



**PROTECTING
THE NATION'S
HEALTH
IN AN ERA OF
GLOBALIZATION**

*CDC's Global
Infectious Disease
Strategy*



**DEPARTMENT OF
HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL
AND PREVENTION**

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Protecting the Nation's
Health in an Era of
Globalization:
CDC's Global Infectious
Disease Strategy



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PREFACE

Since 1994, CDC has been engaged in a nationwide effort to revitalize national capacity to protect the public from infectious disease. Progress continues to be made in the areas of disease surveillance and outbreak response; applied research; prevention and control; and infrastructure-building and training. These efforts are intended to provide protection against endemic diseases like tuberculosis and hepatitis C, as well as against whatever new or drug-resistant diseases arise.

Although safeguarding U.S. health is a domestic goal, its achievement requires international action and cooperation. This is because U.S. health and global health are inextricably linked. As the AIDS epidemic has illustrated, a disease that emerges or reemerges anywhere in the world can spread far and wide. With increased rates of air travel and international trade, infectious microbes have many opportunities to spread across borders, whether carried by businessmen and tourists, by mosquitos that “hitchhike” on airplanes, or by exotic animals imported as pets or livestock. Microbes have additional opportunities for spread on international shipments of fruits, meats, fish, or vegetables.

The international dimension of the effort to combat infectious diseases is reflected in CDC’s growing international role. Whenever a new, highly dangerous, drug-resistant, or reemerging disease is detected anywhere on the globe, U.S. citizens, as well as foreign governments, have come to rely on CDC to provide assistance and public health information. Established diseases such as HIV/AIDS, tuberculosis, and malaria, as well as vaccine-preventable diseases such as polio, demand increasing attention and resources as well. This increased international engagement has stimulated CDC to rethink its infectious disease priorities, keeping in mind that it is far more effective to help other countries control or prevent dangerous diseases at their source than try to prevent their importation.

This document, *Protecting the Nation’s Health in an Era of Globalization: CDC’s Global Infectious Disease Strategy*, represents an important advance in defining CDC’s evolving global mission and in considering how CDC and its international partners can work together to improve global capacity for disease surveillance and outbreak response. We look forward to working with our many partners throughout the nation and the world as we put this strategy into practice.

Jeffrey P. Koplan, M.D., M.P.H.
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EXECUTIVE SUMMARY

It is not possible to adequately protect the health of our nation without addressing infectious disease problems that occur elsewhere in the world. In an age of expanding air travel and international trade, infectious microbes are transported across borders every day, carried by infected people, animals, and insects, and contained within commercial shipments of contaminated food. “Old” diseases such as malaria, measles, and food-borne illnesses are endemic in many parts of the globe, and new diseases such as acquired immunodeficiency syndrome (AIDS; caused by the human immunodeficiency virus (HIV))—as well as new forms of old diseases such as multidrug-resistant tuberculosis (TB)—can emerge in one region and spread throughout the world.

Moreover, unforeseen disease problems continue to appear. Recent examples include vancomycin-resistant infections of *Staphylococcus aureus* in the United States and Japan, avian influenza in Hong Kong, a new disease called Nipah virus encephalitis in Malaysia, and outbreaks of dengue fever in Texas and West Nile encephalitis in New York. Increased CDC engagement in efforts to improve global disease surveillance and outbreak response will help us detect new or unusual diseases of any kind and respond to health emergencies of any kind—including both naturally occurring and intentionally caused outbreaks.

Left unchecked, today’s emerging diseases can become the endemic dis-

eases of tomorrow. This is what happened with HIV/AIDS, which spread from a remote part of Africa to all other continents 20 years ago, and is now entrenched all over the world, necessitating a major international control effort.

Because U.S. and international health are inextricably linked, the fulfillment of CDC’s domestic mission—to protect the health of the U.S. population—requires global awareness and strategic thinking. This document, *Protecting the Nation’s Health in an Era of Globalization: CDC’s Global Infectious Disease Strategy*, describes how CDC and its international partners can collaborate to prevent the emergence and spread of infectious diseases.

U.S. Investment in Global Public Health

The United States must participate more fully in combating infectious disease threats around the world. These efforts will yield multiple benefits:

- **Protecting the health of U.S. citizens at home and abroad.** Controlling disease outbreaks as well as dangerous endemic diseases wherever they occur prevents those diseases from spreading internationally, saving lives and dollars. U.S. citizens cannot be adequately protected from diseases such as measles, HIV/AIDS, and tuberculosis if our public health efforts are restricted to persons residing within our borders.

- **Furthering U.S. humanitarian efforts.** The potential for saving human lives by preventing infectious diseases overseas is tremendous. Every year, an estimated three million infant and child deaths are prevented by vaccination and other preventive health measures. Many families and communities, including refugees and displaced people, also benefit from international investigations that lead to prompt control of outbreaks.
- **Providing diplomatic and economic benefits.** Because health is an area of concern for all nations, international projects that address infectious disease issues can open avenues of communication and ease tensions between the United States and other nations. Improvements in global health will also enhance the U.S. economy and contribute to global prosperity. Reductions in disease burden will promote economic growth in nations that represent growing markets for U.S. products. Investments in global health will also reduce U.S. healthcare costs by decreasing the number of cases of imported diseases and by eradicating diseases currently included in childhood vaccination programs.
- **Enhancing security.** Slowed economic growth fueled by poor health and disease can impede democratic development and political transitions in poor and former communist nations, contributing to military conflicts and humanitarian emergencies. The HIV/AIDS pandemic is already destabilizing poor-

er nations, damaging their economic, social, political, military, and educational infrastructures, and creating vast numbers of orphans. The recent intentional releases of biologic agents in the United States have also intensified international concerns about bioterrorism. Due to the ease and frequency of modern travel, an intentionally-caused outbreak that begins anywhere in the world can quickly become an international problem. A contagious bioterrorist agent such as smallpox can spread rapidly from person to person and from country to country. A noncontagious agent such as anthrax can be spread by unexpected methods, including international mail. The United States must be prepared to work with other nations to prevent illness and deaths caused by acts of bioterrorism.

Although the United States participates in health projects in many parts of the world, much more can be done, at relatively low cost, with political will, national leadership, and a clearly articulated global strategy.

CDC's Role in Promoting Global Public Health

CDC, which is dedicated to the prevention and control of disease and the promotion of health, works by invitation in many different jurisdictions, including U.S. states and cities and other nations. Throughout its history, CDC has provided international leadership in public health, serving as a technical consultant to the World

Health Organization (WHO) and ministries of health on projects that address infectious disease problems related to endemic diseases, wars, famines, or other disasters. Many of these projects have been funded and coordinated by the U.S. Agency for International Development (USAID). CDC has also supported research and public health education on diseases of regional or international importance, provided resources and leadership for the smallpox eradication effort, and established long-term collaborative research partnerships with several developing nations. While considerable effort has been devoted to these international activities, CDC's primary focus has remained on domestic health.

In recent years, however, CDC's overseas role has expanded rapidly. Global polio eradication (<http://www.cdc.gov/nip/global>) and HIV/AIDS control programs (<http://www.cdc.gov/nchstp/od/gap>) have led to substantial investments of CDC personnel and financial resources, as have a succession of complex international emergencies. Between 1990 and 2000, CDC provided outbreak assistance on an ad hoc basis to nations in Asia, Africa, Europe, and Latin America to help investigate outbreaks of unknown, highly dangerous, and highly infectious diseases, and provided diagnostic support for hundreds of local investigations around the globe.

Although there are no formal structures and designated resources for international outbreak response, U.S. citizens—as well as foreign governments—have come to rely on CDC to provide outbreak assistance and pub-

lic health information whenever a new or reemerging disease threat is detected anywhere on the globe. Oubreak assistance by CDC would also be required if an intentionally caused outbreak occurred at home or abroad.

CDC's growing presence overseas presents new opportunities and new challenges. This document—developed in consultation with public and private sector partners, at home and abroad—represents an active effort to further define CDC's evolving global mission. It considers how CDC and its international partners can work together over the long term to improve the capacity to detect, control, and prevent infectious diseases. CDC's ongoing efforts to strengthen U.S. domestic public health infrastructure are critical to the success of these international collaborations.

Six Priority Areas

Protecting the Nation's Health in an Era of Globalization: CDC's Global Infectious Disease Strategy defines CDC's global infectious disease priorities in six areas, selected in consultation with global public health partners. In looking towards the future, CDC envisions increased activity and progress in each area:

1. International Outbreak Assistance.

An underlying principle of the global strategy is the recognition that international outbreak assistance is an integral function of CDC. Supporting this function will require augmenting, updating, and strengthening CDC's diagnostic facilities, as well as its capacity for epidemiologic investigation overseas. In the future, CDC must also be prepared, as a matter of routine, to offer follow-up assistance after each acute emergency response. Such follow-up will assist host-country ministries of health to maintain control of new pathogens when an outbreak is over.

2. A Global Approach to Disease Surveillance.

In the years ahead, regional surveillance networks should expand, interact, and evolve into a global “network of networks” that provides early warning of emerging health threats and increased capacity to monitor the effectiveness of public health control measures. CDC will help stimulate this process by providing technical assistance, evaluating regional progress, and working with many partners to strengthen the networks' telecommunications capacities and encourage the use of common software tools and harmonized standards for disease reporting.

3. Applied Research on Diseases of Global Importance.

A research program on diseases that are of global importance, including some that are uncommon in the United States, is a valuable resource, both for humanitarian reasons and because of the dangers represented by some imported diseases. CDC's laboratorians, epidemiologists, and behavioral scientists will maintain an active research program to develop tools to detect, diagnose, predict, and eliminate diseases of global or regional importance. When a new disease threat is reported anywhere in the world, CDC's laboratorians and field investigators will be available to help answer questions about disease transmission, treatment, control, and prevention.

4. Application of Proven Public Health Tools.

There is often a long delay between the development of a new public health tool and its widespread use. CDC will intensify efforts to couple applied research with research on ways to promote the use of newly developed tools for disease control (“implementation research”). CDC will help identify the most effective tools and actively encourage their international use, applying expertise and resources in laboratory research, public health policy, program management, and health communications to overcome scientific, financial, and cultural barriers.

5. Global Initiatives for Disease Control.

CDC will make sustained contributions to global initiatives to reduce the prevalence of HIV/AIDS in young people by 25% and reduce deaths from tuberculosis and malaria by 50% by 2010. CDC will also work with the Global Alliance for Vaccines and Immunization to reduce infant mortality through enhanced delivery and use of new and underutilized vaccines against respiratory illnesses and other childhood diseases. CDC and its partners will also consult on future international priorities for disease control, elimination, and eradication efforts—as well on monitoring for antimicrobial resistance and planning for pandemic influenza—and help evaluate progress through the collection and analysis of disease surveillance data.

6. Public Health Training and Capacity Building.

CDC will encourage and support the establishment of International Emerging Infections Programs (IEIPs) in developing countries—centers of excellence that integrate disease surveillance, applied research, prevention, and control activities. The IEIP sites will partner with Field Epidemiology Training Programs (FETPS) and other institutions to strengthen national public health capacity and provide hands-on training in public health. Over time, they may help to strengthen capacity in neighboring countries as well as within the host country.

Implementation of specific objectives in these six areas will help realize CDC's vision of a world in which U.S. citizens and people throughout the world are better protected from infectious diseases.

Partnerships and Implementation

CDC's global infectious disease strategy was prepared by the National Center for Infectious Diseases, in collaboration with other CDC centers and offices, including the Office of Global Health, the National Center for HIV, STD, and TB Prevention, the National Immunization Program, the Epidemiology Program Office, and the Public Health Practice Program Office. Many global health organizations and agencies provided consultation and assistance during its development.

The strategy will be implemented incrementally over the next five years, as funds become available, beginning with the highest priorities for 2001-2002 (Box 1). As CDC carries out this strategy, it will coordinate with foreign governments, international organizations (including WHO, the Joint United Nations Programme on AIDS [UNAIDS], and the United Nations Children's Fund [UNICEF]), other U.S. agencies (including USAID, the

National Institutes of Health [NIH], the Food and Drug Administration [FDA], the Department of Defense [DoD], the Department of State, the Department of Veterans Affairs [DVA], the U.S. Department of Agriculture [USDA], the National Oceanic and Atmospheric Administration [NOAA], and the National Aeronautics and Space Agency [NASA]), professional societies, research institutions, and schools of public health, medicine, nursing, and veterinary science. CDC will also participate in international coalitions that support disease eradication efforts and other regional and global health initiatives. These coalitions may include national and local nongovernmental organizations, community-based and faith-based organizations, and communities of color. Other implementation partners will include pharmaceutical and biotechnology companies, non-governmental organizations that address health problems, and development agencies, development banks, foundations, and other organizations that aim to reduce poverty by reducing the incidence of endemic diseases. Website addresses for selected organizations and health publications and reports referred to in this document are provided in Appendix A.

Box 1

Implementation Priorities, 2001-2002

International Outbreak Assistance

Dedicate specific resources—epidemiologic, diagnostic, and logistic—to international outbreak investigations.

A Global Approach to Disease Surveillance

Work with WHO and other partners to provide technical assistance to regional networks in Africa, Asia, and Latin America that can fill gaps in global disease surveillance and become components of a global network of networks.

Applied Research on Diseases of Global Importance

Establish two or more long-term, on-site research collaborations in developing countries to test new strategies for disease control and prevention.

Application of Proven Public Health Tools

Work with a developing-country partner to launch a demonstration project that employs three or more proven public health tools to prevent and control infectious diseases, depending on local priorities.

Global Initiatives for Disease Control

Work with foreign ministries of health and WHO to complete the eradication of polio and guinea worm disease.

Help implement HIV/AIDS control programs on all continents through CDC's Global AIDS Program.

Work with the Roll Back Malaria partnership to help implement and monitor disease control and prevention programs in areas with high rates of transmission.

Work with the Stop TB Initiative to improve global surveillance, prevention, and medical management of TB, including multidrug-resistant TB, in areas with high rates of transmission.

Establish population-based surveillance centers to monitor the impact of vaccine use on diseases targeted by the Global Alliance for Vaccines and Immunization. These surveillance centers may become the nuclei of future International Emerging Infections Program sites.

Public Health Training and Capacity Building

Establish the first International Emerging Infections Program as a partnership among a ministry of health, CDC, a Field Epidemiology Training Program, and one or more local universities or medical research institutes. An initial priority will be to establish training in field epidemiology, applied laboratory science, and public health management.

INTRODUCTION

It is not possible to adequately protect the health of our nation without addressing infectious disease problems that are occurring elsewhere in the world. In an age of expanding air travel and international trade, infectious microbes are transported across borders every day, carried by infected people, animals, and insects (Box 2), and contained within commercial shipments of contaminated food (Box 3). “Old” diseases such as malaria, measles, and foodborne illnesses are endemic in many parts of the globe, and new diseases such as acquired immunodeficiency syndrome (AIDS; caused by the human immunodeficiency virus (HIV))—as well as new forms of old diseases such as multidrug-resistant tuberculosis (TB)—can emerge in one region and spread throughout the world.

Old diseases, as well as new ones, can travel. For example, between July 1999 and January 2000, 56 people in southern Texas fell ill with dengue fever, a mosquitoborne tropical disease endemic to South and Central America and parts of Asia. Seventeen of those people acquired their illness in the United States. In 1999, two Boy Scouts in New York State acquired malaria—eliminated as an endemic disease problem in the United States a half century earlier—from mosquitos at a summer camp in a rural area of Suffolk County. In August and Sep-

tember, 1999, six people in the northeastern United States and a Canadian visiting New York City died from West Nile encephalitis, a viral disease also transmitted by mosquitos. The West Nile virus, which is carried by migratory birds in Asia, Africa, and Europe, had never before been reported in the Western Hemisphere.

These outbreaks present new challenges for U.S. public health agencies at the local, state, and federal levels. They also remind us that millions of people live in tropical areas where mosquitoborne diseases like malaria and dengue are a fact of everyday life.

Because U.S. and international health are inextricably linked, fulfilling CDC’s domestic mission—to protect the health of the U.S. population—requires global awareness and strategic thinking. This document, *Protecting the Nation’s Health in an Era of Globalization: CDC’s Global Infectious Disease Strategy*, describes how CDC and its international partners can collaborate to prevent the emergence and spread of infectious diseases.

The urgency of the situation is illustrated by the emergence of unforeseen disease problems in recent years. These include multidrug-resistant *Streptococcus pneumoniae* throughout the world and vancomycin-resistant *Staphylococcus aureus* in the United States and

Box 2

Infectious Diseases Do Not Recognize Borders

From a public health point of view, domestic and international health are inextricably linked. Examples of disease spread from continent to continent include

- **HIV/AIDS**—This disease apparently emerged in central Africa in the 1950s or earlier¹ and spread through most of Africa, Asia, Europe, and the Americas during the 1970s and 1980s.

Because the AIDS virus weakens an individual's immune defenses, an individual with HIV/AIDS may become coinfecting with malaria, tuberculosis (TB), or pathogens that cause diarrhea or pneumonia.

- **TB**—During the 1980s, this age-old scourge, which had been nearly eliminated in the West by antibiotic treatment, reemerged—sometimes in a multidrug-resistant form—in cities around the world, including in the United States. By 2000, approximately 46% of newly identified U.S. TB cases originated in other countries.

The spread of TB has been hastened by lack of public health surveillance for this disease and by the concurrent HIV/AIDS epidemic.

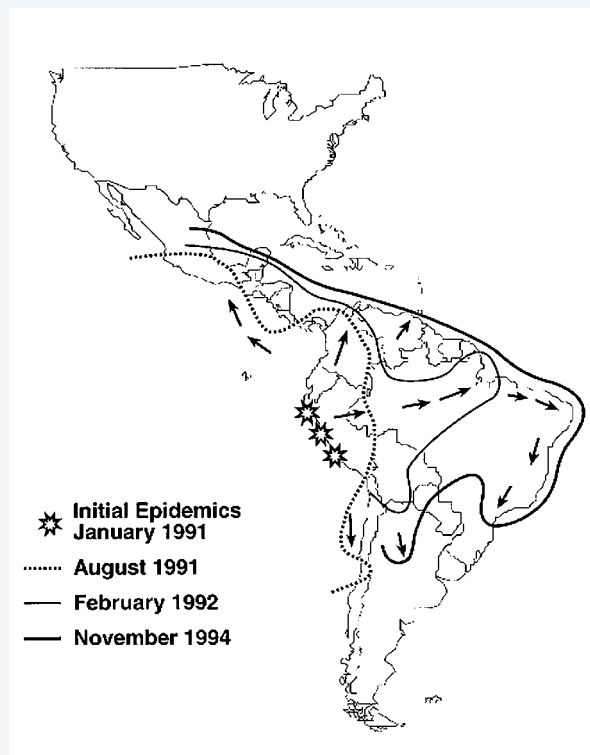
- **Malaria**—Although malaria was eliminated in the United States as an endemic disease by the 1960s (through swamp-draining and vector control programs), approximately 1,500 cases of malaria are reported in the United States each year. One-half occur in U.S. travelers to malaria-endemic countries and the other half occur among foreign nationals who enter the United States already infected.

Over the past 15 years, more than 80 people in the United States were infected by local transmission within our borders. In other countries, the spread of malaria has been augmented by the spread of anti-malarial drug resistance, and many parasite strains are increasingly resistant to preventive antimalarial drugs taken by travelers.

- **West Nile encephalitis**—This mosquito-borne viral disease carried by migratory birds in Asia, Africa, and Europe, caused 79 cases of encephalitis and 7 deaths in the northeastern United States in 1999.

Because the West Nile virus had never before been detected in the Americas—and because it had been mentioned by an Iraqi defector as an organism of interest to the Iraqi bioweapons program—it was speculated that a strain of West Nile virus isolated in New York City might have been deliberately engineered and disseminated to harm U.S. citizens. However, the scientific evidence suggests that the outbreak was caused by a naturally occurring viral strain.²

- ***Vibrio cholerae* O1, El Tor biotype**—A virulent strain of cholera has caused an ongoing pandemic that has lasted 40 years and affected more than 75 countries.



Geographic extent of the Latin American cholera epidemic over time, since its beginning in January 1991. Lines represent the advancing front of the epidemic at different times. Since 1995, most Latin American countries have reported diminishing numbers of cases. Cholera has not yet reached the Caribbean.

Adapted from: Tauxe RV, Mintz ED, Quick RE. Epidemic cholera in the New World: translating field epidemiology into new prevention strategies. *Emerging Infectious Diseases* 1:141-6, 1995.

Box 2

Beginning in 1961, *Vibrio cholerae* O1, El Tor biotype spread from Indonesia through most of Asia into eastern Europe and Africa. From North Africa it spread to the Iberian Peninsula and into Italy in 1973. In the late 1970s, small outbreaks occurred in Japan and in the South Pacific.

In January, 1991, epidemic cholera appeared in Peru and spread rapidly through most of Latin America, causing over 1,000,000 cases by 1994. This was the first time in 100 years that a cholera pandemic had reached the New World.

- **Salmonellosis**—A multistate outbreak carried by contaminated mangoes grown in Brazil caused 79 cases of *Salmonella* Newport infections in 13 states in 1999.

The outbreak was detected and investigated using PulseNet, the U.S. early warning system for food-borne diseases (page 36). PulseNet linked 78 cases in 22 states by comparing the molecular fingerprints of the isolates. Once mangoes were implicated as the common exposure for these cases, FDA traced the source of the mangoes back to a single farm in Brazil. The mangoes had been dipped in warm water in a new process designed to kill fruit-fly larvae before exportation. Unfortunately, the processing water may have been contaminated with *Salmonella*.

- **Coccidioidomycosis**—Outbreaks caused by *Coccidioides immitis*, a soil-dwelling fungus common in arid and semiarid parts of the Western Hemisphere, were reported in 1996 in Washington State and in 2000 in Pennsylvania.

The outbreaks occurred among church mission groups who visited endemic regions of northern Mexico to undertake construction projects. Infected individuals experienced a severe influenzalike disease

with fever, chills and cough. Fungal disease was not initially suspected.

- **Influenza spread on cruise ships**—A 1997 outbreak of the A/Sydney strain of influenza occurred among people on a cruise that made stops in Canada and New England.

The A/Sydney strain had been isolated in Australia too late in the year to be included in the vaccine formulated for the fall/winter flu season in the Northern Hemisphere. Therefore, the cruise ship passengers had not been immunized against it.

- **Measles**—Fifty-six of the 87 cases of measles identified in the United States in 2000 were traced to importations of the virus from outside our borders. Twenty-six were direct importations, 18 were secondary cases, and 8 involved viruses whose DNA sequences suggested a foreign origin.

Comprehensive surveillance and genetic sequencing of all identified strains of the virus allow for tracing of the outbreak strains to the country of origin. The finding that indigenous measles transmission can be interrupted in the United States is an important impetus for supporting a global measles elimination campaign.

- **Polio**—Eliminated from the Western Hemisphere since 1991, paralytic polio was again identified in Haiti and the Dominican Republic in 2000, and attributed to waning immunization coverage rates in those countries.

Unless immunization coverage can be strengthened in other neighboring countries, diseases thought no longer to be a risk for U.S. children may be imported by travelers.

Box 3

Factors That Facilitate the International Spread of Foodborne Disease

- **Globalization of the food supply, particularly of perishable foods, like fresh produce**
U.S. citizens can now eat fresh fruits and vegetables all year round, produced in both Northern and Southern Hemispheres. However, some fresh foods may be contaminated during picking, packaging, transport, or delivery. CDC and FDA are working together to reduce the risk to U.S. consumers.
- **The development of new food production industries in developing nations to meet the needs of the export market**
This includes growing nonindigenous fruits and vegetables that may be susceptible to contamination by indigenous microbes. For example, raspberries were recently introduced into Guatemala with U.S. support as a potentially valuable commercial crop. Some of the exported raspberries were found to be contaminated with *Cyclospora*, a waterborne protozoan parasite not previously associated with foodborne disease. *Cyclospora* outbreaks associated with these raspberries were reported in the United States and Canada.
- **Centralized processing of human and animal foods, followed by widespread distribution**
If an ingredient used in an animal feed, for example, is contaminated with a strain of *Salmonella*, that strain can be quickly disseminated to food animals around the world. Or, if ground beef is contaminated with *E. coli* O157:H7 at a factory, hamburgers sold at fast-food restaurants in many locations (as well as packages of frozen meat sold at grocery stores) may transmit infection.
- **Expanded U.S. market for “ethnic” foods**
There is increased familiarity with—and preferences for—foods from different countries, due to international travel by U.S. citizens, the growing ethnic diversity of our population, and our many immigrant communities. A recent outbreak of typhoid fever was associated with imported frozen mamey fruit pulp, popular among Central Americans living in Florida. Outbreaks of gastroenteritis caused by antibiotic-resistant *Salmonella* have occurred in people who ate traditionally-prepared Mexican cheese made from raw milk and sold informally.
- **Increased international travel**
International tourists and business travelers often develop “traveler’s diarrhea,” caused by foodborne bacteria that generally do not affect local adults, most of whom have acquired immunity from repeated childhood exposures.

Japan (Box 4), avian influenza in Hong Kong (Box 5), a new disease called Nipah virus encephalitis identified in Malaysia, as well as the introduction of West Nile encephalitis into North America (Box 2).

Windows of opportunity for disease control may also close. For example, had smallpox not been eradicated before the global HIV/AIDS epidemic, one of the world’s crowning public

health successes might have been impossible to achieve. There is now evidence that immune suppression such as that caused by HIV/AIDS may lead to a lack of response to smallpox vaccination or (in some cases) to disseminated vaccinal infection that may be life-threatening.

Left unchecked, today’s emerging diseases can become the endemic diseases of tomorrow. This is what hap-

pened with HIV/AIDS, which emerged in a remote part of Africa during the 1970s, spread throughout the world during the 1980s, and is now entrenched on all continents, creating widespread devastation. During the 2000s, HIV/AIDS has become the target of a major international control effort (Box 6).

Box 4

International Spread of Antimicrobial Resistance

Drug-resistant pathogens are a growing menace to all people, regardless of age, sex, or socioeconomic background. They endanger people in affluent, industrial societies like the United States, as well as those in less developed nations. Many pathogens of international importance are becoming resistant to standard therapies, including bacteria that cause pneumonia, ear infections, and meningitis (e.g., *Streptococcus pneumoniae*); food and waterborne infections (e.g., *Salmonella* and *Shigella*); sexually transmitted diseases (e.g., *Neisseria gonorrhoeae*); the human immunodeficiency virus that causes AIDS; and the parasites that cause malaria (*Plasmodium* spp.). Other examples of clinically important microbes that are rapidly developing drug-resistance include *Mycobacterium tuberculosis*; bacteria that cause skin, bone, lung, and bloodstream infections (e.g., *Staphylococcus aureus*) and urinary tract infections (e.g., *Escherichia coli*); and pathogens transmitted in health care settings (e.g., enterococci and *Klebsiella*).

CDC is working with many partners to help improve global capacity to detect and control drug-resistant infections. These efforts include working with WHO to provide quality control and proficiency testing for clinical laboratories in support of surveillance for emerging resistance problems. CDC is also working with FDA, NIH, USAID, DoD, USDA, and other U.S. agencies to develop Part II of the U.S. Public Health Action Plan to Combat Antimicrobial Resistance (<http://www.cdc.gov/drugresistance/actionplan>), which will serve as a blueprint for U.S. government activities to address international antimicrobial resistance issues. U.S. agencies and their partners will implement this blueprint in the context of WHO's *Global Strategy for the Containment of Antimicrobial Resistance* (<http://www.who.int/emc/globalstrategy/strategy.html>).

International Cooperation To Combat Infectious Diseases

The United States must participate more fully in combating infectious disease threats around the world. The urgency of expanding our contributions to infectious disease control was emphasized by an interagency working group of the National Science and Technology Council³ (<http://www.ostp.gov/CISET/html/toc.html>).

There has also been an outpouring of interest in infectious disease issues in other nations, both in the developed and the developing world (Appendix B). In July 2000, at the summit meeting in Okinawa the Group of Eight Industrialized Nations pledged to reduce deaths from infectious diseases in poor countries, agreeing to a set of time-limited objectives (<http://usinfo.state.gov/topical/econ/group8/summit00>). The aim is to reduce the prevalence of HIV/AIDS among young people by 25%, and reduce the number of deaths due to TB and to malaria by 50% by 2010. These goals are based on global health initiatives endorsed by the World Health Organization (WHO) in its effort to address “diseases of poverty” in developing countries (Box 6). Another major initiative, spearheaded by the Global Alliance for Vaccines and Immunization (GAVI; <http://www.vaccinealliance.org/>), aims to increase developing country access to new and underutilized vaccines against hepatitis B, *Haemophilus influenzae* type b, and yellow fever, and to improve delivery of traditional childhood vaccines against measles and other diseases.

Box 5

Avian Influenza in Hong Kong

Influenza viruses are constantly mutating and evolving, and new strains keep emerging. Because few people have immunity to a new strain—and because influenza spreads easily from person to person—new strains can travel quickly around the world. If a strain is particularly virulent, it may cause a pandemic, like the 1918-19 “Spanish flu,” which killed 20 million people, including 500,000 Americans.

The WHO International Influenza Surveillance Network, which includes 110 laboratories throughout the world (including a CDC-based WHO Collaborating Centre), gathers influenza isolates on all continents and collects data on new strains that have the potential for pandemic spread. In 1997, the government of Hong Kong made use of this network to identify a dangerous strain of avian influenza transmitted from chickens to humans that infected 18 persons and killed 6. The authorities feared that the strain (H5N1) might recombine with a human strain and become capable of human-to-human transmission and invited a CDC team to assist with control of the outbreak. Transmission stopped after the government of Hong Kong ordered the destruction of all chickens in Hong Kong that might be carrying the virus (see also Box 15).

This episode suggests that it may be possible to prevent influenza pandemics before they begin, or to mitigate the global impact of an influenza pandemic through early identification of a virulent strain and formulation of a strain-specific vaccine. What is required is continued international vigilance and cooperation (i.e., a global network) and—at the national level—the political will and resources to act on epidemiological and diagnostic evidence. Had the WHO network not been in place, or had the Hong Kong government been unable or unwilling to act, a virulent hybrid chicken/human strain of influenza for which virtually all people lack immunity—and for which there is no vaccine and few drug treatments—might have caused a massive global pandemic.

Our confidence that nations can come together to improve global health is reinforced by the success of the effort to eradicate smallpox, the interruption of measles transmission in the Americas, and the substantial progress made toward the worldwide eradication of polio (Box 7) and guinea worm disease.

U.S. Investment in Global Public Health

Promoting international cooperation to address emerging infectious diseases is a natural role for the United States, whose scientists and business leaders are important members of the biomedical research and telecommunications communities that provide the technical and scientific underpinning for infectious disease surveillance and control. The United States can continue to lead from its strengths in medical science and technology to help protect American and global health.

Moreover, our nation now has a window of opportunity to make public health investments that will pay increasingly valuable dividends in the years to come. As noted in the 1997 Institute of Medicine report, *America’s Vital Interest in Global Health*⁴ (<http://www.nap.edu/books/0309058341/html>), investments in international efforts to detect, control, and prevent infectious diseases can yield multiple benefits:

Box 6

Global Health Initiatives

Four major global health initiatives were launched between 1998 and 2000:

- **Roll Back Malaria**, a global strategy to reduce deaths from malaria by increasing access to prompt and effective treatment (including protective intermittent therapy for pregnant women) and prevention tools (including insecticide-treated bednets); by facilitating rapid response to malaria outbreaks; and by developing new products for the prevention and treatment of malaria.
- **Stop TB**, a global strategy to stop the spread of TB around the world. One of its objectives is to promote implementation of the directly observed therapy short-course strategy (DOTS). The effective implementation of DOT in NYC, in response to the epidemic in the late 1980s and early 1990s, has served as a model in this country and around the world.
- **International Partnership Against AIDS in Africa**, a UNAIDS-led effort to mitigate the effects of the growing HIV/AIDS epidemic. In 1999, as part of this effort, the U.S. government launched the Leadership and Investment for Fighting an Epidemic (LIFE) Initiative, which provides support to the hardest-hit countries for reducing HIV transmission, improving treatment of HIV/AIDS and opportunistic infections,

and strengthening national capacities to collect disease surveillance data and manage national HIV/AIDS programs. The Global AIDS Program is the CDC component of the LIFE Initiative (see Box 21).

- **Global Alliance for Vaccines and Immunization (GAVI)**, a global effort to strengthen childhood immunization programs and bring a new generation of recently licensed vaccines into use in developing countries. These include vaccines against hepatitis B, childhood meningitis, yellow fever, and respiratory infections, which are the leading cause of death in children under age five. Substantial resources for this purpose have been pledged by the Bill and Melinda Gates Foundation and the governments of Norway, Netherlands and the United States.

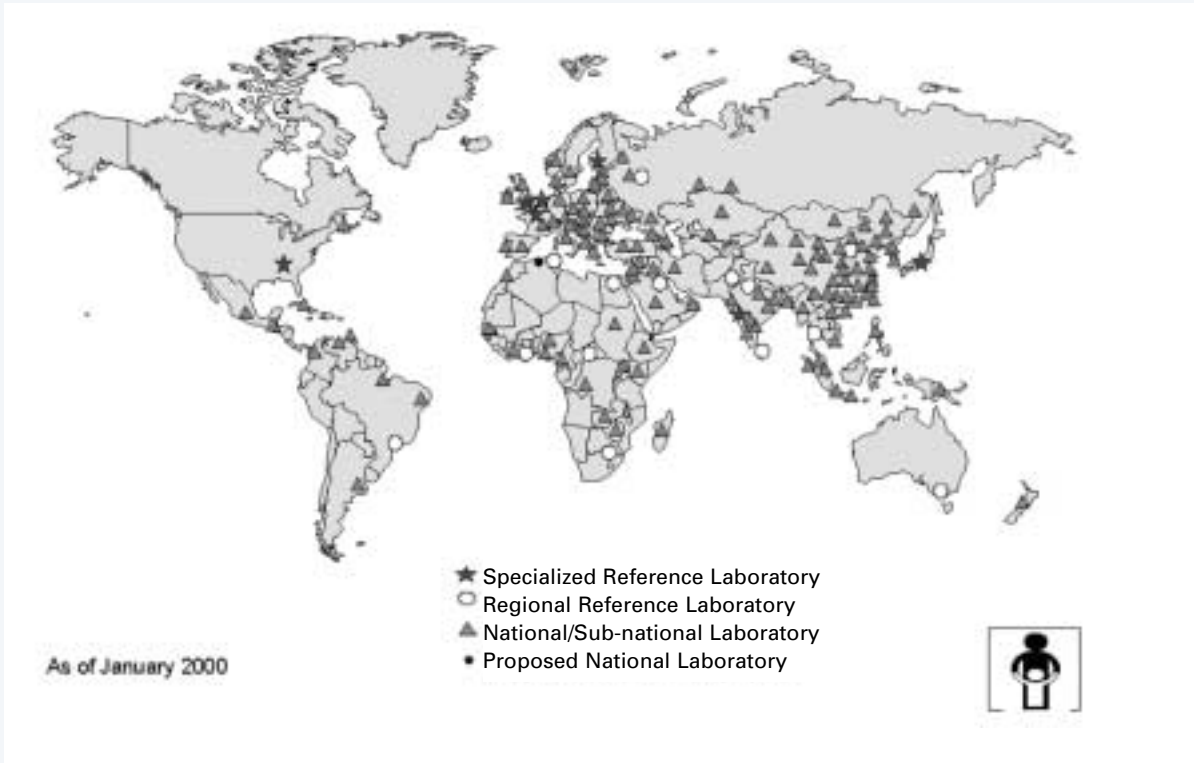
Targets for Disease Reduction

These targets for disease reduction were endorsed at the Group of Eight Industrialized Nations Summit in Okinawa in July 2000:

- HIV/AIDS:** 25% reduction in prevalence in young people by 2010
- TB:** 50% reduction in deaths by 2010
- Malaria:** 50% reduction in deaths by 2010

Box 7

The World Health Organization Global Polio Laboratory Network



Ascertaining whether a disease is still present in a given area (and, therefore, that further prevention efforts are needed) is a critical part of any disease eradication effort. The WHO Global Polio Laboratory Network uses molecular techniques to determine whether wild-type polio is circulating in areas undergoing eradication efforts. Since the worldwide campaign began, cases of polio have declined by 99% (from 350,000 cases to less than 3,000), and the number of countries in which polio is endemic has decreased from 125 to 20.

CDC began training Network virologists in 1986, soon after the Pan American Health Organization declared its goal of eliminating polio from the Americas. CDC will continue to train Network virologists for several more years, as new diagnostic methods are developed to meet the stringent surveillance criteria necessary to obtain certification of global polio eradication.

Protecting the health of U.S. citizens at home and abroad. Seeking to control disease outbreaks as well as dangerous endemic diseases wherever they occur prevents those diseases from spreading internationally, saving lives and dollars. In addition, CDC's sup-

port for outbreak investigations provides U.S. scientists with opportunities to focus on new or drug-resistant pathogens and consider how best to control, prevent, and treat them before they arrive on our shores. Outbreaks and endemic diseases in other

countries also endanger U.S. travelers abroad.

In terms of U.S. health, it is far more effective to help other countries control or prevent dangerous diseases than try to prevent their importation, because it is neither efficient nor feasi-

ble to examine each person who enters or returns to the United States for evidence of infection, or to examine all imported goods for evidence of contamination. Some infections are asymptomatic, and some infected individuals may enter the country during the incubation period of a disease (the time between infection and the appearance of symptoms). Thus, diseases such as measles and TB continue to be imported.

Furthering U.S. humanitarian efforts.

Disease prevention is an investment in the young people of the world and in our collective future. Every year, millions of infant and child deaths are prevented by vaccination and other preventive health measures. Many families and communities also benefit from international investigations that lead to prompt control of outbreaks. These include communities of refugees and displaced persons, who may be especially vulnerable to infectious diseases (see Box 13). CDC is also a major contributor to global efforts to eradicate polio (<http://www.cdc.gov/nip/global>) and dracunculiasis (guinea worm disease; <http://www.cdc.gov/ncidod/dpd/parasites/guineaworm> and <http://www.cartercenter.org/guineaworm.html>).

The potential for saving human lives by preventing infectious diseases overseas is tremendous. For example, an additional three million deaths could be prevented annually by wider worldwide use of childhood vaccines. Although the United States participates in international health projects

in many parts of the world, much more can be done, at relatively low cost, with political will, national leadership, and a clearly articulated global strategy.

Investing in global health is an area in which global humanitarian needs and U.S. national interests coincide. For example, U.S. efforts to help the states of the former Soviet Union rebuild their collapsing public health infrastructures⁵ will also help prevent the resurgence of dangerous diseases (e.g., polio, diphtheria, and drug-resistant TB) that can spread to the Americas. Similarly, U.S. efforts to help China improve surveillance for new strains of influenza may be crucial in preventing or controlling the next influenza pandemic (see Box 5).

Providing economic and diplomatic benefits.

Improvements in global health can also enhance the U.S. economy in direct and indirect ways. Domestic health care costs can be reduced by decreasing the number of cases of imported diseases and by eradicating diseases currently included in childhood vaccination programs. For example, the U.S. saved \$3 billion after investing \$32 million in smallpox eradication, and promises to gain even greater cost savings if the global polio eradication effort is successful. Moreover, a reduction in the infectious disease burden in other countries helps improve the economic well-being of developing nations, which represent the fastest growing markets for U.S. products.

Organizations concerned with economic development, including the

World Bank and the World Trade Organization (www.worldbank.org and www.who.int/inf-pr-2000/en/note2000-wha02.html), have concluded that disease reduction efforts are a necessary part of global development strategies (Box 8). Infectious diseases can sap the strength of a nation's workforce and deplete its medical resources, making it more difficult to participate in the global economy. Promoting political stability and sustainable development in developing nations is a major goal of U.S. foreign policy.

Because health is an area of concern for all nations, international projects that address infectious disease issues can open avenues of communication and ease tensions between the United States and other nations (Box 9). Investments in global health can also help advance specific U.S. foreign policy objectives, such as improving bilateral relationships with Vietnam, China, and the Palestinian Territories, and converting biological weapons plants in the Russian Federation and the newly independent states of the former Soviet Union to peaceful uses.

Enhancing security.

Security experts, including members of the U.S. National Intelligence Council⁶ (<http://www.cia.gov/cia/publications/nie/report/nie99-17d.html>) are concerned that large outbreaks like the HIV/AIDS pandemic may destabilize poorer nations. Slowed economic growth fueled by poor health and disease in developing and former communist countries may challenge democratic development and political transitions and contribute to

Box 8

Infectious Diseases and Economic Development

Infectious diseases like malaria and HIV/AIDS act as a massive societal brake, slowing both economic and human development.

Each year, malaria slows economic growth in several sub-Saharan African countries by as much as 1.3% per person per year.⁷ Besides interfering with individuals' abilities to earn a living or attend school, malaria affects national economies by impeding trade, foreign investment, and commerce. It also interferes with children's mental and physical development and may encourage population growth when parents decide to have bigger families, knowing that some of their children may die young. According to one estimate,⁸ if malaria had been eliminated 35 years ago, Africa's current annual gross domestic product would be \$400 billion, rather than \$300 billion—a loss that is nearly five times greater than all development aid provided to Africa last year.

According to a World Bank report,⁹ HIV/AIDS may subtract an additional 1% a year from GDP growth in some sub-Saharan African countries, due to the continuing loss of skilled and unskilled workers in the prime of life. In South Africa, for example, HIV/AIDS may depress GDP by as much as 17% over the next decade, which is a dangerous burden for a young democracy. The HIV/AIDS pandemic is destabilizing several other hard-hit nations, damaging their economic, social, political, military, and educational infrastructures, and creating vast numbers of orphans.

humanitarian emergencies and military conflicts.

The recent intentional releases of biologic agents in the United States have also intensified international concerns about bioterrorism. Due to the ease and frequency of modern travel, an intentionally-caused outbreak that begins anywhere in the world can quickly become an international problem. A contagious bioterrorist agent such as smallpox can spread rapidly from person to person and from country to country. A noncontagious agent such as anthrax can be spread by unexpected methods, including international mail. The United States must be prepared to work with other nations to prevent illness and deaths caused by acts of bioterrorism.

CDC's Role in Promoting Global Public Health

As its name implies, CDC is dedicated to the control and prevention of disease. The agency grew out of efforts to control malaria in the southern United States and today retains a critical role in addressing domestic infectious disease threats. CDC is known in the United States for

- Working with state and local public health agencies to conduct disease surveillance
- Providing national leadership in times of public health crisis

Box 9

International Disease Control Efforts Can Create New Alliances

Mutual interest in addressing an outbreak or an ongoing infectious disease problem may provide the impetus for collaborations with countries who have not historically cooperated with the United States on public health projects, or with countries whose relationship to the United States is uncertain. One example is Hong Kong during the transfer of sovereignty from the United Kingdom to China (see Box 5).

At times, concern about disease outbreaks may be sufficiently strong to allow national antagonisms to be set aside in the interests of disease control. During the outbreak of Marburg hemorrhagic fever in 1998, for example, an international investigative team was permitted to enter a contested part of the Democratic Republic of the Congo. Similarly, an international guinea worm eradication team sponsored by the Carter Center received safe passage in southern Sudan in 1995, due to a specially negotiated cease-fire between the government of Sudan and rebel forces. Moreover, a polio eradication team was allowed to operate in civil war-torn Sri Lanka during 2 “Days of Peace for National Immunization” that were separated by 30 days of warfare. Three decades earlier, during the height of the Cold War, the United States and the Soviet Union agreed on the need to provide coordinated financial and technical support to the smallpox eradication effort.

- Diagnosing rare, highly dangerous, and previously unknown diseases
- Responding rapidly to requests for outbreak assistance
- Researching public health issues and translating the findings into practical tools for disease control and prevention
- Using surveillance data to drive public health action and inform strategic planning
- Integrating epidemiologic and laboratory expertise to address infectious disease problems
- Implementing programs for disease prevention and control
- Training public health workers

CDC works by invitation in many different jurisdictions, including U.S. states and cities and other nations. Throughout its history, CDC has also provided international leadership in public health, serving as a technical consultant to WHO and ministries of health on projects that address infectious disease problems related to endemic diseases, wars, famines, or other disasters. Many of these projects were funded and coordinated by the U.S. Agency for International Development (USAID). Through the Field Epidemiology Training Programs (see Box 24), the Epidemic Intelligence Service (<http://www.cdc.gov/epo/dapht/eis>), and other programs, CDC has

also supported research and public health education on diseases of regional or international importance. CDC helped lead the smallpox eradication effort in the 1960s, and established collaborative research stations (see Box 10) in Côte D'Ivoire, Guatemala, and Kenya in the 1980s and in Guinea, Botswana, Thailand, and Uganda in the 1990s. Although considerable effort has been devoted to these international activities, CDC's primary focus has remained on domestic health.

An evolving mission. In recent years, CDC's overseas role has expanded rapidly. Global polio eradication and HIV/AIDS control programs have led to substantial investments of CDC personnel and financial resources, as have a succession of complex international emergencies. Between 1990 and 2000, CDC provided rapid response teams to nations in Asia, Africa, Europe, and Latin America to help

investigate outbreaks of unknown, highly dangerous, and highly infectious diseases (Appendix C), and provided diagnostic support for hundreds of local investigations around the globe. Some of these investigations involved epidemic diseases and others involved diseases that afflict refugees and other displaced persons. In many cases, CDC epidemiologists served as members of WHO-coordinated investigative teams supported by CDC-based WHO Collaborating Centre laboratories (Appendix D). In addition to helping with outbreak control, CDC provides on-going public health consultation by placing resident advisors and assignees with key partner agencies and by working with coalitions of national groups on emerging infectious disease issues.

CDC's growing presence overseas presents new opportunities and new challenges. This document, *Protecting the Nation's Health in an Era of Globalization: CDC's Global Infectious*

Disease Strategy, represents an active effort to further define CDC's evolving global mission. It was developed in consultation with public and private sector partners at home and abroad. It considers how CDC and its international partners can work together over the long-term to improve capacity to detect, control, and prevent infectious diseases. This document builds on two ongoing efforts. First, it augments and amplifies the international component of the 1998 CDC plan *Preventing Emerging Infectious Diseases: A Strategy for the 21st Century*¹⁰ (<http://www.cdc.gov/ncidod/emergplan>). CDC's ongoing efforts to strengthen U.S. domestic public health infrastructure are critical to the success of our international collaborations. Second, it fits within the larger framework of CDC's efforts to improve international health, as described in *Working with Partners To Improve Global Health: A Strategy for CDC and ATSDR*¹¹ (<http://www.cdc.gov/ogh/pub/strategy.htm>).

Box 10

Examples of CDC's Long-term Research Collaborations Overseas

CDC manages research collaborations (sometimes referred to as “field stations”) in Côte D'Ivoire, Guatemala, Uganda, Guinea, Kenya, Botswana, and Thailand, and is establishing long-term collaborative projects that may form the basis for a permanent center in Vietnam. In general, CDC provides core funding for the field stations, and USAID and other donors provide additional support for both core activities and special projects.

The field station in Kenya is a collaborative effort between CDC and the Kenya Medical Research Institute (KEMRI). Most of the research takes place in western Kenya, in an area of intense, year-round malaria transmission and high incidence of HIV/AIDS. Major studies have

- Demonstrated that presumptive malaria treatment of pregnant women decreases the number of low birth-weight babies born.
- Demonstrated that use of insecticide-impregnated bednets reduces mortality among children less than 2 years of age in areas of high transmission.
- Provided critical information about the immune response to malaria that is being used to design vaccines.

The field station is also studying the impact of coinfection with HIV and malaria, particularly in pregnancy. Other ongoing activities concern the development of immunity to vaccines among HIV-positive children, defining local spectrum of diarrheal diseases and antimicrobial resistance among diarrheal pathogens, and addressing the consequences of coinfection with HIV and schistosomiasis.

The field station in Guatemala—the Medical Entomology Research and Training Unit/Guatemala, or MERTU/G, is integrated into the Universidad del Valle and works closely with the Guatemalan Ministry of Health. MERTU/G has helped evaluate national prevention and control efforts related to malaria and onchocerciasis. Research on leishmaniasis has led to improved clinical treatment regimens, and research on foodborne and waterborne diseases such as cholera has led to improved prevention methods. To reduce deaths due to Chagas disease—a significant health problem in Guatemala—the Guatemalan Ministry of Health and MERTU/G are conducting nationwide surveys to determine prevalence and risk factors; supporting field and molecular studies of the triatomine insect that carries the disease; and evaluating blood bank practices that may contribute to transmission through blood transfusions.

Future Directions: Capacity Building

The field stations have provided valuable opportunities for CDC scientists to participate in long-term, on-site research on selected diseases of importance in developing countries. Expansion of the field stations and strengthened ties with local ministries of health would facilitate additional opportunities to investigate endemic diseases, respond to new or emerging diseases, and provide a stable training center for epidemiologists and laboratory scientists from CDC and the local region. As part of CDC's global strategy, one of the existing field stations may also provide the nucleus of the first International Emerging Infections Program (page 53).

VISION FOR THE FUTURE

This document defines CDC's global infectious disease priorities in six areas, keeping in mind the intimate relationship between international and U.S. health, selected in consultation with global public health partners. In looking towards the future, CDC envisions increased activity and progress in each area:

1 International Outbreak Assistance.

CDC will maintain the capacity to identify and investigate a broad spectrum of human diseases and serve as an internationally recognized resource that helps maintain global awareness of new and emerging threats.

2 A Global Approach to Disease Surveillance.

Regional and disease-specific surveillance and response networks will increase in number and geographical area until they cover all parts of the world and monitor all infectious diseases of regional or global importance. The networks will link up with each other and evolve into a global "network of networks" that provides early warning of new health threats—including drug-resistant diseases—and increased capacity to monitor the effectiveness of public health control measures.

3 Applied Research on Diseases of Global Importance.

CDC's laboratorians, epidemiologists, and behavioral scientists will maintain an active research program to develop tools to detect, diagnose, predict, and eliminate infectious diseases of global or regional importance. When a new disease threat is reported anywhere in the world, CDC's laboratorians and field investigators will be available to help answer questions about disease transmission, treatment, control, and prevention.

4 Application of Proven Public Health Tools.

The worldwide burden of infectious diseases will be significantly reduced as currently available tools with documented efficacy are rapidly disseminated to the most severely affected populations. Research discoveries will be translated into practical treatments, vaccines, diagnostic tests, and disease prevention strategies that are ready for use by ministries of health and public health agencies. CDC's resources will be effectively marshaled to assist its partners in applying these tools in many countries, saving millions of lives.

5 Global Initiatives for Disease Control.

Sustained global efforts will reduce the prevalence of HIV/AIDS in young people by 25% and reduce deaths from TB and malaria by 50% by 2010. Infant mortality will be reduced in the

poorest countries through enhanced delivery and use of vaccines against respiratory illnesses and other childhood diseases. Polio and dracunculiasis will be eradicated worldwide, paving the way for future efforts to eliminate such diseases as measles, lymphatic filariasis, onchocerciasis, Chagas disease, trachoma, rubella, and hepatitis B.

6 Public Health Training and Capacity Building.

An interconnected group of International Emerging Infectious Disease Programs (IEIPs) will integrate disease surveillance, laboratory studies, and prevention activities, and provide hands-on public health training in disease detection, program management,

and outbreak investigation. The IEIP sites will partner with Field Epidemiology Training Programs (FETPs) and other institutions to perform population-based research on transmission of endemic and emerging diseases and conduct emergency surveillance whenever a new threat appears. The long-term goal of the IEIPs will be to develop sustainable, in-country human capacity to participate in national and regional efforts for disease surveillance and outbreak response.

Implementation of specific objectives in these six areas will help realize CDC's vision of a world in which U.S. citizens and all people everywhere are better protected from infectious diseases.

PARTNERSHIPS AND IMPLEMENTATION

This plan was prepared by CDC's National Center for Infectious Diseases, in collaboration with other major CDC centers and programs involved in addressing emerging infectious diseases. These include the Office of Global Health, the National Center for HIV, STD, and TB Prevention, the National Immunization Program, the Epidemiology Program Office, and the Public Health Practice Program Office. CDC has also worked with global organizations and agencies to develop this strategy. Website addresses providing additional information about partner organizations and health publications and reports referred to in this document are provided in Box 2 and throughout the text of the document.

The strategy will be implemented incrementally over the next five years, as funds become available, beginning with the highest priorities for 2001-2002 (Box 1). As CDC carries out this strategy, it will coordinate with foreign governments, international organizations (including WHO, the Joint Unit-

ed Nations Programme on AIDS [UNAIDS], and the United Nations Children's Fund [UNICEF]), other U.S. agencies (including USAID, the National Institutes of Health [NIH], the Food and Drug Administration [FDA], the Department of Defense [DoD], the Department of Veterans Affairs [DVA], the U.S. Department of Agriculture [USDA], the National Oceanic and Atmospheric Administration [NOAA], and the National Aeronautics and Space Agency [NASA]), professional societies, research institutions, and schools of public health, medicine, nursing, and veterinary science.

CDC will also participate in international coalitions that support disease eradication efforts and other regional and global health initiatives. These coalitions may include national and local nongovernmental organization (NGOs; e.g., Rotary International and CARE), community-based and faith-based organizations, and communities of color. In addition, CDC will work closely with groups that conduct or promote regional disease surveillance, such as the Caribbean Epidemiology Center (CAREC), the Asia-Pacific Economic Cooperation (APEC; see also Appendix E), and the Training in Epidemiology and Public Health Interventions Network (TEPHINET).

Other implementation partners include

- Pharmaceutical and biotechnology companies that develop vaccines, drugs, and rapid diagnostic tests
- NGOs that address related health problems (e.g., maternal and child health, environmental health, occupational health, and chronic illnesses)
- Development agencies, development banks, foundations, and other organizations that aim to reduce poverty by reducing the incidence of endemic diseases
- The primary modality for action will be through partnerships with other institutions.
- CDC will work in technical areas in which it has established expertise and capability.
- CDC will pursue long-term bilateral relationships, because of their enhanced productivity.
- CDC will ensure that it has the workforce and administrative mechanisms required for full implementation of the infectious disease strategy.

As emphasized in *CDC's Working with Partners To Improve Global Health: A Strategy for CDC and ATSDR*¹¹ (<http://www.cdc.gov/ogh/pub/strategy.htm>), CDC's collaborative work overseas will be based on five approaches:

- CDC's activities will be rooted in sound science, bioethical principles, and local needs.

PRIORITIES AND OBJECTIVES

Priority Area 1: International Outbreak Assistance

When a new, highly dangerous, or reemerging disease is detected anywhere on the globe—whether in a developing or industrialized country, in a close ally or a “nation of concern”—U.S. citizens, as well as foreign governments, often rely on CDC to provide outbreak assistance and public health information. CDC is unusual among public health institutions in its comprehensive capacity to identify a wide range of infectious bacteria, viruses, fungi, parasites, and rickettsia.

In past years, however, maintaining this capacity has not always been a priority. Attempts have been made to cut costs by reducing support for laboratory expertise on diseases that are currently uncommon in the United

States, including zoonotic diseases like plague and leptospirosis. However, CDC’s repeated experience with outbreaks of diseases once thought to be archaic or obscure—including a 1994 outbreak of plague in India, a 1995 outbreak of a virulent pulmonary form of leptospirosis in Nicaragua, and a 2000 outbreak of leptospirosis in Malaysian Borneo among athletes at an international competition (Box 11)—has underscored the value of having a comprehensive, integrated ability to identify and investigate most human diseases and to recognize new threats. However, gaps remain in CDC’s repertoire of diagnostic tools in such areas as diseases caused by prions (e.g., new variant Creutzfeldt-Jakob

Outbreak of Ebola hemorrhagic fever, Uganda, 2000. The isolation ward of Gulu Municipal Hospital, Gulu, Uganda, during an outbreak of Ebola hemorrhagic fever in October 2000. There is no known drug treatment or vaccine for this disease, which is transmitted person-to-person through contact with infected bodily fluids and has a case-fatality ratio of 50–90%.

At the invitation of the Ugandan Ministry of Health, CDC sent several teams of scientists to Gulu to participate in a multinational WHO-coordinated response team. The response team helped bring the epidemic under control by providing assistance and consultation to help rapidly identify cases, provide safe care, and interrupt the spread of the virus.

Photographer: Daniel Bausch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, CDC



Box 11

An Outbreak of Leptospirosis Affecting Athletes from 26 Countries Reported by the GeoSentinel Disease Surveillance System

In September 2000, several athletes returning home from the EcoChallenge-Sabah 2000 multisport expedition race in Malaysian Borneo fell ill with leptospirosis, apparently contracted while swimming in a contaminated river. Leptospirosis causes severe fever, headache, chills, muscle pain, and cramps. Left untreated, it can lead to kidney and liver failure, meningitis, and death.

Three clinics that participate in GeoSentinel, the global surveillance network of the International Society of Travel Medicine (Appendix E), reported a cluster of acute febrile illness among Eco-Challenge racers and helped identify its cause. A clinic in London, England, reported four instances of suspected leptospirosis and queried other GeoSentinel sites for similar cases. Clinics in New York City and Toronto responded with reports of five more cases among the same group of athletes, and

all communicated their findings to CDC. Further evaluation indicated that all cases were clinically compatible with leptospirosis.

Leptospirosis is contracted by coming into contact with or swallowing water contaminated with animal urine. During the 12-day Eco-Challenge race, approximately 300 athletes from 26 countries sailed on open ocean and then bicycled and hiked through torrential jungle rain and mud. After that, the racers swam and canoed in a storm-swollen river and waded through caves filled with bat guano. Analysis by CDC suggested that participating in the river swim was significantly associated with illness. At least 44% of the 155 U.S. participants were affected. Additional cases of leptospirosis were identified in athletes from several other countries as well.

disease, the human consequence of infection with bovine spongiform encephalopathy, or “mad cow disease”), and some areas require upgrading to remain effective (e.g., leptospirosis, yellow fever, diphtheria, anthrax, and helminthic diseases).

CDC frequently collaborates on international outbreak investigations conducted in partnership with host nations. CDC participation occurs on an ad hoc basis, in response to requests for assistance from foreign governments or WHO. There is no formal structure for this activity, nor are there designated resources. An underlying principle of the global strategy is the recognition that interna-

tional outbreak assistance is an integral function of CDC. Supporting this function will require augmenting, updating, and strengthening CDC’s diagnostic facilities, including laboratories that participate in the WHO Collaborating Centre network, as well as capacity for epidemiologic investigation overseas, including field logistics and data management.

Outbreak follow-up. In the future, as part of the global strategy, CDC will routinely offer to assist host-country ministries of health and WHO in assessing the public health situation in the aftermath of a major outbreak. If requested, CDC will send a dedicated

prevention team to revisit the outbreak site and suggest additional strategies to improve disease surveillance and outbreak response. The team will share clinical and epidemiologic outbreak data with health authorities and work to strengthen local laboratories. The team may also sponsor local workshops or conferences to consider lessons learned from the outbreak, review local hospital resources, and discuss long-term surveillance efforts. These follow-up efforts will help maintain mutually beneficial relationships and research partnerships between CDC, WHO, and local health authorities (Box 12 and Priority Area 2).

Box 12

Follow-up Activities in the Aftermath of the 1994 Plague Outbreak in India

In September, 1994, rumored outbreaks of bubonic and pneumonic plague in western India caused widespread panic and extensive disruptions in international travel and trade. The Indian Ministry of Health authorized an investigation by a WHO international team that included scientists from CDC, the Russian Federation, and by the WHO South East Asia Regional Office. The work of this team was severely compromised by the inability of Indian laboratories to confirm plague cases by using standard diagnostic methods.

The lack of diagnostic capabilities arose because the Indian Ministry of Health, a former world leader in plague vaccines and diagnosis, believing that plague no longer existed in the country, had allowed its laboratory diagnostic infrastructure to deteriorate. At the suggestion of WHO, the government of India invited CDC team members to return to conduct field training exercises with Indian epidemiologists and hold workshops in plague microbiology at India's National Institute for Communicable Diseases (NICD). Later that year, microbiologists from NICD, the All-India Institute of Medical Science, and the Haffkine Institute in Bombay came to CDC's laboratory in Fort Collins, Colorado, as visiting scientists to learn techniques for confirming infection with *Yersinia pestis* (the causative agent of plague), procedures for preparing standardized diagnostic reagents,

and new and advanced molecular methods for identifying and characterizing *Y. pestis* strains.

The relationships that developed among U.S. and Indian scientists during the 1994 outbreak and subsequent collaborations had lasting scientific and diplomatic effects. During the Cold War, India had maintained few contacts with the U.S. public health community, preferring to collaborate with Russian health officials, who (up until 1989) had sent regular shipments of plague diagnostic reagents to NICD. After 1994, however, India was more open to public health collaboration with the United States. For example, the Indian Ministry of Health worked closely with CDC when it renovated and modernized its national plague laboratory during the late 1990s, and also when it reorganized and computerized its national communicable disease surveillance system. The Indian Ministry of Health also played an active role in two regional and two global workshops on plague organized by WHO and CDC between 1996 and 2000.

International contacts made during the 1994 plague outbreak also led to working relationships with the Kazakh Institute for Research on Plague Control in Almaty, Kazakhstan, the Chinese Academy of Preventive Medicine in Beijing, and the Institute of Endemic Diseases Control and Research in Yunnan, China.

Objectives for Priority Area 1

Dedicate Resources to International Outbreak Assistance

- Facilitate CDC participation in international outbreak investigations by
 - Developing standard operating procedures for responding to governments' requests for outbreak assistance, in coordination with WHO
 - Identifying and purchasing equipment and reagents and increasing capacity for logistical support
 - Establishing standard procedures for distributing and tracking specimens for efficient testing at more than one CDC laboratory when the cause of an outbreak is unknown.
 - Maintaining an inventory of CDC personnel with expertise in diseases of regional or global importance
- Maintaining a registry of disease specialists outside of CDC who have expertise in diseases of regional or global importance ("Active Reserves")
- Developing research protocols that might be used during outbreak investigations for controlled trials of drug treatments or other public health interventions (see Priority Area 3)

Box 13

Outbreaks Among Refugees in Kosovo and the Sudan

Tularemia in Kosovo

In April and May, 2000, an epidemiologist and ecologist from CDC joined a WHO-led investigation of an outbreak of tularemia among displaced persons returning to damaged homes and farms in rural Kosovo. The illness, which affected 500 to 1,000 people, was characterized by fever, severe sore throat, enlarged lymph nodes in the neck, and abscess formation.

The people who fled from Kosovo in March 1999 had left behind unharvested crops and homes with unprotected stocks of food. Over the following months, the local populations of field mice and domestic rats increased exponentially. Returning refugees became ill after ingesting food and water contaminated with

rodent excrement and carcasses containing the bacteria *Francisella tularensis*. The epidemic was halted by instituting simple sanitation measures.

Louseborne Relapsing Fever in the Sudan

In April, 1999, epidemiologists from CDC assisted WHO in investigating an apparent outbreak of hemorrhagic fever in southern Sudan among seminomadic tribes displaced by famine, civil war, and intertribal strife. The causative agent proved to be the spirochete *Borrelia recurrentis*, which is transmitted by body lice. The outbreak affected about 20,000 people and caused about 2,000 deaths before the diagnosis was established and disease control measures were implemented.

- Strengthening the capacity of developing countries to identify outbreaks and to request WHO, CDC, or other outside assistance as needed

Strengthen Diagnostic Capacity

- Strengthen CDC laboratories (including CDC-based WHO Collaborating Centres) that can identify diseases that are rare or unknown, drug-resistant, or highly dangerous.
This effort will include strengthening CDC's capacity to identify animal diseases that can affect humans, working in conjunction with USDA and other partners.
- Strengthen national public health laboratories in developing countries by providing diagnostic refer-

ence reagents, laboratory manuals, and training opportunities for laboratory scientists.

Strengthen Investigative Capacity at CDC

- Rebuild CDC's capacity to respond to international outbreaks.
- Maintain and expand epidemiologic expertise in a wide range of pathogens, helping to create a new generation of experts in infectious disease prevention and control.
- Strengthen international collaboration during investigations, working with many partners, including
 - WHO Global Alert and Response Network (Box 14; <http://www.who.int/emc-documents/surveillance/docs/whodscsr2003.pdf> and

<http://www.who.int/emc-documents/surveillance/docs/whodscsr2002.pdf>).

- European Programme for Intervention Epidemiology Training (EPIET; <http://www.epiet.org/epiet>).
- U.S.-Mexico Border Infectious Disease Surveillance system (BIDS; <http://www.r10.tdh.state.tx.us/obh/bids.htm>).
- Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET <http://asclepius.ic.gc.ca/tephinet/>).
- Improve coordination among the Department of State, CDC, state and local agencies during investigations of infectious disease threats at U. S. ports of entry.

Box 14

WHO and CDC: Collaboration on International Outbreak Assistance

WHO and CDC work in close partnership to help control outbreaks that involve diseases of unknown cause, diseases with high fatality rates, and diseases that are likely to spread across borders:

- As an international entity, WHO is a critical partner in opening doors to U.S. scientists, facilitating U.S. participation in international efforts to identify new threats and contain potential pandemics. WHO also plays a special role in international press management, encouraging nations to share outbreak information while helping to minimize false rumors that cause damage to the trade and tourism industries of affected countries.
- CDC provides WHO with technical guidance, including diagnostic and epidemiologic support. Because

WHO does not maintain laboratory resources of its own, it relies upon an international network of Collaborating Centres that includes more than 30 diagnostic laboratories located at CDC (Appendix D)

At the present time, WHO is strengthening its ability to facilitate international outbreak response efforts, as well as to support global health initiatives that address infectious diseases (see Box 6). As part of this effort, WHO is establishing a Global Alert and Response Network to promote prompt reporting of disease outbreaks and help coordinate offers of outbreak assistance—e.g., supplies, consultation, or on-site support—from public and private sector partners.

- Ensure that the United States is prepared to assist in investigations of international bioterrorist incidents.
- Continue to work with WHO and other partners to investigate epidemics that occur among refugees and displaced persons (Box 13).

Strengthen Control Efforts

- Strengthen CDC's capacity to provide prompt and effective epidemic control, by assigning epidemiologists to help monitor disease spread overseas, laboratory scientists to provide rapid diagnostic testing, and social and behavioral scientists to design and implement community education and mobilization efforts.

- Support efforts to provide supplies during outbreak emergencies by partners such as FDA, WHO, NGOs, pharmaceutical companies, multinational corporations, and other members of the private sector.

Offer Follow-Up

- Offer to conduct follow-up activities at the site of an outbreak, in collaboration with ministries of health, WHO, International Emerging Infections Programs (IEIPs; page 53), and existing national or donor-supported disease control programs. Activities may include

- Sharing data to guide ongoing control programs
- Improving infection control practices
- Building laboratory capacity
- Establishing ongoing surveillance for the outbreak pathogen
- Implementing long-term prevention strategies through the application of proven health tools (see also Priority Area 4)

Priority Area 2: A Global Approach to Disease Surveillance

Stimulated in part by the AIDS pandemic, national and international groups, including the National Science and Technology Council in 1995 and the Group of Eight in 1997, have called for the establishment of a global system for disease surveillance and outbreak response. U.S. agencies are working with international partners to help achieve this goal.

Despite advances in public health telecommunications, however, the global implementation of this goal has not been straightforward. Notable progress has been made at the regional level, with the establishment of such international programs as the Caribbean Epidemiology Center's disease surveillance network, the Amazon and Southern Cone networks in South America, the Integrated Disease Surveillance and Epidemic Preparedness and Response Project in Africa, the Mekong Basin Disease Surveillance system in Southeast Asia, and the International Circumpolar Surveillance system in Alaska, Canada, Greenland, and the circumpolar regions of Europe. These and other

fledgling networks (Appendix E) represent pioneering attempts to work across borders to enhance detection and control of outbreaks of known diseases while maintaining the flexibility to recognize new disease problems. The networks are testing many different approaches (e.g., syndromic surveillance, laboratory-confirmed disease-specific surveillance, hospital-based surveillance, and district-level surveillance), depending on local needs, cultural preferences, and human and technological resources.

In the years ahead, regional disease surveillance networks will grow in number and geographical scope. In the long run, regional and disease-specific networks should expand, interact, and evolve into a global "network of networks" that helps ensure early warning of new and reemerging threats and increased capacity to monitor the effectiveness of public health control measures

CDC can stimulate this process by providing technical assistance, evaluating regional progress, and working with WHO, other U.S. agencies, and other interested groups to strengthen the networks' telecommunications capacities and encourage the use of common software tools and harmo-

nized standards for disease reporting. CDC can also help revise the International Health Regulations, which describe internationally-reportable diseases and syndromes. In addition, CDC will encourage linkages between regional networks and veterinary surveillance systems that monitor illnesses and epidemics among agricultural and feral animals. Several major outbreaks of zoonotic diseases (diseases of animals that also affect humans) involving agricultural animals have occurred in recent years (Box 15). CDC will also support disease surveillance efforts in tropical or heavily forested areas that are likely sources of human infection with unknown zoonotic or vectorborne diseases.

CDC's priorities in global surveillance will be balanced with the priorities of collaborating countries, and CDC's programs will be coordinated with the ongoing efforts of development agencies and NGOs that build disease surveillance capacity at the national level. CDC can best support both national and regional efforts by providing state-of-the-art diagnostic and epidemiologic tools; by developing surveillance standards and guidelines, and by creating new methods for predicting disease risk. CDC can also increase training opportunities by helping establish new or expanded Field Epidemiology Training Programs (FETPs), Public



Disease surveillance personnel at the Caribbean Surveillance System (CARISURV) of the Caribbean Epidemiology Center (CAREC). CARISURV is an electronic disease surveillance system that serves 21 nations: Anguilla, Antigua & Barbuda, Aruba, Bahamas, Barbados, Belize, Bermuda, British Virgin Islands, Cayman Islands, Dominica, Grenada, Guyana, Jamaica, Montserrat, Netherlands Antilles, St. Kitts & Nevis, St. Lucia, St. Vincent & Grenadines, Suriname, Trinidad & Tobago (host country), Turks & Caicos Islands.

CARISURV employs computer-based modules to:

- Track cases of measles as part of PAHO's campaign to eliminate measles in the Americas
- Track cases of HIV/AIDS
- Track cases of unusual or unexplained diseases reported by CAREC's Physician-Based Sentinel Surveillance system

- Compile weekly reports of notifiable diseases
- Maintain a database of deaths caused by infectious agents
- Help provide distance-learning courses for public health and medical personnel

A new module that facilitates hotel-based disease surveillance is under development.

CDC and the Walter Reed Army Institute of Research have worked with CAREC to provide CARISURV members with bioinformatics training, technical support, computer equipment, and public health software, including the Public Health Laboratory Information System (PHLIS) for reporting laboratory-confirmed cases of infectious disease. PHLIS was originally developed at CDC for use by U.S. state health departments.

Information Services Unit, CAREC.

Health Schools Without Walls (PHSWOW; <http://www.tulane.edu/~phswow/>), and Sustainable Management Development Programs (Priority Area 6, Boxes 16 and 24).

The surveillance data gathered by the regional networks will be used not only to detect outbreaks but also to evaluate global health initiatives (Priority Area 5) and to drive national public health programs and decision-making. Disease surveillance data are crucial, for example, in assessing the effectiveness of vaccination programs and the risk factors for underimmunization in a given area.

Objectives for Priority Area 2

Facilitate Regional Disease Surveillance

- Work with WHO and other partners to identify gaps in global disease surveillance by conducting a health situation analysis.
- Provide technical and material assistance to regional networks that can fill global gaps in disease surveillance.
- Host meetings that bring the leaders of regional surveillance networks together on a periodic basis to exchange experiences and methods and facilitate collaboration.
- Develop surveillance modules that can facilitate standardization of disease reporting among regional disease surveillance networks.

Box 15

Agricultural Costs of Controlling Zoonotic Diseases Carried by Food Animals

When a dangerous animal-borne disease spills over into the human population, a government may be forced to slaughter large numbers of food animals as a control measure, despite considerable economic costs.

This happened in 1999 when Malaysian health authorities were faced with an outbreak of encephalitis among farm workers that had a nearly 50% mortality rate. The cause of the outbreak turned out to be a previously unknown paramyxovirus called the Nipah virus, which is carried by swine. To control the outbreak, millions of pigs were slaughtered within a few weeks, severely harming the Malaysian meat industry. Two years before, a similar precautionary measure was taken by the government of Hong Kong, which arranged the culling of all 1.6 million chickens on Hong Kong Island and the New Territories to prevent chicken-to-human transmission of a virulent avian form of influenza (Box 5).

The costs of measures to control the outbreak of bovine spongiform encephalopathy (BSE, or “mad cow disease”) in the United Kingdom and continental Europe, and the related outbreak of an invariably fatal human neurodegenerative disease (new variant Creutzfeldt-Jakob disease [nvCJD]) have also been high. Ingestion of beef containing the causative agent of BSE (a prion) can result in the development of nvCJD many years later. The export of live cattle and cattle products (other than milk) from the UK has been temporarily banned by the European Commission, and trade in these products has been affected on a global basis. Gov-

ernment officials have come under fire, and consumers across Europe have changed their eating habits due to concern over the spread of BSE. Control measures, including the slaughter of affected cows, have thus far cost the U.K. government an estimated 3.5 billion pounds (about 5 billion U.S. dollars).

The rapidly spreading outbreak of foot-and-mouth disease in Great Britain and continental Europe in 2001 threatens to dwarf the economic costs of the BSE epidemic and devastate the centuries-old British livestock industry. Foot-and-mouth disease does not infect humans but can be spread by travelers who have contaminated soil on their shoes or clothing or who carry contaminated food products. The St. Patrick’s Day parade in Ireland was cancelled due to concerns about spreading the virus, and the British army has been drafted to help bury the carcasses of animals slaughtered because of potential exposure to the disease. Officials credit high-quality animal health surveillance and importation restrictions for the absence of foot-and-mouth disease in the United States, but remain concerned because similar measures have failed to contain the spread of the disease in continental Europe.

These examples demonstrate the potential impact an infectious disease outbreak can have on commerce as well as on human and animal health. If the United States were forced to destroy a significant number of cattle, sheep, pigs, or chickens to control an epidemic, the costs might easily rise into the billions.

Modules may cover sentinel disease surveillance, disease-specific surveillance, and syndromic disease surveillance.

- Help WHO strengthen WHO country and regional offices by providing CDC scientists, as needed, to assist with national and regional disease surveillance efforts.
- Assign epidemiologists and laboratory scientists from CDC to DoD laboratories in Indonesia, Kenya, and Thailand, in addition to those already in Egypt and Peru, to support DoD efforts to help strengthen regional disease surveillance (Appendix E).
- Engage nontraditional partners, such as medical missionary organizations and multinational corporations, in regional disease surveillance activities, particularly in regions that lack adequate public health infrastructures.

Use State-of-the-Art Tools

- Work with DoD, USAID, development banks, foundations, and other partners to provide public health agencies in developing countries with hardware (e.g., hand-held computers for field use), specialized software (e.g., EPI INFO 2000, PHLIS, and LITS+), and reliable Internet access to facilitate participation in regional infectious disease networks and training activities.

- Work with many partners to provide regional networks with field-friendly diagnostic tests (e.g., dipsticks).
- Work with WHO and other partners to develop laboratory standards for diagnostic testing and data standards for disease and syndrome reporting.

Promote New Paradigms for Global Disease Surveillance

- Establish mechanisms for regular information exchange between veterinary and agricultural organizations and public health agencies on new and re-emerging animal diseases that might affect humans.
- Work with NOAA, NASA, DoD, NIH, the National Science Foundation, and many other partners to create models that predict the risk of zoonotic and vectorborne disease by integrating climatic, environmental, veterinary, entomologic, and epidemiologic data. CDC can play a major role in providing epidemiologic data.
- Encourage the use of molecular methods for microbial subtyping and outbreak detection, such as PulseNet methods for the detection of foodborne disease outbreaks (see Surveillance for Foodborne and Waterborne Diseases).

Strengthen WHO's Disease-Specific Global Surveillance Networks

- Provide technical assistance to WHO-sponsored networks that monitor specific diseases of global importance, such as polio, measles, influenza, and TB (Appendix E).
- Work with WHO to help establish a global network for surveillance and control of plague, using the WHO Influenza Surveillance Network as a model.
- Work with WHO and other partners to help draft a new set of International Health Regulations (IHR) that includes a set of internationally-reportable diseases or disease syndromes.

Facilitate Surveillance for Foodborne and Waterborne Diseases

- Improve global surveillance for foodborne and waterborne diseases by
 - Establishing sentinel surveillance sites for foodborne and waterborne disease at International Emerging Infections Programs (IEIPs; page 53).
 - Working with PAHO and FDA to expand PulseNet—the U.S. early warning system for foodborne diseases—into a regional system for detecting outbreaks of foodborne disease throughout

the Americas. PulseNet compares the molecular fingerprints of bacterial isolates from many different sources. It can trace the source of an outbreak to shipments of contaminated food bought and consumed at different geographic locations. (See Box 2.)

- Establishing a mechanism for the regular exchange of surveillance information on foodborne diseases (e.g., salmonellosis, shigellosis, and *E. coli* O157:H7 infection), including PulseNet fingerprinting data, with European Union partners.
- Seek WHO approval for establishing a CDC-based WHO Collaborating

Center for Salmonella Surveillance that provides support to WHO's Global Salmonella Surveillance system (Global Salm-Surv).

Facilitate Surveillance for Antimicrobial Resistance

- Provide technical assistance to help implement WHO's Global Strategy for the Containment of Antimicrobial Resistance (<http://www.who.int/emc/globalstrategy/strategy.html>).
- Work with other U.S. agencies to draft and implement Part II of the U.S. Public Health Action Plan To Combat Antimicrobial Resistance (Box 4), which will consider the role of the U.S. Government in

addressing global resistance problems, such as the spread of multidrug-resistant TB.

- Increase the number of regional laboratories that conduct state-of-the-art testing for drug resistance, working through the WHO External Quality Assurance System and the WHO Collaborating Centre for Antimicrobial Resistance and using the new WHO/CDC laboratory manual for standardized susceptibility testing.
- In collaboration with WHO, the European Union, and other partners, explore the possibility of establishing an expert working group that sets international standards for detecting and reporting drug-resistant threats.

Box 16

A Growing Community of International Public Health Leaders

By fostering contacts between CDC staff and scientists from other countries (during outbreak investigations, scientific conferences, training courses, and disease prevention projects), CDC is helping build an international community of epidemiologists and laboratory scientists who are prepared to respond to emerging infectious disease threats, whenever and wherever they arise. Often linked by e-mail, as well as by phone and fax, these individuals are part of an informal network that shares outbreak alerts and research data and provides assistance and consultation during infectious disease emergencies.

In addition to these informal exchanges, CDC offers formal training programs in epidemiology (e.g., through Field Epidemiology Training Programs, the Public Health Schools Without Walls, and the Epidemic Intelligence Service), laboratory diagnostics (e.g., through fellowships and disease-specific training workshops), and public health management (e.g., through the Sustainable Management Development Program) that support the development of public health leaders around the world.

Priority Area 3: Applied Research on Diseases of Global Importance

CDC's researchers have a dual role. They not only identify the microbes, risk factors, and epidemiologic conditions that lead to outbreaks, but also conduct applied research on ways to detect, prevent, and control them. Maintaining a comprehensive diagnostic and investigative capacity goes hand-in-hand with maintaining a broad-based research program on endemic and epidemic diseases that includes studies in applied epidemiology, microbiology, and behavioral and social science.

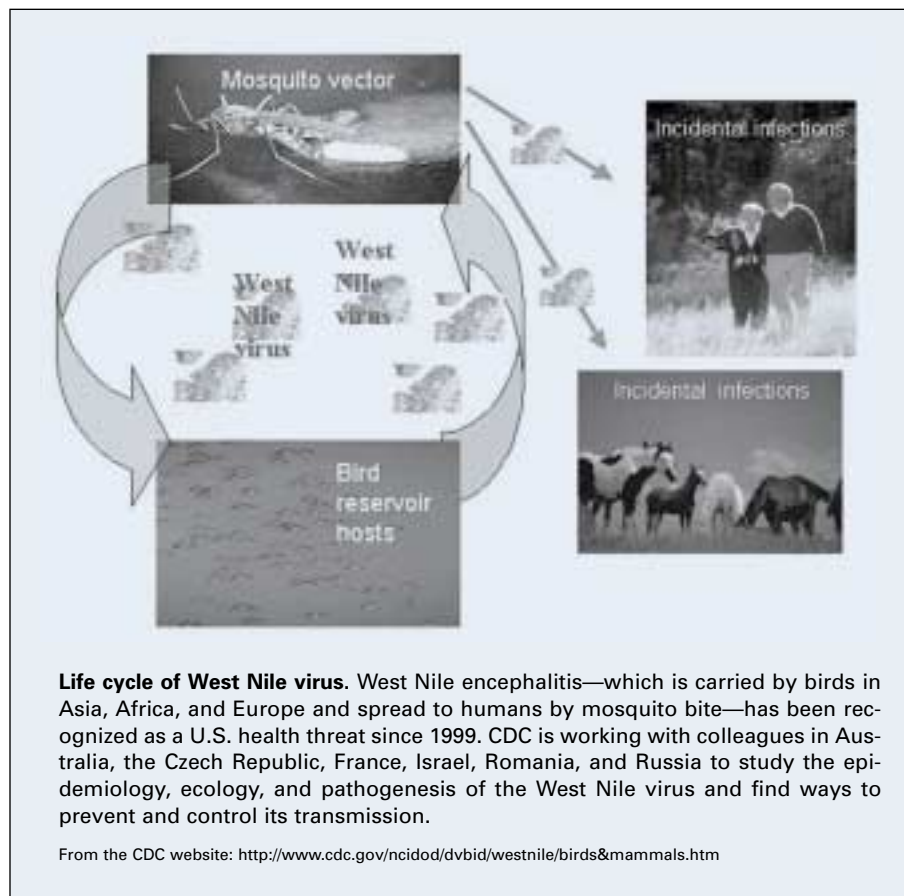
A research program on diseases that are uncommon in the United States is a valuable resource, both for humanitarian reasons and because of the dangers represented by some imported diseases. Had scientists begun to study "slim disease"—now known as AIDS—when the syndrome was described in central Africa in the late 1970s,¹² the world health community might have learned much earlier how HIV is acquired and what can be done to prevent its spread.

An in-depth knowledge of a wide range of infectious pathogens can also facilitate the identification and characterization of new microbes that emerge in the United States. One example concerns hantavirus pulmonary syndrome (HPS), an often-fatal disease first identified in 1993 in the Four Corners region of the United States. In 1993 hantavirus research was a low priority

in the United States, because hantavirus-associated disease had never before been recognized in the Western Hemisphere. However, a few laboratories supported by DoD had continued to collect information on a hantaviral disease called Korean hemorrhagic fever or hemorrhagic fever with renal syndrome (HFRS) that killed a significant number of United Nations troops during the Korean Conflict. Because of these HFRS studies, the CDC out-

break team in Four Corners was armed with sophisticated serologic and molecular tools that allowed them to diagnose HPS in a short time. Because it was known that the HFRS hantavirus is transmitted by rodents, the team rapidly honed in on the animal reservoir of the HPS virus and provided disease prevention guidelines to the people in the area.

Several fundamental precepts inform CDC's infectious disease



research collaborations with other countries. First, the overriding purpose of CDC's research work overseas is to lead the way in demonstrating how individuals and governments can best prevent and control disease. Second, it is important for CDC to help strengthen international research capacity by supporting extramural research at home and abroad, through collaborations, cooperative agreements, and peer-reviewed grants. Third, CDC's research activities must be rooted in bioethical principles, respecting the needs and rights of human research subjects. Fourth, CDC must strive to engage new research partners, in addition to its traditional partners at universities and schools of public health. Research collaborators may include scientists from private companies, NGOs, and other U.S. agencies (e.g., NIH, FDA, DoD, NASA, NOAA, and USDA).

Long-term, on-site research collaborations are especially important, because it is often very difficult to study new and hazardous pathogens while an outbreak is in progress. Long-term partnerships with in-country research institutions may be mutually beneficial, facilitating collaborative field research and clinical studies, providing opportunities for technology transfer and training, and building international friendships and trust within the scientific and public health communities.

Objectives for Priority Area 3

Strengthen Overseas Research Collaborations by Establishing IEIPs

- Establish an inventory of existing and potential sites for long-term, on-site research collaborations to address infectious disease problems of regional importance. The inventory should evaluate:
 - How the site might fill geographical and disease-specific research gaps
 - The site's potential as a center for research training
 - Opportunities to engage multiple partners, including in-country partners (e.g., public health agencies and universities) and U.S. agency partners (e.g., NIH and DoD)
 - Opportunities to leverage resources and ensure sustainability
- Create International Emerging Infections Programs (IEIPs), using the information from the inventory described above. (See also Priority Area 6.)

Conduct Research on Vector-borne and Zoonotic Diseases

- Support the development of field-friendly diagnostic tests for the detection of zoonotic and vector-borne disease, as well as new methods for animal and vector control.
- Support research on the epidemiology, ecology, and pathogenesis of vectorborne and zoonotic diseases of current international concern, including malaria, West Nile fever, dengue fever, Nipah virus encephalitis, rabies, Q fever, leishmaniasis, typhus, plague, and Chagas disease.
- Search for the animal or insect reservoirs of Ebola and Marburg hemorrhagic fevers, working through the CDC-based WHO Collaborating Centre for Viral Hemorrhagic Fevers and collaborating with the South African National Institute of Virology and other partners.
- Investigate the relationship between environmental conditions and the emergence of zoonotic and vector-borne diseases.

Conduct Vaccine Research

- Encourage and support the development and evaluation of vaccines against diseases of global health importance (Boxes 17 and 18).
- Support research on ways to decrease the cost of expensive vaccines like conjugate *Haemophilus influenzae* type b and pneumococcal vaccines in developing countries (e.g., administering them less frequently or in lower doses).
- Help define the epidemiology and public health burden (illness, mortality, and cost) of vaccine-preventable diseases in developing countries, and monitor the declining burden of disease associated with widespread vaccination. (See also the next section.)

Conduct Research in Support of Global Initiatives for Disease Control

- Encourage and support basic research to improve our understanding of the genetics, physiology, and pathogenesis of parasites, bacteria, and viruses that cause illnesses targeted by global initiatives for disease control.

Box 17

CDC's Role in the Development of Vaccines Against Diseases of Global Importance

CDC supports the vaccine development goals of the Global Alliance for Vaccines and Immunization (GAVI), the International AIDS Vaccine Initiative, the DHHS Blueprint for TB Vaccine Development, and the Malaria Vaccine Initiative. Over the next 5 years, CDC will work with NIH, FDA, USAID, DoD, and many other public and private partners to help develop:

- A multistage vaccine against malaria, as part of the Malaria Vaccine Initiative, funded by the Bill and Melinda Gates Children's Vaccine Program
- A DNA-based vaccine against HIV/AIDS, in collaboration with the Emory Vaccine Center in Atlanta, Georgia
- Strain-specific vaccines against dengue and dengue hemorrhagic fever, in collaboration with Mahidol University in Salaya, Nakhonpathom, Thailand
- Conjugate vaccines against meningococcal meningitis group A, in collaboration with WHO and the Bill and Melinda Gates Children's Vaccine Program
- An Ebola vaccine, in collaboration with NIH
- Third generation vaccines against *Streptococcus pneumoniae* using proteins common to all pneumococcal serotypes. (Second generation conjugate vaccines are currently under evaluation [see Box 18].)



CDC vaccine researcher working in a biosafety level 4 (BSL-4) containment facility. BSL-4 laboratories are used for work on infectious agents for which there are no current vaccines or treatments (e.g., Ebola virus).

Box 18

CDC's Role in the Evaluation of Vaccines Against Diseases of Global Importance

Over the next 5 years, CDC will work with many different partners to help implement:

- Phase III trials in Thailand of an HIV vaccine based on the glycoprotein-20 antigen developed by the VaxGen company
- Studies to evaluate the effectiveness of 7-valent pneumococcal conjugate vaccines on
 - Herd immunity among Native American communities that have high rates of invasive disease. This is a phase III, cluster-randomized trial of conjugate pneumococcal vaccine conducted in collaboration with Johns Hopkins School of Public Health.
 - Nasopharyngeal carriage of pneumococci in Alaska
 - Invasive pneumococcal disease throughout the United States, using the Active Bacterial Core Surveillance (ABCs) system.
- Phase III trial in the Gambia of a 9-valent conjugate pneumococcal vaccine against all-cause mortality and acute-respiratory-infection-specific mortality, conducted in collaboration with the Medical Research Council-Gambia, USAID, NIH, the Bill and Melinda Gates Children's Vaccine Program, and WHO's Vaccine Development, Vaccines and Biologicals program.
- USAID-supported Phase I trials of two vaccines against *Schistosomiasis mansoni*, conducted by the Schistosome Vaccine Development Project, a partnership involving the Government of Egypt, CDC, NIH/NIAID, NAMRU-3, academic centers, and private industry.
- A multisite rotavirus vaccine trial in Southeast Asian countries using an attenuated human rotavirus vaccine produced in India.

- Help develop and evaluate
 - Tools and strategies to prevent transmission of TB, malaria, and HIV/AIDS
 - Treatments for drug-resistant cases of TB, malaria, and HIV/AIDS
 - Improved methods for the detection of TB, HIV/AIDS-related opportunistic infections, and early-stage HIV infections
- Assess the impact of coinfection with HIV and malaria and with HIV and TB on disease control efforts.

Conduct Research on Foodborne and Waterborne Diseases

- Evaluate diagnostic strategies for foodborne and waterborne infections that are common in developing countries, but for which current diagnostic procedures are slow, expensive, or difficult.
- Conduct targeted research studies in sentinel IEIP sites (page 53) to determine the sources of, and risk factors for, specific foodborne and waterborne infections so that appropriate prevention measures can be developed.
- In collaboration with WHO and others, assess the efficacy, safety, and utility of vaccination to prevent selected foodborne and waterborne infections (e.g., typhoid fever) in combination with other prevention strategies. (See also Conduct Vaccine Research.)

Conduct Research on Diseases of Pregnant Women and Newborns

- Develop point-of-care diagnostic methods suitable for use in prenatal and obstetric healthcare settings in developing countries and provide quality assurance programs for their use.
- Field test new treatments and prevention measures, such as
 - Drug combinations for the treatment or prophylaxis of malaria in infants and in pregnant women, for use in areas in which chloroquine-resistance is common.
 - Simple and inexpensive regimens for the treatment and prevention of HIV/AIDS that can be administered to mothers and babies during labor and the first week of life.
- Explore ways to extend the benefits of intrapartum or neonatal prophylaxis (e.g., for prevention of HIV/AIDS and hepatitis C infection) to pregnant women with little or no prenatal care.
- Explore the effectiveness of perinatal application of topical antimicrobial agents in preventing neonatal sepsis and tetanus.
- Assess the relationship between particular maternal infections and low birthweight or preterm babies.

Conduct Research on Antimicrobial Resistance

- Encourage and support the development of drug susceptibility tests and surveillance systems to detect emerging resistance problems.
- Evaluate the impact of new vaccines (such as the conjugate pneumococcal vaccines) on the control of antimicrobial resistance and infection. (See also Conduct Vaccine Research.)
- Determine how disease prevention programs that include mass chemotherapeutic treatments can be optimized to minimize potential for the emergence of drug resistance. Examples include the use of praziquantel to prevent schistosomiasis, albendazole to prevent lymphatic filariasis, ivermectin to prevent onchocerciasis, azithromycin to prevent trachoma, trimethoprim-sulfamethoxazole to prevent AIDS-associated opportunistic infections, and nevirapine or zidovudine to prevent mother-to-child transmission of HIV/AIDS.
- Encourage efforts by WHO and other partners to
 - Evaluate the quality of commercially available antibiotic stocks and determine whether low-potency stocks are hastening the emergence of drug-resistant strains of pneumococci, *Mycobacterium tuberculosis*, *Plasmodium* spp., *Neisseria gonorrhoeae*, or other pathogens.

- Determine whether antibiotics purchased over the counter in developing countries (and often used in subtherapeutic doses) are hastening the emergence of drug resistance.

FDA supports these efforts.

Conduct Research on Healthcare-Acquired (Nosocomial) Infections

- Develop methods for identifying nosocomial infections and reducing their transmission in hospitals with limited resources for infection control.
- Provide technical assistance to hospital staff in assessing risk factors for acquiring
 - *Mycobacterium tuberculosis* (e.g., transmitted from patients to health care workers or to other patients).
 - Nosocomial respiratory and enteric infections (e.g., inadequate barrier nursing practices)
 - Nosocomial bloodborne infections (e.g., re-use of medical devices or surgical equipment)

Conduct Research on Infectious Causes of Chronic Diseases

- Conduct research on infectious agents of international importance that cause or may cause chronic diseases (e.g., hepatitis B and C viruses and hepatocellular carcinoma, *Helicobacter pylori* and peptic ulcer disease or gastric carcinoma, *Chlamydia pneumoniae* and cardiovascular disease, and human papillomaviruses and cervical cancer)

Conduct Research on Sexually Transmitted Diseases

- Study the contribution of herpes simplex virus type 2 infection and other genital ulcer diseases on HIV transmission, and devise appropriate intervention strategies.
- Develop more standardized diagnostic reagents and assays for syphilis to enhance the capacity to control neonatal syphilis worldwide.
- Monitor the development of antimicrobial resistance among strains of *Chlamydia trachomatis* and devise appropriate alternative treatments.

Priority Area 4: Application of Proven Public Health Tools

Another major priority for CDC is to translate research innovations into practical public health tools and ensure that they are disseminated widely and rapidly for the benefit of people all over the world. Examples of public health tools that have had a major impact on global infectious disease control are antibiotics, childhood vaccines, oral rehydration therapy, and vitamin supplements.

There is often a long delay between the development of a new public health tool and its widespread implementation. A country may lack the means to buy a new medical product or it may lack a public health delivery system and trained workers to administer it. There may be low demand, because the public is not informed about a new drug or vaccine, or low political interest, because the national government is not convinced that the drug or vaccine will be cost-effective.

CDC can use its experience in disease surveillance to demonstrate the value of public health tools to ministries of health and finance and to the public, using pilot studies, demonstration projects, and health education campaigns (Box 19). For example, CDC will continue to work with USAID, WHO, and other partners to demonstrate that mechanisms for the prevention or control of malaria (via

vector control, chemotherapy, and insecticide-treated bednets) are ready for national or regional implementation, pending the availability of resources and political commitment (see Priority Area 5). CDC can also help development agencies, NGOs, and other partners address problems related to public health training and to drug or vaccine delivery (see also Priority Area 6).

As part of the global strategy, CDC will intensify efforts to couple applied research with research on ways to promote the use of newly developed tools for disease control (“implementation research”). CDC will help identify the most effective tools and actively encourage their international use, applying expertise and resources in laboratory research, public health policy, program management, and health communications to overcome scientific, financial, and cultural barriers.

Examples of new tools with the potential for significant worldwide impact include point-of-use disinfection and safe water storage to prevent waterborne diseases; auto-disable (one-use) syringes to prevent blood-borne transmission of hepatitis B and C viruses and HIV; and diethylcarbamazine and albendazole therapy to eliminate lymphatic filariasis.



Bednets protect children from malaria. Nightly use of insecticide-impregnated bednets¹³ reduces childhood mortality by 20–30%, and use in one village protects children in neighboring villages by reducing the number of infectious mosquitos. Nevertheless, bednets are used by fewer than 10% of persons at risk, due to lack of knowledge, unavailability of bednets, and other logistical constraints.

Objectives for Priority Area 4

Promote Effective Drug Use

- Conduct implementation research and demonstration projects to promote the use of therapeutic drugs such as
 - Ivermectin to eliminate onchocerciasis in West Africa and Central America
 - Diethylcarbamazine and albendazole or mebendazole therapy to eliminate lymphatic filariasis in the Americas
 - Single-dose azithromycin to eliminate blinding trachoma in endemic regions in Africa, Middle East, Asia, and Central America

- Single-dose nevirapine to prevent perinatal HIV transmission. (See also Priority Area 5.)
- Praziquantel to treat schistosomiasis
- Promote the widespread use of the directly observed therapy short-course strategy (DOTS) to treat TB. (See also Priority Area 5.)

Improve Immunization

- Use CDC resources to strengthen routine immunization services and to encourage the introduction of new and underutilized vaccines, including vaccines against hepatitis B, yellow fever, *Haemophilus influenzae* type b, and other childhood diseases. (See also Priority Area 5.)

Promote the Use of Proven Disease Prevention Strategies

- Work with ministries of health and PAHO to encourage the adoption of vector control measures to eliminate Chagas disease from Central America and reduce morbidity and mortality from dengue and dengue hemorrhagic fever (<http://www.cdc.gov/ncidod/dpd/parasites/chagasdisease> and <http://www.cdc.gov/ncidod/dvbid/dengue>).
- Work with private and public sector partners to promote widespread implementation of CDC's Safe Water System, which uses point-of-use disinfection and safe water storage to prevent cholera, dysentery, and other waterborne diseases (Box 20; <http://www.cdc.gov/safewater>).

Box 19

Narrowing the Interval Between the Invention and Use of an Effective Public Health Tool

In the past, the time between the development of a new public health tool and its widespread use was often extremely long. For example, the tetanus toxoid vaccine, developed in 1926 and used to protect soldiers during World War II, was not widely administered to children in industrialized countries until the 1940s and 1950s, and did not reach high levels of coverage in developing countries until the mid-1980s, a 60-year interval.

Today, this gap is narrowing. After the hepatitis B vaccine was licensed in 1981, universal infant hepatitis B vaccination projects were initiated in many countries, including five U.S.-affiliated Pacific islands where HBV infection is highly endemic and HBV-induced chronic liver disease is a leading cause of death. After a decade of successful demonstration projects, routine childhood hepatitis B vaccination was recommended by the World Health Assembly for all countries. During the 1990s, more than 100 countries (including the United States) implemented hepatitis B immunization programs, although lack of financing hindered vaccine use in the poorest countries. In 2000, financial assistance for the purchase of hepatitis B vaccine became available through The Vaccine Fund, and the Global Alliance for Vaccines and Immunization (GAVI) targeted hepatitis B vaccine for universal introduction into developing countries by 2007.

The history of the hepatitis B vaccine provides a good example of how the gap in time between introduction and widespread use of a new public health tool can be shortened through strategic planning, a rapid sequence of efficacy studies and demonstration projects, active advocacy and funding. As future vaccines and other public health innovations are developed, it should be possible to narrow the gap further. CDC can play an important role in this area.

A man being immunized against hepatitis B virus. Expanded use of the hepatitis B vaccine will decrease mortality from cirrhosis, liver failure, and hepatocellular carcinoma, which is the 4th leading cause of cancer death worldwide.

Adapted from: Centers for Disease Control and Prevention. Preventing emerging infectious diseases: Addressing the issue of vaccine development and use. Atlanta, GA: U.S. Department of Health and Human Services, 2001.



Box 20

CDC's Safe Water System

In the poorest, least industrialized nations, diarrheal diseases caused by contaminated food and water remain a leading cause of death in childhood. Many of these deaths could be prevented by simple sanitation measures.

With assistance from ministries of health, funding from USAID and Rotary International, and special expertise from nongovernmental organizations and the private sector, CDC has developed a sustainable way to improve the safety of household drinking water. The components of CDC's safe water system, as implemented in pilot projects in Zambia, include

- **Water disinfection.** Population Services International (PSI) has marketed a locally produced disinfectant solution for water treatment (CLORIN) to communities in the southern, eastern, and western regions of Zambia. A CDC case-control study documented a 65% reduction of risk of cholera in Zambian households that use CLORIN.
- **Safe storage of water.** CDC, the Procter and Gamble Company, and Rotary International have contributed to the design of a narrow-mouthed vessel for safe storage of water. The mold for the new vessel was shipped to South Africa in January 2000, where vessels have been produced for use in Zambia, Madagascar, Kenya, Côte d'Ivoire, and Pakistan.
- **Social marketing.** PSI has trained public health workers in Lusaka, Kitwe, and Ndola, Zambia, on how to involve their communities in the safe-water effort.

USAID has increased funding for the safe water project in Zambia to permit nationwide coverage within the next few years, and the CARE/CDC Health Initiative is funding similar projects in western Kenya and in Antananarivo, Madagascar. Each CARE/CDC Health Initiative project will target a population of 200,000 people and combine the methods of the Zambian project with the community organizing techniques of CARE.

In the future, the elements of the Safe Water System may also be used to promote:

- Safe preparation of foods and beverages by street vendors
- Safe preparation of medications, such as oral rehydration solutions to treat cholera
- Safe preparation of formula for use by HIV-infected women who choose not to breast-feed their infants
- Handwashing and improvements in hygiene
- The addition of nutritional supplements to drinking water



A safe water storage vessel employed by participants in an ongoing Safe Water System implementation project in Homa Bay, Kenya, initiated in October 2000 in collaboration with CARE Kenya. The vessel was designed to eliminate a major source of diarrheal disease contamination that results when hands, cups, ladles, or other objects are dipped into open buckets to remove water for drinking. Because the local population in Homa Bay preferred to use vessels made of clay rather than plastic, CDC and CARE Kenya incorporated a narrow mouth, lid, and spigot into traditional clay pots to ensure safe water storage. The use of plastic vessels with similar characteristics, in combination with water disinfectants, has reduced diarrheal diseases by 30–50% in communities in Zambia, Pakistan, and Bolivia.¹⁴

Photographer: Bobbie Person, Office of Health Communication, National Center for Infectious Diseases, CDC

- Work with WHO and ministries of health in central African countries to provide training in hospital barrier nursing practices that prevent nosocomial spread of viral hemorrhagic fevers like Ebola and Marburg.
- Continue to support the Safe Injection Global Network (SIGN) and work with development agencies and other partners to promote safe injection practices to prevent the spread of hepatitis B and C, HIV/AIDS, and other bloodborne diseases.
- Work with the Roll Back Malaria partnership to promote the use of insecticide-impregnated bednets for the prevention of malaria and other mosquito-borne diseases. (See Priority Area 5.)
- Work with ministries of health and WHO to provide public health education and mobilize communities to use proven public health tools.

Disseminate Diagnostic Tests

- Work through the WHO Collaborating Centre laboratory network to provide proven diagnostic reagents for the detection of endemic diseases to national public health laboratories and regional surveillance networks. (See Priority Area 1.)
- Work with WHO and donor agencies to provide national public health laboratories with state-of-the-art laboratory tests that measure antimicrobial resistance in *Mycobacterium tuberculosis* and other common bacterial pathogens, as well as in malaria parasites and in the AIDS virus. (See Priority Area 5.)
- Work with ministries of health to transfer technology for molecular subtyping of common bacterial pathogens (e.g., PulseNet techniques; page 36) to national public health laboratories for use in detecting outbreaks of foodborne diseases).

Use Surveillance Data To Direct Public Health Policy

- Work with ministries of health and ministries of finance, WHO, and NGOs to
 - Conduct disease surveillance to assess national public health needs and recommend specific public health tools to address them.
 - Demonstrate the use of specific surveillance methods for detecting outbreaks, for evaluating public health programs, and for driving public health decision-making.
- Work with global partners to evaluate the progress of global initiatives to combat malaria, TB, AIDS, and vaccine-preventable diseases. (See Priority Area 5.)

Priority Area 5: Global Initiatives for Disease Control

Dr. Gro Bruntland, Director-General of WHO, has said that “solutions, like problems, have to be global in scope.” In accord with this idea, WHO is helping to coordinate major global initiatives to reduce deaths from malaria, TB, and HIV/AIDS—diseases that contribute to poverty and economic stagnation. This approach was endorsed by the Group of Eight Industrialized Nations at the Okinawa summit in July 2000. WHO is also helping to coordinate global initiatives to increase developing-country access to vaccines against acute respiratory diseases, yellow fever, hepatitis B, and other diseases, through the Global Alliance for Vaccines and Immunization (GAVI; <http://www.vaccinealliance.org>).

Although these global initiatives have clearly stated goals and are supported by multiple private and public sector partners (Box 6), the details of

their implementation are still under discussion. Previous efforts to eradicate malaria by using a narrow approach to vector control ended in failure. Because no proven vaccines are yet available against malaria, TB, or AIDS, “one-shot” solutions are not feasible, and it will be necessary to employ multiple control strategies, including behavioral interventions that require a high degree of cooperation and trust in affected communities. The incidence of TB, HIV/AIDS, and acute respiratory infections is high in poor, war-torn, or post-Communist countries in which public health infrastructures have deteriorated. Moreover, emerging drug resistance complicates the treatment and control of each of these diseases.

A new priority for CDC will be to elevate the level of its participation in these and other global initiatives

(Box 6). CDC and its partners will also consult on future international priorities for disease control, elimination, and eradication efforts—as well as for antimicrobial resistance monitoring and pandemic influenza preparedness planning—and help evaluate progress through the collection and analysis of disease surveillance data.

Increased participation in global health initiatives will require long-term partnerships with host countries, as well as improved coordination with public health partners throughout the world. CDC will build on its strengths in disease surveillance, laboratory science, and program evaluation to assist development agencies, international organizations, NGOs, and development banks that support international programs to strengthen healthcare systems and control disease. As a partner in the Global AIDS alliance (Boxes 6



Children from villages hard-hit by AIDS. Thirteen million children in sub-Saharan Africa have lost one or both parents to AIDS, and the number is expected to reach 40 million by 2010.¹⁸ The number of AIDS orphans is also growing in Asia and Latin America.

Global efforts are underway to help these children and prevent further devastation from HIV/AIDS and other infectious diseases. These global initiatives involve complex alliances among public and private groups, health and trade experts, and national and international donor organizations.

Photographer: Bobbie Person, Office of Health Communication, National Center for Infectious Diseases, CDC

and 21), for example, CDC has a special opportunity to work with UNAIDS and USAID to implement HIV/AIDS control programs on all continents (<http://www.unaids.org/africapartnership/files/mrpretoria.doc>). As a partner in Roll Back Malaria (<http://www.rbm.who.int>), Stop TB (<http://www.stoptb.org>), and GAVI, CDC can contribute to the Shared Agenda for Health in the Americas (<http://wbln0018.worldbank.org/external/lac/lac.nsf>)¹⁶ developed by PAHO, the Inter-American Development Bank, and the World Bank.

Increased participation in global health initiatives also will require additional staff to work on projects overseas, as well as to provide diagnostic support from CDC laboratories in the United States. Full participation in GAVI, for example, will require increased programmatic support and technical expertise in acute respiratory diseases, yellow fever, hepatitis B, and meningococcal meningitis. There remains a shortage of U.S. and world expertise in many infectious disease areas. (See also Priority Area 6.)

CDC staff will also continue to work with ministries of health, WHO, PAHO, USAID, and other partners on disease elimination or eradication campaigns. In addition, CDC staff will help further efforts to reduce illness and death from acute respiratory diseases and diarrheal diseases,

Box 21

The Global AIDS Program

Thirty-six million people worldwide have been infected with HIV, the virus that causes AIDS, and more than 21.8 million have died. Eighty-five percent of all AIDS deaths have occurred in the countries of sub-Saharan Africa. In at least five of these countries, more than 20% of adults are HIV-positive. Infection rates are also climbing in parts of Asia, Latin America, the Caribbean, and the former Soviet Union countries and Eastern Europe. Only a concerted global effort coordinated by WHO and led by the United States and other industrialized countries can stop this pandemic.

Through the Global AIDS Program (GAP), CDC is working with USAID and other DHHS agencies to assist ministries of health. In 2001, the program targeted 17 of the hardest-hit African countries (Angola, Botswana, Côte d'Ivoire, the Democratic Republic of the Congo, Ethiopia, Kenya, Malawi, Mozambique, Namibia, Nigeria, Rwanda, Senegal, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe), as well as India, Brazil, Cambodia, Guyana, Haiti, Thailand, and Vietnam. GAP's mission is to implement the U.S. Leadership and Investment for Fighting an Epidemic (LIFE) Initiative, which is the U.S. contribution to the International Partnership Against AIDS in Africa and to AIDS efforts on other continents.

The goals of the Global AIDS program are to

- Reduce HIV transmission through primary prevention of sexual, mother-to-child, and bloodborne transmission
- Improve community and home-based care and treatment of HIV/AIDS, sexually transmitted infections, and opportunistic infections
- Strengthen national capacities to collect and use surveillance data and manage national HIV/AIDS programs

Additional information on the Global AIDS Program is available at <http://www.cdc.gov/nchstp/od/gap>

which—in addition to HIV/AIDS, TB, and malaria—are the leading infectious causes of death, worldwide. CDC will also continue to conduct applied research to improve our understanding of the genetics, physiology, and pathogenesis of microbes that cause illnesses targeted by global initiatives for disease control. (See Priority Area 3.)

Objectives for Priority Area 5

Establish a Solid Foundation for Global Initiatives

- Expand the cohort of public health professionals at CDC who have international expertise and can provide support for global initiatives to combat infectious diseases. (See also Priority Area 6)
- Help suggest international priorities for current and future global initiatives for disease control. Future initiatives might include antimicrobial resistance monitoring, pandemic influenza preparedness planning, and campaigns to control or eliminate measles, lymphatic filariasis, onchocerciasis, trachoma, rubella, neonatal tetanus, or hepatitis B.
- Provide technical assistance to national health authorities in public health management of diseases targeted by global health initiatives, working through the Sustainable Management Development Program and other mechanisms. In

some countries this will include integrating specialized HIV, TB, and STD surveillance programs into national surveillance and laboratory service systems for infectious diseases.

- Improve coordination among CDC personnel who work overseas in the same country or region.

Enhance Support for Disease Control, Elimination, and Eradication Programs

- Help complete the eradication of polio by 2005. The global effort to eradicate polio is led by WHO, in partnership with an international coalition that includes CDC, Rotary International, UNICEF, and the governments of many countries (<http://www.cdc.gov/nip/global>). The WHO Global Polio Laboratory Network (Box 7), which uses molecular techniques to determine whether wild-type polio is circulating in areas undergoing eradication efforts, should be expanded to include monitoring for other vaccine-preventable diseases, such as measles and rubella.
- Help complete the eradication of dracunculiasis, working in partnership with the Carter Center's Global 2000 Program, UNICEF, WHO, and other groups (<http://www.cdc.gov/ncidod/dpd/parasites/guineaworm> and <http://www.cartercenter.org/guineaworm.html>).
- Work with PAHO to complete the elimination of indigenous (i.e., non-

imported) cases of measles in the Americas, and work with WHO, UNICEF, the UN Foundation, USAID, the American Red Cross, the International Federation of Red Cross and Red Crescent Societies (IFRC), and other partners to reduce by 50% by 2005 the nearly 900,000 annual measles deaths worldwide.¹⁷

Participate in the Roll Back Malaria Initiative

- Contribute to Roll Back Malaria (RBM; <http://www.rbm.who.int>) through full endorsement and active promotion of RBM strategies in malaria-endemic countries in sub-Saharan Africa, Southeast Asia, and the Americas. Although RBM strategies vary by region and by local malaria transmission dynamics, 90% of the world's malaria is in sub-Saharan Africa, where the strategies for malaria prevention and control include
 - Prompt effective case management of malaria illness
 - Prevention of malaria and its consequences in pregnancy, through prophylaxis or preventive intermittent treatment regimens with an effective anti-malarial drug
 - Widespread use of insecticide-treated bednets, particularly by young children and pregnant women
 - Prompt recognition and management of malaria epidemics

- Conduct operations research on
 - Antimalarial drug efficacy and the management and prevention of antimalarial drug resistance
 - Malaria prevention in pregnancy
 - Transmission reduction through the use of insecticide-treated bednets and other strategies
 - Malaria assessment in complex emergencies, such as outbreaks that occur among refugees or outbreaks that occur after hurricanes or other natural disasters
 - Malaria diagnostics
 - Social attitudes and practices that facilitate or hinder the effectiveness of malaria control programs
 - Malaria surveillance, monitoring, and evaluation strategies
 - Provide technical assistance to the African Integrated Malaria Initiative (<http://www.usaid.gov/regions/afr/abic/sddev/sddspr96/sddspr96.htm>; see also Appendix A), a USAID-sponsored initiative that enhances integrated malaria treatment and prevention in Kenya, Malawi, Zambia, and Benin by promoting the use of interventions in the home (e.g., insecticide-impregnated bednets), in healthcare facilities (e.g., chemoprophylaxis), and among pregnant women (e.g., protective intermittent chloroquine therapy, as recommended by the USAID Safe Motherhood Initiative). During 2001, the African Integrated Malaria Initiative will be extended to the Democratic Republic of the Congo, Nigeria, Senegal, and Uganda.
 - Assist ministries of health in malaria control efforts and in the monitoring and evaluation of antimalarial drug efficacy. CDC is currently working on national malaria control programs in Kenya, Tanzania, Peru, and Nepal.
- Strengthen the Stop TB Program**
- Contribute to Stop TB (<http://www.stoptb.org>) by
 - Assigning an epidemiologist to WHO's Stop TB secretariat
 - Providing technical assistance to facilitate the use of the directly observed therapy short-course strategy (DOTS) for TB. (See also Priority Area 4)
 - Strengthening TB treatment programs in LIFE Initiative/Global AIDS Program countries (see below)
 - Supporting demonstration projects on the medical management of drug-resistant TB
 - Providing technical assistance to improve hospital TB control and detect hospital and community outbreaks in communities with high HIV prevalence
 - Assigning a medical officer to the International Union Against TB and Lung Diseases (IUATLD) to train a cadre of international TB experts, as a joint effort with USAID and WHO
 - Providing technical assistance and laboratory support to implement global antituberculosis drug resistance surveys
 - Consult with ministries of health in Russia, Vietnam, and other countries on training issues related to TB diagnosis and treatment.
 - Conduct operations research on
 - TB surveillance, program management, and program evaluation strategies
 - Multidrug-resistant TB treatment approaches and evaluation strategies
 - Treatment strategies for latent TB among persons with HIV infection
 - Factors that improve adherence to antituberculosis therapy
 - New diagnostic methods, drugs, and vaccine for TB
- Expand the LIFE Initiative and Other International Efforts To Address HIV/AIDS**
- CDC will work with foreign ministries of health and public and private sector partners in countries targeted by the LIFE Initiative/Global AIDS Program (Boxes 6 and 21; <http://www.cdc.gov/nchstp/od/gap>) to
- Prevent primary transmission of HIV by
 - Expanding voluntary counseling and testing programs for youth and other vulnerable populations

- Building large-scale programs to reduce mother-to-child transmission
- Strengthening programs to reduce bloodborne HIV transmission
- Strengthening medical management of sexually transmitted infections (STIs)
- Supporting and strengthening national education and mobilization efforts for disease prevention
- Improve community and home-based care and treatment by
 - Expanding and strengthening TB prevention and care
 - Enhancing care and treatment of HIV/AIDS and AIDS-related opportunistic infections
 - Exploring the innovative use of antiretroviral therapy
- Build public health and medical infrastructure by
 - Expanding and strengthening surveillance for HIV, STIs, and TB
 - Providing laboratory support for diagnosis and surveillance of HIV, STIs, TB, and opportunistic infections, as well as for HIV screening of blood supplies
 - Expanding and strengthening public health information systems
 - Providing training in managing and implementing HIV treatment and prevention programs (see also page 55).
 - Enhancing evaluation of HIV/AIDS prevention and care programs.

Support Global Vaccine Initiatives

- Help GAVI partners (<http://www.vaccinealliance.org/>) develop and implement strategies to strengthen routine immunization services and monitor their effectiveness.
- Provide assistance to GAVI in assessing the burden of hepatitis B, yellow fever, *Haemophilus influenzae* type b, pneumococcus, rotavirus, meningococcus A, measles, and congenital rubella syndrome in developing countries and use this information to design, implement, and evaluate immunization programs against these infections.
- Support efforts by GAVI partners—including pharmaceutical companies, foundations and development banks—to develop and evaluate new vaccines that are needed in developing countries, and to promote their availability. (See also Priority 3.)

Priority Area 6: Public Health Training and Capacity Building

CDC's growing visibility as an international outbreak consultant has also led to increased participation in efforts to build global public health capacity. Although CDC is not a development agency, CDC has traditionally assisted USAID with the public health and research components of development projects (Box 22) and has consulted with private foundations and development banks on efforts to strengthen public health infrastructures (Box 23). Over the past decade, CDC has also helped strengthen healthcare systems in developing countries, working with hospital administrators and physicians to improve infection control practices and ensure safe blood supplies. CDC has also managed overseas field stations that facilitate on-site collaborative research on diseases of regional and global importance (Box 10). In addition, several foreign scientists enroll each year in CDC's Epidemic

Intelligence Service and the Emerging Infectious Disease Laboratory Fellowship Program, which is a joint effort between CDC and the Association of Public Health Laboratories (APHL).

In recent years, in the aftermath of outbreaks and other infectious disease crises, CDC has responded to requests from more than 80 foreign governments for epidemiologic, laboratory, or research assistance to ensure preparedness for future emergencies. However, most of these efforts—which included training courses, research collaborations, program evaluations, health education campaigns, and the provision of laboratory reference support—were limited in scope and duration and were not integrated into a larger effort to build public health capacity.

As part of the global strategy, CDC will propose the establishment of a series of International Emerging Infections Programs (IEIPs) in developing

countries—centers of excellence that will integrate disease surveillance, applied research, prevention, and control activities. Each site will represent a partnership between a ministry of health and CDC, with additional partnerships involving local Field Epidemiology Training Programs (FETPs) and one or more local universities or medical research institutes. The IEIP sites will build on existing CDC overseas activities to strengthen national public health capacity and provide hands-on training in public health. Over time, they may have a regional as well as a national impact on health.

The IEIPs will be broad-based public health collaborations between the ministry of health of the host country and CDC, with both parties contributing resources and reaching agreement on the priorities of the program. Each site will be built on existing CDC field capacity in that country. Some IEIPs may be based at research institutions



Presentation of certificates: Workshop on HIV/AIDS Epidemiology, Surveillance, and Prevention, May 2000, Nha Trang City, Khanh Hoa Province, Vietnam. Since Vietnam and United States renewed diplomatic relations, Vietnamese and U.S. scientists and public health workers have collaborated on workshops, training courses, and research projects that build national capacity to detect and prevent HIV/AIDS, TB, malaria, typhoid fever, influenza, hospital-acquired infections, plague, and dengue and dengue hemorrhagic fever.

Photographer: Nguyen Thi Thu Hong, HHS/CDC/Hanoi

Box 22

USAID and CDC: Collaboration on Capacity Building

The U.S. Agency for International Development (USAID) and CDC are longstanding partners in the effort to combat emerging diseases overseas. Twenty years ago, CDC and USAID collaborated with WHO and other partners to eradicate smallpox. Today, CDC and USAID are helping eradicate polio; reduce deaths from malaria, HIV/AIDS, TB, and acute respiratory infections; and improve global surveillance for emerging threats.

In many countries, CDC partners with USAID on evaluations of infectious disease problems related to wars, famines, or other disasters, as well as on development projects that involve epidemiologic or diagnostic research. CDC also helps implement USAID-supported programs in the four key areas of USAID's emerging infectious disease initiative:

- **Antimicrobial resistance:** Developing and implementing strategies and interventions for detecting, studying, and containing emerging resistance problems.
- **TB:** Working for a sustainable reduction in the incidence of TB among key populations in selected countries through by the introduction of directly observed therapy short-course strategy (DOTS; see Box 6).
- **Malaria:** Improving the diagnosis and treatment of malaria; promoting effective preventive strategies; addressing the challenges of malaria in pregnancy; containing malaria outbreaks; responding to malaria during complex emergencies; slowing the emergence and spread of drug-resistant malaria; and accelerating the development of tools for malaria control.
- **Disease surveillance and response:** Improving public health capacity to obtain and use good quality data for disease surveillance and effective response to infectious diseases.

As part of the global strategy, CDC will intensify its efforts to work with USAID to develop mutually reinforcing ways of working together at the country level to maximize the impact of U.S. investments in global health.

where CDC has long-standing collaborations. Others may be based at CDC field stations or adjacent to other U.S. institutions abroad, such as NIH's Tropical Medicine Research Centers or DoD's overseas laboratories. Each site will maintain close ties with WHO country and regional offices, and, if possible, will collaborate with one of the Field Epidemiology Training Programs (FETPs) that CDC has helped establish in more than 16 countries (Box 24).

The IEIPs will be modeled in part on the U.S. Emerging Infections Program (EIP; <http://www.cdc.gov/ncidod/osr/EIP.htm>) whose nine sites conduct population-based surveillance, provide emergency outbreak assistance, invest in cutting-edge research, and address new problems whenever they arise. Because the EIP sites combine specialized epidemiologic and laboratory expertise, they are able to go beyond the routine functions of local health departments to address important issues in infectious diseases and public health. For example, when "mad cow disease" was reported in the United Kingdom in 1996, the EIP surveillance sites were able to reassure the U.S. public within a short time that the disease had not spread to the United States.

Like the domestic EIPs, the International EIP sites will perform multiple functions, including research on endemic diseases and emergency surveillance when a new threat appears.

They will also provide disease surveillance data to ministries of health and finance to help assess the burden of specific diseases and evaluate the cost-effectiveness of national public health programs. Also like the EIPs, the IEIPs will incorporate preexisting sites (e.g., U.S. institutions, public health agencies, research institutions, and non-governmental organizations); use the sites in an integrated fashion; and establish an international steering committee to provide guidance for core projects conducted at all of the IEIP network sites. Areas in which IEIP sites might play an especially important role are in surveillance for drug-resistant forms of malaria, TB, pneumonia, and dysentery. All of the sites will be linked by electronic communications to keep health experts around the world in close contact with one another.

The long-term goal of the IEIPs will be to develop sustainable, in-country capacity for disease surveillance, outbreak investigation, and research on diseases of regional or global importance by fostering the next generation of international public health leaders (Box 16). The implementation of this goal will require extensive scientific, human, and financial resources from both private and public sources, as well as sustained efforts over many years. However, the costs will be low in relation to potential benefits, in terms of both human health and increased global prosperity.

Objectives for Priority Area 6

Establish International Emerging Infections Programs (IEIPs)

- Help create International Emerging Infections Programs (IEIPs) that
 - Train local scientists and CDC personnel
 - Provide diagnostic and epidemiologic resources when outbreaks occur
 - Serve as platforms for regional infectious disease control activities
 - Conduct public health research of global importance
 - Disseminate proven health tools

Expand Training in Epidemiology, Public Health Management, and Laboratory Diagnostics

- Increase training opportunities for foreign scientists in epidemiology, public health management, and state-of-the-art laboratory techniques. For example, CDC will provide training in
 - PulseNet's methods for fingerprinting strains of foodborne bacteria (page 36)
 - Methods for identifying foodborne viruses
 - Drug susceptibility testing of pathogens of public health importance

- DPDx, an Internet-based system to help confirm diagnoses of parasitic diseases
- International public health management
- Managing and implementing HIV treatment and prevention programs in Global AIDS Program countries (see page 52)
- Work through TEPHINET and other mechanisms to provide technical assistance to health authorities in countries that are establishing or expanding national schools of public health, new Field Epidemiology Training Programs (FETPs), new Sustainable Management Development Programs, or the Rockefeller Foundation-supported Public Health Schools Without Walls (PHSWOW). TEPHINET is a public health network network that links FETP and PHSWOW staff.
- Help increase the number of public health workers in developing countries who are trained in vaccine work by
 - Encouraging training efforts by foreign governments, foundations, and donor organizations (e.g., the WHO public health training project in Lyon, France)
 - Incorporating training components into such projects as the U.S.-India Vaccine Plan, the Egyptian Schistosomiasis Vaccine Development Project, and the HIV vaccine trials in Kenya and Côte D'Ivoire (Box 18)

Box 23

The World Bank and CDC Sign a Memorandum of Understanding

Infectious diseases are not just a result of, but also a *cause* of, poverty (see Box 8). In recognition of this fact, the World Bank, a leading global development lender, signed a memorandum of understanding with CDC in February 2001, to intensify joint efforts to prevent and control diseases that take a heavy toll in developing countries.

Under the agreement, CDC and the World Bank will collaborate on a broad range of global health activities, related to nutrition, maternal and child health, endemic diseases such as HIV/AIDS, TB, and malaria, public health, health surveillance, health policy and statistics, research, and healthcare technology. Over the next year, for example, CDC will transfer technical experts to the World Bank to help design, implement, and evaluate projects to control the spread of malaria in Africa and promote worldwide use of vaccines against many childhood diseases.

The memorandum will also facilitate previously established collaborations between the World Bank and CDC, including an ongoing project to upgrade the surveillance infrastructure for infectious diseases in Argentina and Brazil, from the local to the national level. That effort includes

- Training public health workers in epidemiology, management, and laboratory science
- Establishing electronic reporting networks and sentinel sites for disease surveillance
- Enhancing laboratory capacity
- Strengthening outbreak response
- Instituting measures to prevent the spread of TB and other priority diseases

- Training national and regional health workers in vaccine program planning, monitoring, and evaluation as part of GAVI's effort to improve routine immunization services and to introduce new and underutilized vaccines into developing countries
- Provide training opportunities that increase international expertise in the detection and treatment of prenatal and perinatal infections.
- Expand the cohort of public health professionals at CDC who have international infectious disease expertise, by
 - Creating an inventory of CDC staff to identify gaps in international expertise
 - Developing an international infectious disease training program or seminar series for CDC staff, in collaboration with public health and medical schools
 - Establishing an exchange program that enables visiting scientists from other countries to work at CDC and vice versa
 - Working with the Association of Schools of Public Health and the Association of Teachers of Preventive Medicine to increase the number of graduate courses that cover global infectious disease issues
- Expand opportunities for training in-hospital infection control and clinical surveillance by providing
 - Train-the-trainer courses in hospital epidemiology
 - Technical assistance to hospital staff in designing and implementing programs to reduce transmission of nosocomial pathogens

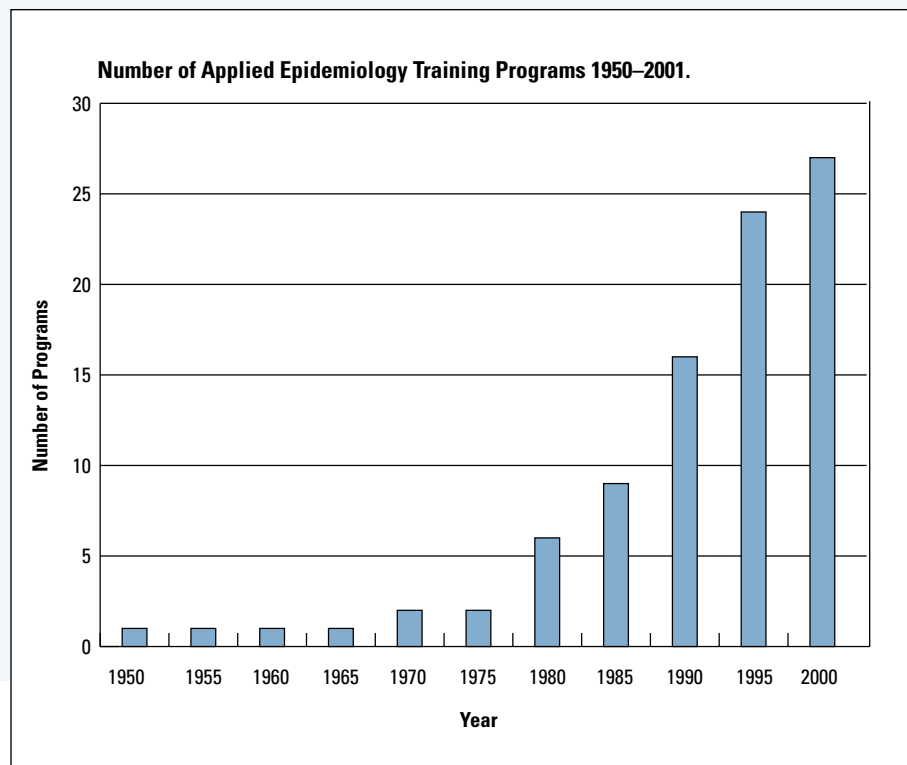
Box 24

Applied Field Epidemiology Training Programs

For more than 20 years, CDC has collaborated with ministries of health around the world to establish Field Epidemiology Training Programs (FETPs) for specialists in epidemiology. These programs are modeled on the Epidemic Intelligence Service, CDC's primary applied epidemiology training program, which was founded in 1951. Canada established a field epidemiology training program in 1975, and Thailand launched one in 1980, in collaboration with CDC and WHO. CDC partners who have helped establish other FETPs include the World Bank (Brazil), PAHO (a regional FETP in Central America), and USAID (Egypt, Jordan, Peru, Philippines, and Central America).

CDC has also provided consultants to **Public Health Schools Without Walls (PHSWOW)**, which helps post-graduate-level public health personnel attain the epidemiologic, managerial and leadership competencies required to run increasingly decentralized health systems. The PHSWOWs are funded by the Rockefeller Foundation with technical support from Tulane University. The first PHSWOW was launched in Zimbabwe in 1993 at the University of Zimbabwe; the second in Uganda in 1994 at Makerere University; and the third in Ghana in 1995 at the University of Ghana. In 1997, Vietnam started a PHSWOW in collaboration with the Hanoi School of Public Health.

As of 2000, in addition to EIS, there were 27 Applied Epidemiology Training Programs, including 20 FETPs, 4 PHSWOWs, and 3 other Applied Epidemiology Training Programs (the European Programme for Intervention Epidemiology Training [EPIET], the WHO Global Health Leadership Officers Programme [GHLOP], and the WHO/AFRO Programme d'Epidemiologie Pratique [PEP]). Of 19 programs over 4 years old, 18 (95%) continue to produce graduates. Thus far, it is estimated that the 27 Applied Epidemiology Training Programs have trained more than 900 international public health leaders in epidemiology and outbreak investigation. Approximately 420 more are currently in training.



- Consultation to USAID and other donor organizations on infectious disease projects that build infrastructure to improve the provision of prenatal and perinatal care in developing countries.

Enhance Availability of Guidelines and Other Publications

- In collaboration with WHO and international experts, draft regional health care guidelines on the judicious use of antibiotics, including antibiotics that are purchased

over-the-counter. Regional health care guidelines can be used to mount public health education campaigns on antibiotic usage to help retard the development of drug resistance.

- Provide consultation to ministries of health in developing national guidelines for
 - Hospital infection control, including prevention of hospital-acquired pneumonia, TB, HIV/AIDS, and other nosocomial infections of local concern.

- Management of exposures to bloodborne pathogens like HIV and hepatitis B and C.

- Disseminate new information on infectious disease issues through the *Morbidity and Mortality Weekly Report (MMWR)*, the *Emerging Infectious Diseases* journal, and the CDC website.

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ACRONYMS

AFRIMS	Armed Forces Research Institute of Medical Science, Bangkok, Thailand
AIDS	acquired immunodeficiency syndrome
AIMI	African Integrated Malaria Initiative
AMREF	African Medical and Research Foundation
APEC	Asia-Pacific Economic Cooperation
APHL	Association of Public Health Laboratories
ATSDR	Agency for Toxic Substances and Disease Registry
BIDS	U.S.-Mexico Border Infectious Disease Surveillance system
CAREC	Caribbean Epidemiology Center
DoD	Department of Defense
DOTS	directly observed therapy short-course strategy
DVA	Department of Veterans Affairs
ELISA	enzyme-linked immunosorbent assay
EPI	Expanded Programme on Immunization
EPIET	European Programme for Intervention Epidemiology Training
EIP	Emerging Infections Program
EWORS	Early Warning Outbreak Recognition System
FDA	Food and Drug Administration
FETP	Field Epidemiology Training Program
GAP	Global AIDS Program
GAVI	Global Alliance for Vaccines and Immunization
GHLOP	WHO Global Health Leadership Officers Programme
HIV	human immunodeficiency virus
HIV/AIDS	human immunodeficiency virus infection/acquired immunodeficiency syndrome
HFRS	hemorrhagic fever with renal syndrome
HPS	hantavirus pulmonary syndrome
IFRC	International Federation of Red Cross and Red Crescent Societies
IHR	International Health Regulations
IPAA	International Partnership Against AIDS in Africa
IUATLD	International Union Against TB and Lung Diseases
KEMRI	Kenya Medical Research Institute
LIFE	Leadership and Investment for Fighting an Epidemic initiative
LITS	Laboratory Information Tracking System

MERTU/G	Medical Entomology Research and Training Unit/Guatemala
NAMRU-2	Naval Medical Research Unit No. 2, Jakarta, Indonesia
NAMRU-3	Naval Medical Research Unit No. 3, Cairo, Egypt
NASA	National Aeronautics and Space Agency
NGO	nongovernmental organization
NIH	National Institutes of Health
NMRC	Naval Medical Research Center Detachment, Lima, Peru
NOAA	National Oceanic and Atmospheric Administration
PacNET	Pacific Public Health Surveillance Network
PAHO	Pan American Health Organization
PEP	WHO/AFRO Programme d'Epidemiologie Pratique
PHLIS	Public Health Laboratory Information System
PHSWOW	Public Health Schools Without Walls
RBM	Roll Back Malaria initiative
SIGN	Safe Injection Global Network
STD	sexually transmitted diseases
STI	sexually transmitted infections
TB	tuberculosis
TEPHINET	Training in Epidemiology and Public Health Interventions Network
UNAIDS	Joint United Nations Programme on AIDS
UNESCO	United Nations Educational, Scientific, and Cultural Organization
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
USAMRU-K	United States Army Medical Research Unit, Nairobi, Kenya
USDA	United States Department of Agriculture
WHO	World Health Organization
WHO/AFRO	World Health Organization Regional Office for Africa
WHO/EMRO	World Health Organization Regional Office for the Eastern Mediterranean

APPENDIX A

GLOBAL HEALTH WEBSITES

Organization	Publication	Web Address
Carter Center	Guinea Worm Eradication Program	http://www.cartercenter.org/guineaworm.html
Center for Strategic and International Studies	Contagion and Conflict: Health as a Global Security Challenge	http://www.csis.org
Centers for Disease Control and Prevention	The HIV/AIDS Collaboration, CDC and The Ministry of Public Health Thailand	http://www.hac.or.th/
Centers for Disease Control and Prevention	Global Polio Eradication Initiative	http://www.cdc.gov/nip/global
Centers for Disease Control and Prevention	Guinea Worm Disease Fact Sheet	http://www.cdc.gov/ncidod/dpd/parasites/guineaworm
Centers for Disease Control and Prevention	Global AIDS Program	http://www.cdc.gov/nchstp/od/gap
Centers for Disease Control and Prevention	Working with Partners to Improve Global Health: A Strategy for CDC and ATSDR	http://www.cdc.gov/ogh/pub/strategy.htm
Centers for Disease Control and Prevention	International Health Data Reference Guide, 1999	http://www.cdc.gov/nchs/data/ihdr99.pdf
Centers for Disease Control and Prevention	U.S.-Mexico Border Infectious Diseases Surveillance	http://www.r10.tdh.state.tx.us/obh/bids.htm
Centers for Disease Control and Prevention	Preventing Emerging Infectious Diseases: A Strategy for the 21st Century	http://www.cdc.gov/ncidod/emergplan
Centers for Disease Control and Prevention	Biological and Chemical Terrorism: Strategic Plan for Preparedness and Response	http://bt.cdc.gov/documents/btstratplan.pdf
Centers for Disease Control and Prevention	Protecting the Nation's Health in an Era of Globalization: CDC's Global Infectious Disease Strategy	http://cdc.gov/globalidplan.htm
Council on Foreign Relations and Milbank Memorial Fund	Why Health Is Important to U.S. Foreign Policy	http://www.cfr.org//public/pubs/Kassalow_Health_Paper.htm
Department of Defense	Global Emerging Infections System	http://www.geis.ha.osd.mil
Department of Health and Human Services	DHHS Global Health Website	http://www.globalhealth.gov
Bill and Melinda Gates Foundation		www.gatesfoundation.org
Global Alliance for Vaccines and Immunization		http://www.vaccinealliance.org/
Institute of Medicine	Emerging Infections from the Global to Local Perspective	http://www4.nationalacademies.org/iom/iomhome.nsf
Institute of Medicine	America's Vital Interest in Global Health	http://www.nap.edu/books/0309058341/html
Joint United Nations Programme for AIDS (UNAIDS)		http://www.unaids.org
National Institute of Allergy and Infectious Diseases, National Institutes of Health	Global Research Plan for HIV/AIDS, Malaria, and Tuberculosis	http://www.niaid.nih.gov/publications/globalhealth/global.pdf
National Intelligence Council	The Global Infectious Disease Threat and Its Implications for the United States	http://www.cia.gov/cia/publications/nie/report/nie99-17d.html

Organization	Publication	Web Address
National Science and Technology Council, Committee on International Science, Engineering, and Technology, Working Group on Emerging and Reemerging Diseases	Infectious Disease—A Global Health Threat	http://www.ostp.gov/CISET/html/toc.html
Rockefeller Foundation	Program on Health Equity	http://www.rockfound.org/display.asp?context=3&SectionTypeID=18
Roll Back Malaria		http://www.rbm.who.int
Safe injection Global Network		http://www.injectionsafety.org
Stop TB Initiative		http://www.stoptb.org
United Nations Foundation		http://www.unfoundation.org
United States Agency for International Development	Infectious Disease Strategy	http://www.usaid.gov/pop.health/ID/index/html
World Bank, Pan- American Health Organization, and Inter- American Development Bank	Shared Agenda for Health in the Americas	http://wbln0018.worldbank.org/external/lac/lac.nsf
World Bank	World Development Report 2000/2001	http://www.worldbank.org/poverty/wdrpoverty/report
World Health Organization	Removing Obstacles to Healthy Development	http://www.who.int/infectious-disease-report/index-rpt99.html
World Health Organization	WHO Antimicrobial Resistance Infobank	http://oms2.b3e.jussieu.fr/arinfobank
World Health Organization	WHO Report on Global Surveillance of Epidemic-prone Infectious Diseases	http://www.who.int/emc-documents/surveillance/docs/whocdscsr2001.html/Tableofcontents/about.htm
World Health Organization	Overcoming Antimicrobial Resistance	http://www.who.int/infectious-disease-report/2000/index.html
World Health Organization	Global Strategy for the Containment of Antimicrobial Resistance	http://www.who.int/emc/globalstrategy/strategy.html
World Health Organization	The World Health Report 2000	http://www.who.int/whr/2000/en/report.htm
World Health Organization, Rotary International, Centers for Disease Control and Prevention, United Nations Children Fund (UNICEF)	Global Polio Eradication Initiative	http://www.polioeradication.org
World Health Organization, UNICEF, UNAIDS, World Bank, United Nations Educational, Scientific, and Cultural Organization (UNESCO), United Nations Population Fund	Health a Key to Prosperity	http://www.who.int/inf-new/

APPENDIX B

DIPLOMATIC FORUMS THAT ADDRESS EMERGING INFECTIOUS DISEASE ISSUES

Emerging infectious diseases are a topic of discussion at many high-level international meetings, including

Group of Eight Industrialized Nations (G8)^a
<http://usinfo.state.gov/topical/econ/group8>

Asia-Pacific Economic Cooperation (APEC)^b
<http://www.apecsec.org.sg>

Common Agenda with Japan
<http://www.mofa.go.jp/region/n-america/us/agenda>

Transatlantic Agenda with the European Union
<http://www.eurunion.org/partner/agenda.htm>

U.S.-Mexico Binational Commission
<http://www.r10.tdh.state.tx.us/obh/bids.htm>

The Arctic Council
<http://www.arctic-council.org>

-
- a. The Group of Eight Industrialized Nations includes: Canada, France, Germany, Italy, Japan, the Russian Federation, the United States, and the United Kingdom.
- b. The economies of the Asia-Pacific Economic Cooperation include Australia, Brunei, Canada, Chile, China, Hong Kong China, Indonesia, Japan, Republic of Korea, Malaysia, Mexico, New Zealand, Papua New Guinea, Peru, the Philippines, Russia, Singapore, Chinese Taipei, Thailand, the United States, and Vietnam.
- c. The Arctic Council includes: Canada, Finland, Greenland/Denmark, Iceland, Norway, Russia, Sweden, and the United States.

APPENDIX C

EXAMPLES OF INTERNATIONAL OUTBREAK ASSISTANCE

During the 1990s, CDC participated in numerous outbreak investigations in other countries, sometimes as part of an international WHO team and sometimes in direct response to a request from an affected nation. These investigations included

1990	Japanese encephalitis in Saipan
1990	Epidemic dysentery in Burundi
1991	Hepatitis E in Kenya and Somalia
1991-92	Epidemic dysentery in Zambia
1991	Cholera in Bolivia, Ecuador, El Salvador, Guatemala, and Peru
1991	Cholera in Brazil
1991	Polio in Romania
1991	Polio in Bulgaria
1992	Polio in Jordan
1992-96	Diphtheria in Ukraine
1993-96	Diphtheria in Russia
1993	Polio in Namibia
1993	Polio in Uzbekistan
1994	Dengue in Nicaragua
1994	Plague in India
1994-95	Measles in Palau, Guam, and the Federated States of Micronesia
1995	Diphtheria in Georgia, Kyrgyzstan, Kazakhstan, Uzbekistan, and Turkmenistan
1995	Leptosporosis in Nicaragua
1995	Ebola fever in the Democratic Republic of the Congo (then Zaire)
1996	Epidemic dysentery in South Africa
1996	West Nile encephalitis in Romania
1996	Typhoid fever in Tadjikistan
1996	<i>E. coli</i> O157:H7 infection in Japan
1996	Polio in Albania
1997	Polio in Turkey
1997	Botulism in Argentina
1997	Cholera in Kenya
1997	Avian influenza in Hong Kong
1997	Rift Valley fever in Kenya
1997	O'nyong-nyong fever in Uganda

1997	Nosocomial HIV-associated multidrug-resistant TB in Argentina
1997	Multidrug-resistant TB in Colombia
1998	Measles in Romania
1998	Bolivian hemorrhagic fever in Bolivia
1999	Louseborne relapsing fever in southern Sudan
1998	Plague in Ecuador
1998	Dengue in Palau
1998	Dengue in Yap
1998	Amebiasis in the Republic of Georgia
1998-99	Influenza outbreaks on cruise ships (U.S.-Canada)
1999	Dengue fever on U.S.-Mexico border
1999	Epidemic poststreptococcal glomerulonephritis in Brazil
1999	Typhoid fever in Nauru
1999	Nipah virus encephalitis in Malaysia
1999	Marburg fever in the Democratic Republic of the Congo
1999	Polio in Angola
1999	Measles in Costa Rica
1999-2000	Hantavirus pulmonary syndrome in Panama
2000	Polio in the Democratic Republic of the Congo
2000	Tularemia in Kosovo
2000	Cholera in Pohnpei State, Federated States of Micronesia
2000	Rift Valley fever in Saudi Arabia and Yemen
2000	Ebola hemorrhagic fever in Uganda
2000	Measles in Haiti, Dominican Republic, Bolivia
2000	Polio in Haiti and the Dominican Republic
2000	Measles in Zambia
2000	Diphtheria in Latvia
2000	Dengue hemorrhagic fever in El Salvador

APPENDIX D

WHO COLLABORATING CENTRES (WHOCCS) BASED AT CDC

WHOCC for Antimicrobial Resistance
WHOCC for Arthropod-Borne Viruses in the Western Hemisphere
WHOCC for *Clostridium botulinum*
WHOCC for Dengue and Dengue Hemorrhagic Fever
WHOCC for Research, Training, and Eradication of Dracunculiasis
WHOCC for HIV/AIDs
WHOCC for Reference and Reagents for Human Immunoglobulin Subclasses
WHOCC for Foodborne Disease Surveillance
WHOCC for Surveillance, Epidemiology, and Control of Influenza
WHOCC for Evaluating and Testing New Insecticides
WHOCC for Leptospirosis
WHOCC for Control and Elimination of Lymphatic Filariasis
WHOCC for Malaria Control in Africa
WHOCC for Production and Distribution of Malaria Sporozoite ELISAs
WHOCC for Mycoses in North America
WHOCC for Reference and Research on Plague Control
WHOCC for Poliovirus and Enterovirus Surveillance
WHOCC for Reference and Research on Rabies
WHOCC for Respiratory Viruses Other Than Influenza
WHOCC for Rickettsial Diseases
WHOCC for *Shigella*
WHOCC for Smallpox and Other Poxvirus Infections
WHOCC for Reference and Research in Syphilis Serology
WHOCC for Viral Hemorrhagic Fevers
WHOCC for Reference and Research on Viral Hepatitis

Tentative WHO Approval:

WHOCC for Lyme Borreliosis
WHO/PAHO Collaborating Center for Rotavirus and the Agents of
Viral Gastroenteritis
WHOCC for Public Health Systems and Practice

Proposed New Centers:

WHOCC for Cysticercosis
WHOCC for Molecular Identification and Typing of Insect Disease Vectors
WHOCC for Measles Virus Diagnostics (also serves as the PAHO
Regional Measles Reference Laboratory)
WHOCC for Prevention and Control of Epidemic Meningitis
WHOCC for Prevention and Control of *Mycobacterium ulcerans* (Buruli ulcer)
WHOCC for Insecticide Resistance
WHOCC for Infectious Disease Pathology
WHOCC for Salmonella Surveillance
WHOCC for Streptococcus
WHOCC for *Vibrio cholerae* O1 and O139

APPENDIX E

REGIONAL AND DISEASE-SPECIFIC SURVEILLANCE NETWORKS

A. Regional Networks for Disease Surveillance & Outbreak Response

Africa

- Integrated Disease Surveillance and Epidemic Preparedness and Response Project, led by WHO/AFRO
- International Disease Survey for diseases of epidemic potential (e.g., meningitis, yellow fever, cholera, measles, and polio), supported by USAID

Other disease surveillance activities in Africa:

The disease surveillance component of UNAIDS' International Partnership Against HIV/AIDS in Africa (IPAA) monitors progress in reducing infection rates and deaths from HIV/AIDS, TB, and opportunistic infections.

As part of USAID's African Integrated Malaria Initiative (AIMI), CDC helps ministries of health in Benin, Kenya, Malawi, and Zambia monitor progress in reducing illness and deaths from malaria. During 2001, AIMI surveillance activities will also be conducted in collaboration with the ministries of health of the Democratic Republic of the Congo, Nigeria, Senegal, and Uganda.

The U.S. Army Medical Research Unit in Nairobi (USAMRU-Kenya) is coordinating an effort to enhance surveillance for HIV/AIDS, malaria, yellow fever, and enteric illnesses in east Africa. Partners include ministries of health in Kenya and Uganda, the Kenya Medical Research Institute (KEMRI), the African Medical and Research Foundation (AMREF), and CDC's Kenya Field Station.

The Americas and the Caribbean

- Amazon Basin Network
Includes 7 laboratories from 5 nations
- Southern Cone Network
Includes 8 laboratories from 6 nations
- Caribbean Epidemiology Center (CAREC) disease surveillance system
Includes the 21 members of CAREC
- Middle America Network
- U.S.-Mexico Border Infectious Disease Surveillance System
- U.S./Canada International Circumpolar Surveillance project to enhance surveillance for invasive bacterial infections among indigenous peoples in sub-arctic regions of northern Canada and Alaska. This project is conducted in association with the International Circumpolar Surveillance project in Europe (see: **Europe**).

Other disease surveillance activities in the Americas and the Caribbean:

The U.S. Naval Medical Research Center Detachment (NMRCD) in Lima is coordinating an effort to enhance surveillance for malaria, yellow fever, dengue, and other hemorrhagic fevers in South America. Planners include ministries of

health of Peru, Ecuador, and Bolivia, WHO/PAHO, and CDC. An epidemiologist from CDC is currently stationed at NMRCDC.

Asia

- Mekong Delta Surveillance Network.
Includes China (Yunan), Cambodia, Laos, Thailand, Myanmar, and Vietnam
- Pacific Public Health Surveillance Network (PacNet)
Includes 20 Pacific Islands
- Early Warning Outbreak Recognition System (EWORS)
A collaboration between the Indonesian Ministry of Health and U.S. Naval Medical Research Unit No. 2 (NAMRU-2). It currently involves hospitals throughout Indonesia and is expanding to include hospitals in Cambodia.

Other disease surveillance activities in Asia:

Disease Surveillance and Electronic Networking are two of six “pillars” in a strategy to fight HIV/AIDS and infectious diseases endorsed at the 2001 summit meeting of the Asia Pacific Economic Cooperation (APEC). (The other pillars are: Outbreak Response, Capacity Building, Partnering Across Sectors, and Political and Economic Leadership.) As part of this effort, work has begun toward the creation of an Asia-Pacific network of networks that will knit together existing electronic infectious disease networks and facilitate timely transmission of public health information across APEC economies. The cooperative system will build on existing APEC projects that enhance surveillance for influenza, *E. coli* O157 infection, dengue, and dengue hemorrhagic fever.

The first International Emerging Infectious Program (IEIP) was established in Bangkok in September 2001, as a collaboration between CDC and the Ministry of Health of Thailand. This IEIP site will serve as a resource for infectious disease surveillance networks in Asia.

The United States participates in binational projects to improve disease surveillance with Vietnam, Thailand, and Cambodia. These collaborations are coordinated by CDC, the Armed Forces Research Institute of Medical Science (AFRIMS-Thailand) in Bangkok, and NAMRU-2 in Jakarta. For example, an epidemiologist from CDC stationed at NAMRU-2 and a satellite laboratory in Phnom Penh is working with the Cambodian Ministry of Health to establish a school of public health. An epidemiologist from CDC has also been assigned to China to facilitate collaborative projects that address the prevention and control of viral hepatitis, which is a major public health concern in China.

Europe

- E.U.’s EnterNet system for surveillance of international foodborne outbreaks
- International Circumpolar Surveillance project to enhance monitoring of invasive bacterial infections in the circumpolar regions of Europe (Iceland,

Greenland [Denmark], Norway, Sweden, Finland and Russia). This project is conducted in association with the U.S./Canada International Circumpolar Surveillance project (see: **The Americas and the Caribbean**).

The Middle East

- WHO Middle East Initiative to enhance disease surveillance in Israel and the Palestinian territories

Other disease surveillance activities in the Middle East:

The U.S. Naval Medical Research Unit No. 3 (NAMRU-3) in Cairo is coordinating a collaborative effort to enhance surveillance for diseases of importance in the Middle East (e.g., meningitis, influenza, acute febrile illnesses, and antibiotic-resistant enteric organisms). Partners include the Egyptian Ministry of Health and Population, health authorities in Yemen, Pakistan, and the Palestinian Territories, WHO/EMRO, and CDC. An epidemiologist from CDC is currently stationed at NAMRU-3.

B. Selected Global Networks for Infectious Disease Surveillance & Outbreak Response

- WHO Influenza Surveillance Network
- WHO Global Network for Polio Eradication/Measles Elimination
- WHO Supranational Reference Laboratory Network for Antituberculosis Drug Resistance
- WHO Global Salmonella Surveillance (Global Salm-Surv)
- WHO Global Alert and Response Network (see Box 14)
- Surveillance in support of the worldwide eradication of guinea worm disease
- Surveillance for vaccine-preventable diseases under the Expanded Programme on Immunization (EPI)
- GeoSentinel, the global surveillance network of the International Society of Travel Medicine

Includes 26 travel and tropical medicine clinics, 15 in the United States, 2 in the United Kingdom, 2 in Australia, and 1 each in Canada, Germany, Israel, Italy, Nepal, New Zealand, and Switzerland

As mentioned above, the first International Emerging Infectious Program (IEIP) was established in 2001 in Thailand. As new IEIP sites are founded (see page 53), they will provide technical assistance to local disease surveillance networks and become members of a global IEIP network.

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