, in 2009, representatives from NIAID and China’s Henan Provincial Bureau of Health signed an implementation arrangement to foster research on tuberculosis, including clinical research on new treatments for multidrug-resistant tuberculosis.

NIAID also recently established the International Centers of Excellence for Malaria Research program to expand basic and clinical research capacity in malaria-endemic areas. NIAID views international research and partnerships as fundamental to its mandate and essential for global efforts to manage, control, and eliminate infectious diseases. In addition to infectious disease challenges, NIAID-supported investigators continue to pursue research opportunities to reduce the global burden of immune-mediated diseases, including autoimmune disorders and allergy and asthma.

We celebrate our successes, while acknowledging the enormous challenges that lie ahead. Global health research is a priority for NIAID, and we are confident that our sustained cooperative efforts will continue to help improve the health of citizens throughout the world.

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
About NIAID

The National Institute of Allergy and Infectious Diseases (NIAID) is one of the 27 institutes and centers that constitute the National Institutes of Health (NIH), an agency of the U.S. Department of Health and Human Services (HHS). NIAID is one of the largest institutes at NIH, with an operating budget of approximately $4.5 billion in fiscal year 2010. More than 11 percent of the NIAID operating budget supports international research and training, and NIAID is one of the few NIH institutes to have an Associate Director for International Research Affairs to facilitate international activities.

As with other large NIH institutes, most of the NIAID budget supports biomedical research at academic and research institutions outside NIAID through grants, contracts, and cooperative agreements (called extramural research). The remaining budget funds research within NIAID’s own laboratories (called intramural research) and supports administrative functions.

NIAID Extramural Research

Extramural research is managed by the following NIAID divisions:

- **Division of Acquired Immunodeficiency Syndrome**—supports research aimed at improving basic understanding, prevention, and treatment of HIV/AIDS and its complications and co-infections.

- **Division of Allergy, Immunology, and Transplantation**—supports research on basic immunology and the etiology, treatment, and prevention of immune-mediated conditions, including autoimmune diseases; asthma and allergic diseases; and the rejection of transplanted organs, tissues, and cells.

- **Division of Microbiology and Infectious Diseases**—supports research to control and prevent diseases caused by virtually all human infectious agents except HIV; major priorities include emerging and re-emerging infectious diseases and biodefense.

- **Division of Extramural Activities**—serves NIAID and its extramural research community by overseeing policy and management for grants and contracts, managing NIAID’s research training and international programs, and conducting initial peer review of grant applications.

NIAID supported biomedical research in more than 100 countries during fiscal year 2010.
NIAID Intramural Research

Most NIAID intramural laboratories are located on the NIH campus in Bethesda, Maryland, and in nearby Rockville, Maryland. NIAID also has a large research campus in Hamilton, Montana, known as the Rocky Mountain Laboratories, and research collaborations at sites in Mali, Uganda, India, and many other countries.

The NIAID intramural program includes the following divisions:

- **Division of Intramural Research**—conducts basic and clinical research in a wide range of disciplines related to immunology, allergy, and infectious diseases. Its global activities include HIV, malaria, and dengue vaccine development; research to develop better therapies for tuberculosis; and lab and field research on neglected tropical diseases, such as filariasis and leishmaniasis.

- **Dale and Betty Bumpers Vaccine Research Center**—conducts research that facilitates the development of effective vaccines for human disease. Its global activities include studies on HIV, Ebola and Marburg viruses, and avian influenza.

- **Division of Clinical Research**—facilitates the efficient performance of NIAID clinical research programs in the United States and abroad. Its global activities include support for research projects in Mali, Mexico, South Africa, and Southeast Asia.

NIAID Office of Global Research

The Office of Global Research (OGR), within the NIAID Office of the Director, facilitates and coordinates international activities and collaborative research programs. OGR works closely with other NIH institutes and centers such as the Fogarty International Center and with other offices and agencies of HHS, including the Office of Global Health Affairs within the Office of the Secretary, the Centers for Disease Control and Prevention, and the Food and Drug Administration. OGR also collaborates with other U.S. government agencies, such as the Department of State and the Agency for International Development, and with numerous foreign government agencies.

**Online Resources**

- NIAID Organization [www.niaid.nih.gov/about/organization](www.niaid.nih.gov/about/organization)
- NIAID Director’s Page [www.niaid.nih.gov/about/directors](www.niaid.nih.gov/about/directors)
- NIAID Global Research [www.niaid.nih.gov/topics/globalresearch](www.niaid.nih.gov/topics/globalresearch)
- Office of Global Research [www.niaid.nih.gov/about/organization/odoffices/omo/ogr](www.niaid.nih.gov/about/organization/odoffices/omo/ogr)
- Division of Acquired Immunodeficiency Syndrome [www.niaid.nih.gov/about/organization/daids](www.niaid.nih.gov/about/organization/daids)
- Division of Allergy, Immunology, and Transplantation [www.niaid.nih.gov/about/organization/dait](www.niaid.nih.gov/about/organization/dait)
- Division of Clinical Research [www.niaid.nih.gov/about/organization/dcr](www.niaid.nih.gov/about/organization/dcr)
- Division of Extramural Activities [www.niaid.nih.gov/about/organization/dea](www.niaid.nih.gov/about/organization/dea)
- Division of Intramural Research [www.niaid.nih.gov/about/organization/dir](www.niaid.nih.gov/about/organization/dir)
- Division of Microbiology and Infectious Diseases [www.niaid.nih.gov/about/organization/dmid](www.niaid.nih.gov/about/organization/dmid)
- Vaccine Research Center [www.niaid.nih.gov/about/organization/vrc](www.niaid.nih.gov/about/organization/vrc)
NIAID’s International Involvement:
Taking the Lead To Improve Global Health Research

Issues related to global health have captured the attention of world leaders, philanthropists, policy makers, academia, and the general public. Developed nations have realized that disease outbreaks in distant countries can have worldwide social, economic, and political ramifications. This heightened awareness has presented a welcome opportunity for those in biomedical research and public health to emphasize international collaboration and promote new and existing global health programs.

NIAID has embraced its leadership role in global health with innovative scientific research programs that seek to not only advance knowledge of ever-changing pathogens, but also help translate new scientific discoveries into medical tools that improve diagnosis, prevention, and treatment of infectious diseases.

NIAID accomplishes its mission by fostering collaborations between domestic and international scientists and by supporting development of research capacity in regions with high burdens of disease. Through partnerships with academia, private industry, philanthropic organizations, and other research-supporting agencies, NIAID helps guide and enhance medical research that improves the quality of human life around the world.
ICER Program Fosters Research Collaborations in Developing Countries

The NIAID International Centers for Excellence in Research (ICER) program was launched in 2002 to develop and sustain research programs in resource-poor countries through partnerships with local scientists. NIAID has developed core programs at the ICER sites—currently located in Mali, Uganda, and India—and, over time, has facilitated the expansion of research capacity by training young scientists, improving laboratory and clinical infrastructure, and enhancing information technology capabilities.

The ICER program builds on experience gained from NIAID’s long-standing malaria research collaboration with scientists in Mali. Initially, the collaboration focused on the genetics of malaria mosquitoes, but it has expanded significantly over the years.

Today, Malian researchers collaborate with NIAID scientists on multiple projects, including studies on mosquito vectors, malaria drug resistance, and candidate malaria vaccines; research on neglected tropical diseases such as filariasis and leishmaniasis; and immunologic and microbiologic studies of patients co-infected with HIV and tuberculosis. NIAID and Malian colleagues have recently initiated research programs on relapsing fever and Lassa fever.

The ICER site in Uganda, which includes a state-of-the-art field laboratory in the Rakai District and facilities at Makerere University in Kampala and the Uganda Virus Research Institute in Entebbe, conducts basic and clinical research on HIV and sexually transmitted infections, including studies on viral pathogenesis, transmission kinetics, treatment, and prevention. The ICER site in India, located at the Tuberculosis Research Centre in Chennai, conducts collaborative studies on filariasis and, more recently, on tuberculosis-filarial and HIV-filarial co-infections.
Since its recognition in 1981, AIDS has claimed approximately 30 million lives, the majority of them in the developing world. While extraordinary scientific, medical, and public health accomplishments have been made in the battle against HIV/AIDS, major challenges remain, especially in the delivery of therapies and prevention tools to the resource-poor countries that need them the most.

NIAID played an important role in the design and early implementation of the President’s Emergency Plan for AIDS Relief and continues to serve as a scientific partner for that program. NIAID has led much of the research that supports the program, engaging scientists from all parts of the world and many U.S. biomedical and public health research institutions.

NIAID’s investment in HIV/AIDS research has generated promising findings in preventing and treating HIV/AIDS and in advancing scientific understanding of the disease. In 2010, a study cosponsored by NIAID and the Bill & Melinda Gates Foundation and conducted at 11 sites in Brazil, Ecuador, Peru, South Africa, Thailand, and the United States found that a daily dose of an oral antiretroviral drug approved to treat HIV infection reduced the risk of HIV acquisition among men who have sex with men by 44 percent. The study, known as iPrEx, found even higher rates of effectiveness, up to 73 percent, among study participants who adhered most closely to the daily drug regimen. This landmark finding followed closely on the heels of another breakthrough international study, CAPRISA 004, which found that the use of a microbicide gel containing a 1 percent concentration of the antiretroviral drug tenofovir resulted in 39 percent fewer HIV infections compared with a placebo gel. NIAID was among the organizations that provided substantial support and resources to establish the infrastructure and training for the Centre for the AIDS Programme of Research in South Africa, which conducted the study. Ongoing and future clinical trials will build on these study results with the goal of bringing a safe and effective microbicide to the general public.

Conducting AIDS research in international settings allows NIAID-supported scientists to study the disease under a variety of environmental and social conditions. For example, the NIAID-funded HIV Prevention Trials Network (HPTN) comprises more than 20 clinical sites in the United States, Africa, Asia, and South America. HPTN evaluates the effectiveness of multiple HIV prevention strategies—from the use of antiretroviral therapy to prevent HIV and other sexually transmitted infections to community education and counseling—in different populations to better understand and ultimately control the spread of HIV on a global scale.
Clinical Trials Network Evaluates Microbicides To Reduce Spread of HIV

Women and girls account for half of all people living with HIV, according to UNAIDS estimates. In 2009, HIV/AIDS was the leading cause of disease and death among women between the ages of 15 and 44. Globally, the vast majority of women with HIV/AIDS became infected through heterosexual intercourse, frequently in settings where refusing to have sex or insisting on condom use is not an option because of cultural factors, lack of financial independence, and even the threat of violence.

In response to these and other issues, NIAID established the Microbicide Trials Network (MTN) in 2006 to develop and evaluate products that could be applied topically by women to prevent infection with HIV and other sexually transmitted agents. Safe and effective microbicides would give women the ability to protect themselves when negotiating with sexual partners is difficult or impossible.

The MTN conducts its multicenter studies at sites in Malawi, South Africa, Uganda, Zambia, Zimbabwe, India, and the United States. Its international trials include the Vaginal and Oral Interventions to Control the Epidemic (VOICE) study, which compares the safety and effectiveness of a microbicide to pre-exposure prophylaxis (PrEP), another experimental approach to HIV prevention. PrEP involves administering antiretroviral drugs to uninfected people who are at high risk of HIV infection. Like microbicides, PrEP is viewed as a potential HIV prevention method that women can use independently and proactively. VOICE will evaluate these experimental approaches in 5,000 women at sites in South Africa, Uganda, Zambia, and Zimbabwe.

The MTN is structured to allow for active representation and participation by community stakeholders in every stage of clinical study development and implementation. In addition to including a community representative on its executive committee, the MTN has established a Community Working Group (CWG), comprising one Community Advisory Board member and one community educator from each site. The CWG aims to ensure the successful conduct of studies through community and researcher partnerships and to build capacity within local communities for providing input into the planning and conduct of MTN trials.

As part of its effort to be more responsive to the needs and perspectives of local communities, the MTN also has adopted the Regional Physician Model, a successful component of the Bill & Melinda Gates Foundation-funded Partners in Prevention. Regional physicians are the MTN’s local ambassadors in Africa, providing support to clinical sites and educating local providers and community groups about microbicide research, MTN-specific trials, and safety measures designed to protect all trial participants.
Scientists have made extraordinary progress toward containing or nearly eliminating many infectious diseases, such as diphtheria, tetanus, polio, and measles. Despite these advances, the world still faces numerous threats from new microbes that emerge naturally and from familiar pathogens that re-emerge with enhanced properties or in unusual settings. Tuberculosis, including drug-resistant forms, and influenza viruses with pandemic potential are of particular concern.

NIAID research programs combating these threats emphasize collaborations with domestic and international partners to improve knowledge; stimulate the pipeline of new drugs, diagnostics, and preventive measures; and enhance existing research infrastructure to effectively confront outbreaks where they occur.

Tuberculosis

In 2009, an estimated 9.4 million new cases of tuberculosis (TB) were reported worldwide, and an estimated 1.7 million people died of the disease. Antiquated techniques for diagnosing TB, complex drug regimens, an increase in the prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains of Mycobacterium tuberculosis, and the interplay between TB and HIV/AIDS continue to present major challenges to effective TB control.

NIAID TB research programs include domestic and international efforts to develop new tools and strategies to help control TB. NIAID is leading and sponsoring research activities to create a foundation of knowledge for the discovery of new diagnostics, drugs, and vaccines for drug-resistant and drug-sensitive TB. Many of these programs are providing critical information to advance our scientific understanding of TB.
For example, a recent clinical study of a TB diagnostic that was developed through a public-private partnership with NIAID support showed that the test provides highly accurate and much more rapid results than what is possible with current TB diagnostics. In the study of 1,730 patients with suspected drug-sensitive or MDR pulmonary TB, the Cepheid Xpert MTB/RIF TB test success fully identified 98 percent of all confirmed TB cases and 98 percent of patients with rifampin-resistant bacteria in less than 2 hours. These results were achieved directly from patient samples without the need to first culture or visualize the bacteria. NIAID continues to support expansion of this technology to detect other resistance markers for XDR TB.

Other diagnostic tests initially supported through NIAID small-business grants are now being considered for rollout in countries with high burdens of TB. To further improve the pipeline of new TB diagnostics, NIAID recently established the TB Clinical Diagnostics Research Consortium (CDRC), which will assist in the clinical evaluation of early-stage TB diagnostic tests and with strategies in countries where TB is a public health concern.

NIAID also supports preclinical and clinical development of promising new TB drugs. SQ109, an anti-TB drug candidate initially identified through a partnership between NIAID intramural laboratories and the biopharmaceutical company Sequella, currently is being evaluated in early-stage clinical trials through NIAID extramural support. Other drug candidates and new combinations such as PA-824 and fluoroquinolone antibiotics have been supported through NIAID’s preclinical development resources and animal model services.

U.S.-South Korean Collaboration Seeks To Advance TB Care

In 2003, NIAID scientists and clinical researchers at South Korea’s National Masan Tuberculosis Hospital joined forces to develop potential new drug regimens for effective TB treatment and to identify new rapid means of diagnosing drug resistance. The hospital is the national referral center for TB treatment failures in South Korea and has one of the largest numbers of in-patient MDR TB cases in the world.

The United States and South Korean researchers have conducted numerous research studies and have more than 800 patients participating in clinical trials. Trials of existing drugs in patients with highly drug-resistant TB are ongoing using PET/CT imaging technologies. In addition, researchers are collecting information about rates and causes of MDR and XDR TB in two groups of patients: those who are having an initial episode of active TB and those who have recurrent TB. Investigators also are studying the human and M. tuberculosis genomes to further understand the relationship between the expression of specific bacterial and human genes and the acquisition and development of XDR TB infection. More than 10 manuscripts describing these studies were published in 2010.

Other scientists have been drawn to collaborate with the successful South Korean center. For example, a consortium of five groups with funding from the Bill & Melinda Gates Foundation is attempting to define correlates of response to TB therapy that may prove useful in determining the point at which cessation of drug therapy does not pose a risk of disease reactivation. Additionally, NIAID scientists and researchers from the University of Cape Town, South Africa, with funding from the Wellcome Trust, are using advanced imaging techniques to attempt to understand the development and containment of latent TB disease using paired clinical studies in South Africa and South Korea.

IN 2009, AN ESTIMATED 9.4 MILLION NEW CASES OF TB WERE REPORTED WORLDWIDE, AND AN ESTIMATED 1.7 MILLION PEOPLE DIED OF THE DISEASE.
Malaria continues to pose an enormous global health burden, particularly in countries in tropical and subtropical regions. The World Health Organization (WHO) estimates that in 2009 there were 225 million cases of malaria worldwide. That same year, more than 780,000 people, mostly young children in Africa, died from the disease.

NIAID has a longstanding commitment to malaria research and supports global efforts to reduce death and suffering from the disease. NIAID works closely with organizations such as the U.S. Agency for International Development, WHO, the European Malaria Vaccine Initiative, the Program for Appropriate Technology in Health Malaria Vaccine Initiative, the Wellcome Trust, and the Bill & Melinda Gates Foundation. Additionally, NIAID has joined with the NIH Fogarty International Center, the National Library of Medicine, and other institutions to form the Multilateral Initiative on Malaria, whose mission is to enhance worldwide research on malaria by facilitating multinational cooperation and by supporting the career development and research efforts of African scientists working in malaria-endemic areas.

Such collaborations have yielded notable successes. For example, NIAID-supported scientists have sequenced the genomes of the malaria parasites *Plasmodium falciparum* and *Plasmodium vivax* as well as *Anopheles gambiae*, the mosquito species that is the primary vector of malaria in Africa. These and similar studies promise to reveal potential new targets for drug and vaccine development.

In Malawi, NIAID-funded research has suggested that chloroquine, the once-standard medication for preventing and treating malaria, may again be effective in that country, thanks to the reduced prevalence of the genetic mutation responsible for parasitic resistance to the drug. This finding may
eventually lead to low-cost chloroquine being reintroduced in parts of Africa for use in combination with other drugs. NIAID also supports discovery and development of new antimalarial drugs, through investigator-initiated research and collaborations with public-private partnerships. For example, NIAID recently funded the preclinical development of the drug AQ-13, which may be effective against chloroquine-resistant parasites. This drug is now progressing through clinical trials.

Finally, NIAID remains committed to developing safe and effective vaccines for malaria. Several vaccine candidates that target different lifecycle stages of the malaria parasite are in development, including those designed to either destroy parasites in the bloodstream or inhibit parasites from infecting red blood cells. NIAID supports clinical trials of these and other vaccine candidates in malaria-endemic countries.

NIAID-Funded Centers Seek To Enhance Malaria Control

Malaria has been eliminated from many parts of the globe, yet approximately half of the world’s population remains at risk of contracting the disease. In July 2010, NIAID awarded funds to establish the International Centers of Excellence for Malaria Research (ICEMR), which form a network of independent research institutions in malaria-endemic regions of Africa, Asia, the Pacific Islands, and Latin America. These regions include some of the focus countries of the President’s Malaria Initiative, an effort that since 2005 has worked to fight malaria in the regions most affected by the disease.

The ICEMR program is based on the need for sustainable, multidisciplinary strategies to control malaria. The centers will integrate clinical and field approaches with laboratory-based immunologic, molecular, and genomic methods. They will adapt their research to changes in malaria epidemiology and emerging research needs as well as to opportunities within the specific regions. Findings are expected to help inform how new interventions and control strategies are designed and evaluated in the future.

The ICEMR program will support malaria research in more than 20 countries and will provide the knowledge, tools, and evidence-based strategies to support researchers working in a variety of settings, especially within governments and healthcare institutions. The program is expected to bring critical infrastructure to malaria-endemic regions and help build the needed training and research capacity to combat malaria around the world.
Seasonal influenza, caused by viruses that vary slightly from year to year, is a classic example of a re-emerging infectious disease. Influenza viruses also can undergo more dramatic genetic changes to cause outbreaks in humans who have no immunity or only limited pre-existing immunity. If these viruses spread from person to person, they can cause a pandemic, such as the 2009 H1N1 influenza pandemic, which is estimated to have killed more than 18,000 people worldwide.

NIAID supports a broad portfolio of influenza research, including studies that inform the development of vaccines, diagnostics, and therapeutics against both seasonal and pandemic influenza. For example, NIAID clinical trials provided information that became the foundation for the U.S. 2009 H1N1 immunization program that protected millions of people during the H1N1 pandemic. NIAID trial data offered key scientific evidence essential for public health decision making, including determining optimal dosage and number of doses for individuals in different age brackets and for specific high-risk groups such as pregnant women.

NIAID also helped initiate and conduct pediatric studies of the antiviral drug oseltamivir that provided critical data to the U.S. Food and Drug Administration for an Emergency Use Authorization of the drug against H1N1. This authorization allowed oseltamivir to be prescribed for the treatment of 2009 H1N1 influenza in children less than 1 year of age, providing treatment for those who were infected and protecting others by preventing the spread of disease. These data also were shared with international regulatory agencies and used to support the use of oseltamivir in infants around the world. The data gathered and experience gained from successfully responding to a pandemic will be invaluable for subsequent influenza research and for future pandemic preparedness efforts.

The South East Asia Infectious Disease Clinical Research Network (SEAICRN), cosupported by NIAID and the Wellcome Trust, brings together hospitals and institutions in Indonesia, Thailand, the United Kingdom, the United States, and Vietnam to advance scientific knowledge and clinical management of influenza and other infectious diseases. SEAICRN studies aim to improve patient care and help inform public health policy.
on the treatment of influenza and other emerging infectious diseases. The network also works with national ministries of health and other authorities to facilitate the sharing of samples of influenza viruses for research purposes.

NIAID-funded research projects and repositories are providing researchers around the world with vital data to help improve the understanding of how influenza viruses evolve, spread, and cause disease. For example, the NIAID Influenza Genome Sequencing Project helps scientists identify sequences in the influenza genome that could be potential targets for vaccines or therapies. To date, more than 6,000 complete influenza virus genomes have been sequenced and made available in the public domain.

Centers Expand Global Reach of Influenza Research and Surveillance

In 2007, NIAID established the Centers of Excellence for Influenza Research and Surveillance (CEIRS) to expand its worldwide influenza surveillance program and bolster influenza research in key areas, including understanding how the virus causes disease and how the immune system responds to infection with the virus. The goal of the CEIRS program is to provide essential information for the development of public health strategies crucial to both lessening the impact of seasonal influenza and responding to a pandemic.

Following the 2009 H1N1 influenza outbreak, the CEIRS sites quickly began work with the virus. Within 4 months, several important findings had been generated, providing essential information and basic characterization of the virus. The basic research performed by CEIRS investigators helped explain how a new influenza virus emerged; its pathogenicity, transmissibility, and susceptibility to antiviral agents; and what to expect during recurrences of pandemic virus circulation.

Current activities of the CEIRS program seek to expand the NIAID influenza virus surveillance program, both internationally and domestically, and to conduct research on the prevalence of avian influenza; how influenza viruses evolve, adapt, and are transmitted; and the immunological factors that influence the course of influenza infection. Some sites will continually monitor international and domestic cases of animal and human influenza to rapidly detect and characterize viruses that may have pandemic potential and to develop pandemic vaccine candidates. These activities help lay the groundwork for new and improved control measures for emerging and re-emerging influenza viruses.
Though of low prevalence in most of the United States, tropical diseases such as dengue fever, lymphatic filariasis, leishmaniasis, and schistosomiasis take a tremendous toll on global health. According to recent estimates, more than 1 billion people—one-sixth of the world’s population—suffer from at least one neglected tropical disease (NTD). These diseases tend to thrive among impoverished populations in developing regions of the world, where water quality, sanitation, and access to health care are substandard.

NIAID supports a robust program of research devoted to better understanding, preventing, and treating NTDs. Studies conducted and supported by NIAID have led to important new discoveries about the microbes that cause these diseases, the identification of targets for potential new drugs and vaccines, and the development of strategies for controlling the vectors that transmit NTD-causing agents to humans. For example, NIAID-supported investigators have sequenced the genomes of *Trypanosoma brucei*, *Trypanosoma cruzi*, and *Leishmania major*, the parasites that cause the diseases African sleeping sickness, Chagas’ disease, and leishmaniasis, respectively. Researchers also have sequenced the genome of *Aedes aegypti*, the mosquito species that transmits dengue and yellow fever. Currently, NIAID investigators are working on sequencing the genomes of two other important NTD vectors: the tsetse fly, which transmits *T. brucei* to humans, and the freshwater snail *Biomphalaria glabrata*, which transmits a parasite that causes schistosomiasis.

This new genetic information promises to help researchers design better ways to diagnose, treat, and prevent NTDs. The genome of *A. aegypti* is particularly important because the mosquito has become increasingly resistant to insecticides. Researchers hope that studies of the sequence will help them develop new methods of controlling the mosquito, such as genetically altering the species so that it is resistant to agents that cause disease.

Through its Partnerships with Public-Private Partnerships program and Tropical Disease Research Units, NIAID is actively supporting the discovery and development of treatments for parasitic tropical diseases. For example, researchers in these programs are developing a low-cost treatment for visceral leishmaniasis, the most severe form of the disease, and identifying new drugs for African sleeping sickness and Chagas’ disease. One drug, called K777, has recently completed early testing to evaluate its effect on *T. cruzi*, the Chagas’ disease parasite. K777 was found to be effective against the parasite in vitro and in vivo and is now moving into preclinical studies to further assess its safety and efficacy.

Recently, scientists supported in part by NIAID identified cellular components in mosquitoes and in humans that dengue viruses use to multiply inside both hosts. Their findings could lead to the development of drugs that would inhibit one or more of these components, thus limiting infection and the development of dengue fever. The search for anti-dengue therapies is vital, as no specific drugs or vaccines are available to fight dengue infection, which afflicts up to 50 million people worldwide each year.
Basic immunology is the foundation for much of the research being conducted on HIV/AIDS, malaria, tuberculosis, and other global infectious diseases. NIAID supports a wide variety of research projects on the immunology underlying infection and vaccination outcomes. For example, the Population Genetics Analysis Program is an international effort to identify genetic differences among individuals within a given population and relate these differences to disease severity or vaccine efficacy and adverse events. Diseases of interest among these investigators include cholera, typhoid, smallpox, anthrax, tuberculosis, and influenza.

Immunology also is vital in the fight against transplant rejection, autoimmune and allergic diseases, asthma, and other disorders of the immune system that cause chronic disease and disability on a global scale. NIAID supports and conducts basic and clinical immunology research to advance understanding of the mechanisms that underlie immune system disorders and to develop new strategies to detect, prevent, and treat them. For example, the NIAID Immune Tolerance Network, an international collaboration of more than 80 researchers, is making steady progress toward reducing the need for costly and potentially risky immunosuppressive drugs that are the current standard of care for many autoimmune disorders and for preventing rejection of transplanted organs and tissues. To date, more than 20 kidney and liver transplant recipients are surviving without immunosuppressive drugs, some for as long as 4 years.

NIAID also supports clinical trials in food allergy, including studies aimed at preventing the development of allergies to particular foods and reversing established allergies to milk, eggs, peanuts, and others. For instance, an Immune Tolerance Network study of children in the United Kingdom is exploring whether early-life exposure to peanuts will prevent the emergence of peanut allergy. Children enter the study between the ages of 4 and 10 months and, until they are 5 years old, they either avoid peanuts completely or eat a peanut snack three times a week. At the close of the study, children will be assessed for the occurrence of allergic disorders, including allergies to peanut and other foods, by clinical history and an oral peanut challenge.
NIAID funds biomedical research through various mechanisms such as grants, cooperative agreements, and contracts.

**Grants**

Grants are used to foster creative scientific research with minimal NIAID involvement. Cooperative agreements are types of grants NIAID uses to fund projects in which substantial NIAID scientific or programmatic involvement is needed to guide and coordinate the research.

Investigators need not be U.S. citizens to apply for select NIH research grants, including the following:

- **R01s**—support biomedical research and development based on the NIH mission
- **R03s**—support small research projects that can be carried out in a short period of time with limited resources
- **R21s**—encourage exploratory research projects by supporting the early and conceptual stages of development

Another opportunity for funding is the NIH Pathway to Independence Award (K99/R00), which is available to investigators with a clinical or research doctorate and no more than 5 years of postdoctoral research training at the time of application.

The K99/R00 does not require citizenship or permanent U.S. residency, but the applicant should have a visa that allows him or her to be in the country for the duration of the grant.

**NIAID IRIDA Program**

The NIAID International Research in Infectious Diseases including AIDS (IRIDA) Program solicits R01 applications from organizations/institutions in eligible foreign countries that propose research related to infectious diseases. NIAID funds up to 10 IRIDA grants each year to encourage the development of scientific expertise and research infrastructure and to increase collaborative research partnerships at NIAID-funded international sites.

Studies may be proposed for the IRIDA program on any aspect of infectious diseases (except clinical trials). The following are some examples:

- Epidemiology, pathogenesis, and immunopathogenesis of infectious diseases
- Identification of resistance patterns
- Characterization of susceptible cohorts for a particular pathogen
- Pilot and feasibility studies in preparation for larger studies
How To Apply for Grant Funding

Research funds are paid to institutions only, not to individual scientists. Foreign institutions must be registered with Grants.gov and with the NIH Electronic Research Administration Commons Web site prior to applying for NIAID or other NIH grants. It may take 4 to 6 weeks to complete the registration process, so interested institutions should start well in advance of the application due date.

Before applying, institutions should read current NIAID funding opportunity announcements and consider whether their projects fit within the NIAID mission. Successful grant applications often depend on collaborations. Scientists from foreign countries may find it helpful to partner with U.S. institutions when applying.

Contracts

NIAID uses contracts to purchase items it needs or to perform research and development. Through contracts, NIAID funds clearly defined projects of scientific need or interest. NIAID closely supervises projects funded by contracts. NIAID uses a variety of contract mechanisms to accomplish its research goals, such as contracts for developing animal models, developing and testing vaccines, conducting clinical trials, and developing and maintaining reagent and specimen repositories for investigators.

CRADAs

NIAID often uses Cooperative Research and Development Agreements (CRADAs) to facilitate the development of specific technologies or projects that originate in NIAID laboratories. Under a CRADA, NIAID may provide personnel, services, facilities, equipment, or other resources. See the CRADA Web site listed at right for more information.

Online Resources

NIAID International Awards
funding.niaid.nih.gov/researchfunding/int/pages/default.aspx

IRIDA Program Announcement
grants.nih.gov/grants/guide/pa-files/PAR-08-130.html

K99/R00 Program Announcement
grants.nih.gov/grants/guide/pa-files/PA-10-063.html

Grants.gov
www.grants.gov

Foreign Grants Information
grants.nih.gov/grants/foreign/index.htm

Electronic Research Administration Commons
commons.era.nih.gov/commons

CRADAs
Training at NIH

The NIH Visiting Program provides opportunities for foreign postdoctoral scientists to train and conduct collaborative research. Annually, more than 2,000 scientists from other nations conduct research in the basic and clinical science laboratories on the NIH campus in Bethesda, Maryland, and in several field units across the United States. NIH has long considered close interaction with foreign scientists in the conduct of collaborative research to be an essential ingredient in achieving its objectives.

There are two categories of Visiting Program participants: Visiting Fellows, who receive awards for research training, and Visiting Scientists, who receive appointments to conduct research. Each participant works closely with a senior NIH investigator who serves as a sponsor or supervisor during the period of award or appointment.

Visiting Scientists and Visiting Fellows hosted by NIAID receive a salary or stipend according to their particular appointment.

How To Apply for Training Opportunities

Foreign postdoctoral scientists who wish to participate in the Visiting Program must first secure an invitation from a senior scientist at NIH. The award (Visiting Fellow) or appointment (Visiting Scientist) is offered based on a candidate’s qualifications and the research needs of the host laboratory.

Individuals interested in an NIAID fellowship or appointment should write to a senior scientist at an NIAID laboratory who works in the same research field, enclosing a resume and brief description of their particular research area and interests.

Guest and Volunteer Researchers

Foreign predoctoral and postdoctoral scientists may work at NIAID without salary or stipend as Volunteer Researchers. It also is possible for foreign scientists to receive a salary or stipend from their home institution and work at NIAID as Guest Researchers. Interested individuals should contact a senior scientist at an NIAID laboratory who works in the same research field, enclosing a resume and brief description of their particular research area and interests.

ICSSC Assists Clinical Investigators in Developing Countries

The International Clinical Sciences Support Center (ICSSC) provides support to clinical investigators funded by the NIAID Division of Microbiology and Infectious Diseases and whose work focuses on treatment, prevention, and control of infectious diseases in developing countries.

This support includes the following:

- Assistance with research planning, protocol development, and study implementation
- Training and workshops on topics such as study design, data management, and ethical conduct of trials
- Opportunities to communicate and share experiences with other investigators

The ICSSC Web site includes a service-request form and links to resources such as protocol templates, informed consent checklists, and online tutorials.

Online Resources

International Clinical Sciences Support Center
www.ICSSC.org

Training in NIAID Labs
www.niaid.nih.gov/labs/training

Opportunities at the NIH for Non-U.S. Citizens
www.jobs.nih.gov/jobsearch/noncitizen.htm