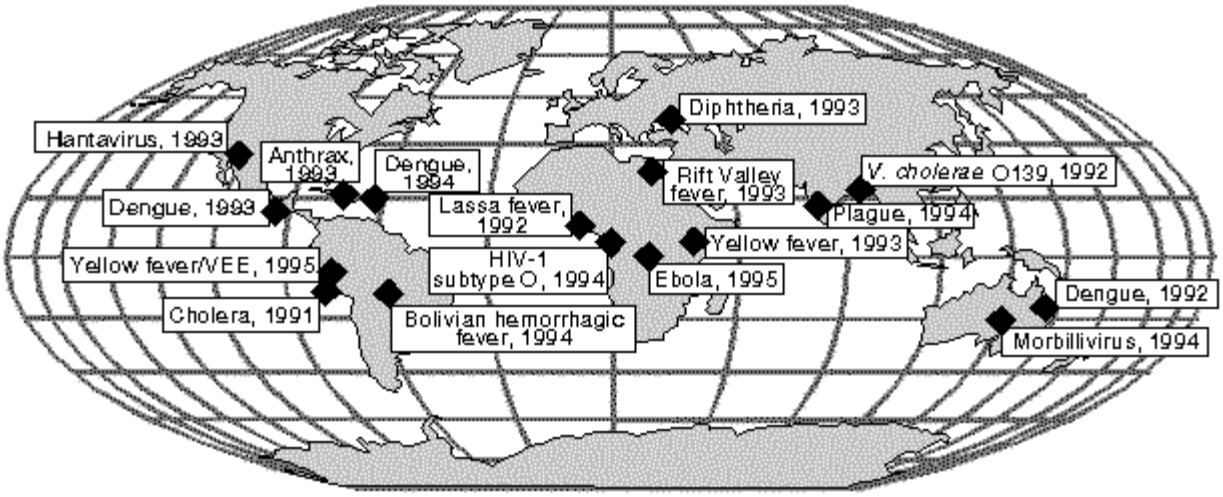
# Global Microbial Threats in the 1990s




***Report of the NSTC Committee on International Science, Engineering, and Technology (CISET) Working Group on Emerging and Re-emerging Infectious Diseases***

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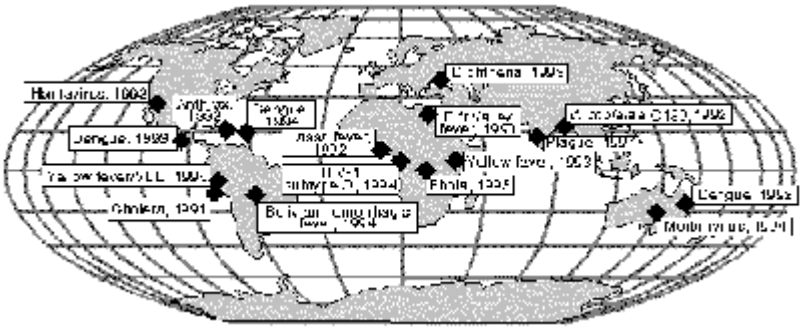


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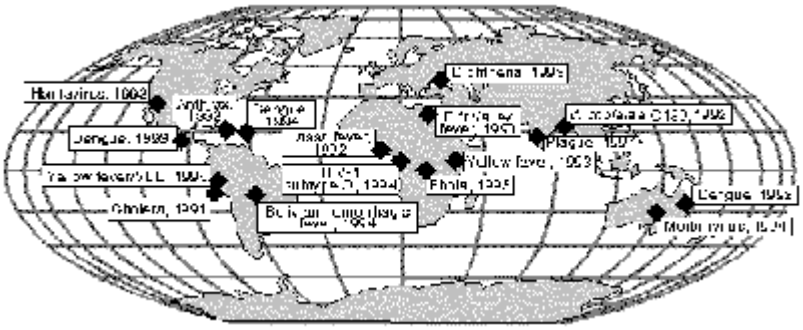
# *Global Microbial Threats in the 1990s*

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## Executive Summary

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### Emerging Infectious Diseases

Thirty years ago, the threat of infectious diseases appeared to be receding. Modern scientific advances, including antibiotic drugs, vaccines against childhood diseases, and improved technology for sanitation, had facilitated the control or prevention of many infectious diseases, particularly in industrialized nations. The incidence of childhood diseases such as polio, whooping cough, and diphtheria was declining due to the use of vaccines. In addition, American physicians had fast-acting, effective antibiotics to combat often fatal bacterial diseases such as meningitis and pneumonia. Deaths from infection, commonplace at the beginning of the twentieth century, were no longer a frequent occurrence in the United States. Meanwhile, in other parts of the world, chemical pesticides like DDT were lowering the incidence of malaria, a major killer of children, by controlling populations of parasite-carrying mosquitoes.

As it turned out, our understandable euphoria was premature. It did not take into account the extraordinary resilience of infectious microbes, which have a remarkable ability to evolve, adapt, and develop resistance to drugs in an unpredictable and dynamic fashion. It also did not take into account the accelerating spread of human populations into tropical forests and overcrowded mega-cities where people are exposed to a variety of emerging infectious agents.

Today, most health professionals agree that new microbial threats are appearing in significant numbers, while well-known illnesses thought to be under control are re-emerging. Most Americans are aware of the epidemic of the acquired immunodeficiency syndrome (AIDS) and the related increase in tuberculosis (TB) cases in the United States. In fact, there has been a general resurgence of infectious diseases throughout the world, including significant outbreaks of cholera, malaria, yellow fever, and diphtheria. In addition, bacterial resistance to antibiotic drugs is an increasingly serious worldwide problem. Furthermore, the number of people infected with the human immunodeficiency virus (HIV) that causes AIDS is increasing in many countries and may reach 40 million by the year 2000. Most recently, Ebola virus, which causes an often fatal hemorrhagic illness, has appeared again in Africa, and a formerly unknown virus of the measles family that killed several horses in Australia also infected two men, one of whom died.

New diseases have also appeared within the United States, including Lyme disease, Legionnaires' disease, and most recently hantavirus pulmonary syndrome (HPS). HPS was first recognized in the southwestern United States in 1993 and has since been detected in more than 20 states and in several other countries in the Americas. Other new or re-emerging threats in the United States include multidrug-resistant TB; antibiotic-resistant bacteria causing ear infections; pneumonia; meningitis; rabies; and diarrheal diseases caused by the parasite *Cryptosporidium parvum* and by certain toxigenic strains of *Escherichia coli* bacteria.

### Why are new infectious diseases emerging?

The reasons for the sharp increase in incidence of many infectious diseases - once thought to be under control - are

complex and not fully understood. Population shifts and population growth; changes in human behavior; urbanization, poverty, and crowding; changes in ecology and climate; the evolution of microbes; inadequacy of public health infrastructures; and modern travel and trade have all contributed. For example, the ease of modern travel creates many opportunities for a disease outbreak in remote areas to spread to a crowded urban area. Human behavioral factors, such as dietary habits and food handling, personal hygiene, risky sexual behavior, and intravenous drug use can contribute to disease emergence. In several parts of the world, human encroachment on tropical forests has brought populations with little or no disease resistance into close proximity with insects that carry malaria and yellow fever and other, sometimes unknown, infectious diseases. In addition, local fluctuations in temperature and rainfall affect the number of microbe-carrying rodents in some areas. Finally, in many parts of the world there has been a deterioration in the local public health infrastructures that monitor and respond to disease outbreaks.

## Are infectious disease surveillance and control cost-effective?

The costs of infectious diseases at home and abroad are staggering, and the cost-effectiveness of disease prevention has been demonstrated again and again. Every year, billions of dollars are lost in the United States in direct medical costs and lost productivity, due to intestinal infections, sexually transmitted diseases, influenza, and other viral, bacterial, or parasitic diseases. When diseases are controlled or prevented, tremendous savings can be achieved. For instance, a timely epidemiologic investigation in Washington State in 1993 led to the prompt recall of 250,000 hamburgers contaminated with *E. coli* O157, saving millions of dollars as well as preventing human suffering and death. Since smallpox was eradicated in 1977, the total investment of $32 million has been returned to the United States every 26 days. Based on the current rate of progress towards eradication of poliomyelitis, the World Health Organization predicts "global savings of half a billion dollars by the year 2000, increasing to $3 billion annually by the year 2015." Furthermore, every dollar spent on the vaccine against measles, mumps, and rubella, saves $21, while every dollar spent on the vaccine against diphtheria, tetanus, and pertussis saves $29. Clearly, public health measures that prevent or control infectious diseases are extremely cost-effective.

Today, two of the largest U.S. infectious disease health-care expenses are for the treatment of TB and AIDS. When the first cases of AIDS and drug-resistant TB were detected in the United States control measures were delayed, partly due to a lack of surveillance information. TB is an ancient disease, known throughout human history, that re-emerged in the United States in the late 1980s, sometimes in a drug-resistant or multidrug-resistant form. Government spending on infectious disease control had declined during the 1980s, and in 1986 the surveillance system for drug-resistant TB was discontinued. By 1993, multidrug-resistant TB had became a public health crisis and millions of federal dollars were necessary to control the emergency.

Unlike TB, AIDS is a newly emergent disease, unrecognized before the 1980s. AIDS might have been identified before it became established in the United States if a global surveillance system with the capacity to identify new diseases had been in place in the 1970s. As early as 1962, African doctors apparently witnessed cases of what was then known as "slim disease." Had the international community taken notice, epidemiologists might have gained a head start in learning how AIDS is transmitted and prevented, and many lives might have been saved.

Disease prevention is an investment in the young people of the world and in our collective future. Every year, an estimated four million infant and child deaths are prevented by vaccination and other preventive health measures, due to multilateral efforts. At the same time, many countries have dramatically strengthened their health-care delivery systems, even in the face of economic stagnation. On the other hand, the AIDS pandemic and the resurgence of malaria and TB are impeding economic development in many of the world's poorest countries.

## Need for U.S. leadership

The modern world is a very small place; any city in the world is only a plane ride away from any other. Infectious microbes can easily travel across borders with their human or animal hosts. In fact, diseases that arise in other parts of the world are repeatedly introduced into the United States, where they may threaten our national health and security. Thus, controlling disease outbreaks in other countries is important not only for humanitarian reasons. It also prevents those diseases from entering the United States, at great savings of U.S. lives and dollars. Moreover, U.S. support for disease investigations in other countries provides U.S. scientists with opportunities to bring U.S. capacity to focus on new pathogens like Ebola virus and consider how best to control, prevent, and treat them internationally before they arrive on our shores. Thus, U.S. interests are served while providing support to other nations.

Actively promoting the effort to develop an international partnership to address emerging infectious diseases is a natural role for the United States. American business leaders and scientists are in the forefront of the computer communications and biomedical research communities that must provide the technical and scientific underpinning for disease surveillance. The United States maintains more medical facilities and personnel abroad than any other country, in terms of both civilian and military, and public and private sector institutions. Furthermore, American scientists and public health professionals have been among the most important contributors to the international efforts to eradicate smallpox and polio. This position of leadership should be fostered.

Our earlier successes in controlling infections have bred complacency. Consequently, the component of the public health system that protects the public from infectious microbes has been neglected, both here and abroad, and its focus has narrowed. In the United States, federal, state, and local efforts to control communicable diseases are concentrated on a few targeted illnesses, with few resources allocated to address new or re-emerging diseases. This limits the ability of the U.S. medical community to detect and respond to outbreaks of newly emerging diseases, whether here or in foreign countries.

## International coordination of infectious disease prevention efforts

The challenge ahead outstrips the means available to any one country or to international organizations. The elimination of smallpox would not have been possible without a truly global effort. Similarly, multilateral leadership and resources propel the international program to eradicate polio. Both examples demonstrate the value to American citizens of resources invested in global disease prevention.

In addition, an effective global disease surveillance and response network will enable the United States to respond quickly and effectively in the event of terrorist incidents involving biological or chemical agents. The experience gained in controlling naturally occurring microbes will enhance our ability to cope with a biological warfare agent, should the need arise. The release of nerve gas in the Tokyo subway system in March 1995 has underscored our need to be well prepared to counteract deliberate attempts to undermine human health.

To address the growing threat of emerging infectious diseases the U.S. Government must not only improve its public health infrastructure, but also work in concert with other nations and international bodies, particularly WHO. The work and cost of protecting the world's people from infectious diseases must be shared by all nations. Some industrialized countries have already decided to devote substantial resources to a surveillance effort, and some less developed nations may also be ready to engage in an international effort that is so clearly in their own interests. President Clinton and the other leaders of the G7 nations recently endorsed 11 pilot projects of the Global Information Infrastructure at the Halifax Summit, including a project entitled, "Toward a Global Health Network." This project is designed to help public health institutions in their fight against infectious diseases and major health hazards. In addition, the World Health Assembly recently passed a resolution that focuses on national capacity building related to detecting and controlling emerging infectious diseases. The U.S. Agency for International Development (USAID), other donors, and the WHO, are continuing to assist developing countries in establishing disease prevention and control programs and to encourage the development of disease reporting systems.

Although international efforts must be coordinated to prevent global pandemics, disease surveillance is first of all the responsibility of each sovereign nation. However, individual governments may not only lack the means to respond but may also be reluctant to share national disease surveillance information, fearing losses in trade, tourism, and national prestige. Nevertheless, because the United States is widely respected as the world's foremost authority on infectious disease recognition and control, we do learn about most major disease outbreaks in other countries, although not always in an official or timely fashion. Individual doctors, laboratories, or ministries of health often seek United States assistance when they are confronted with a disease problem that they cannot solve. To ensure that we continue to be notified when an unusual outbreak occurs, we must encourage and support other countries' efforts in national disease surveillance and respond when asked for assistance. We must strive to develop a sense of shared responsibility and mutual confidence in the global effort to combat infectious diseases.

The effort to build a global surveillance and response system supports other foreign policy goals of the United States. Obviously, such a system will help protect the health of American citizens and of people throughout the world. In the post-Cold War period, a major objective of U.S. foreign policy is the promotion of political stability through sustainable economic development around the globe. Helping other countries to help themselves _ to improve the lives of their

citizens, develop their economies, and find niches in the global economy _ is a major goal for U.S. foreign assistance. Healthy people are more productive and better able to contribute to their country's welfare.

## Building a global infectious diseases network

### Surveillance

At the present time, a formal system for infectious disease surveillance does not exist on a global scale. When a cluster of cases of a new disease occurs in a remote part of Africa, Eastern Europe, Asia, or the Americas, the international community may or may not learn about it. If a new disease of unknown cause occurs in a part of the world that lacks modern communications, it may spread far and wide before it is recognized and brought under control. In most cases, however, news of a major outbreak spreads informally. When international resources are successfully mobilized, assistance in diagnosis, disease control and prevention can be made available to local health authorities. Clinical specimens can be sent to a diagnostic "reference" laboratory to rule out known disease agents. Epidemiologists can be sent into the field to help investigate the source of the new infection and determine how it is transmitted. Public health officials can use this information to implement appropriate control measures. Once the infectious agent has been identified, which is often a difficult task, experimental scientists can start to develop diagnostic tools and treatments if the disease is carried by a previously unknown agent.

The elements of a global network for disease surveillance already exist but need to be strengthened, linked, and coordinated. For instance, many U.S. Government departments and agencies maintain or support field stations and laboratories in Africa, Asia, and the Americas that may be electronically linked to provide an initial framework for a network for global infectious disease reporting. In partnership with other countries and with WHO, this skeletal surveillance network could be expanded over time to include many international resources, including national health ministries, WHO Collaborating Centers, hospitals, and laboratories operated by other nations, and American and foreign private voluntary organizations.

Information technology is revolutionizing communications worldwide; this technology needs to be applied to disease control programs, not only to effectively monitor program performance and progress, but also to detect and report emerging problems.

### Response

The process of response encompasses a multitude of activities, including diagnosis of the disease; investigation to understand its source and modes of transmission; implementation of control strategies and programs; research to develop adequate means to treat it and prevent its spread; and production and dissemination of the necessary drugs and vaccines.

The international community does not always have adequate resources to respond to localized disease outbreaks and control them before they can spread across borders. If an "old" disease re-emerges, there may be a need for epidemiologic investigations and/or for emergency procurement or production of medical supplies. If the disease is new, efforts will be needed to identify the causative microbe and determine how to stop its transmission. To make the best possible use of U.S. expertise and resources, it is necessary to establish clear lines of authority and communication among U.S. Government agencies.

Response to infectious disease outbreaks, whenever and wherever they occur requires international preparation and planning. A goal of the WHO is to assist each country to develop its ability to provide laboratory diagnosis of diseases endemic to its area and to refer specimens from suspected newly emergent or re-emergent diseases to an appropriate regional reference laboratory. To reach this goal, each country must train medical workers and laboratory technicians and supply them with appropriate equipment and diagnostic resources.

In addition, several international elements must be in place to provide the wherewithal for effective and timely disease control and prevention efforts. First, regional reference laboratories must be maintained to provide diagnostic expertise and distribute diagnostic tests. Second, an international communications mechanism must be made available to receive and analyze global disease surveillance information. Third, regional procedures should be instituted to facilitate the production, procurement, and distribution of medical supplies, including vaccines for disease eradication programs.

Fourth, enhanced public education in simple health measures in both industrialized and developing countries is very important.

Through programs administered by USAID and other agencies, the United States has invested in assisting developing countries to establish disease prevention and control programs, trained thousands of individuals, and strengthened scores of institutions. As a consequence, developing country researchers are better prepared to solve their own disease problems and contribute to solving global ones. Strengthening this foundation will be critical to facilitating timely and effective responses to disease outbreaks and minimizing the impact of emerging disease threats.

**Research**

An effective system for disease surveillance and control is critically dependent on a strong and stable research infrastructure. Scientific studies of infectious agents and the diseases they cause provide the fundamental knowledge base used to develop diagnostic tests to identify diseases, drugs to treat them, and vaccines to prevent them. Traditionally, this has been an area of U.S. strength and international leadership. To meet the new challenges represented by emerging diseases, a strong research and training effort must be sustained and strengthened. The current level of support for research and training in laboratory and field work on infectious diseases, other than AIDS and TB, is very limited. To combat new diseases for which no treatments are available, it is essential to maintain an active community of well-trained epidemiologists, laboratory scientists, clinical investigators, behavioral scientists, entomologists, and public health experts ready and able to seek new solutions for disease threats. At the present time, many of the brightest young microbiologists in the United States are leaving the field, discouraged by the lack of jobs and research funds.

USAID, National Institutes of Health (NIH), and Centers for Disease Control and Prevention (CDC) support has fostered the capacity of less developed countries to identify and solve their infectious disease problems. Applied research in these countries is aimed at preventing disease transmission through control of insect and animal vectors, environmental factors, and behavior, and at evaluating new or improved therapeutic and preventive measures. In addition, the National Oceanic and Atmospheric Administration is developing tools to predict local changes in weather that effect the incidence of vector-borne diseases.

**Training**

Many research programs routinely incorporate training opportunities for graduate students and postdoctoral fellows. In addition, there is an urgent need to augment specialized training programs in such areas as the handling of hazardous microbes, public health management, and field epidemiology.

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**Summary of Recommendations of the CISET Working Group**

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An interagency Government working group on emerging infectious diseases was formed in December 1994 under the auspices of the National Science and Technology Council's Committee on International Science, Engineering, and Technology (CISET). Led by CDC, the Department of State, USAID, Food and Drug Administration, NIH, and the Department of Defense, the working group makes the following recommendations for action by the U.S. Government.

Work in partnership with other countries, with WHO, and with other international organizations to improve worldwide disease surveillance, reporting, and response by

1. Establishing regional disease surveillance and response networks linking national health ministries, WHO regional offices, U.S. Government laboratories and field stations abroad, foreign laboratories and medical centers, and WHO Collaborating Centers.
2. Ensuring that reliable lines of communication exist between local and national medical centers and between national and regional or international reference facilities, especially in parts of the world where modern communications are lacking.
3. Developing a global alert system whereby national governments can inform appropriate worldwide health authorities of outbreaks of infectious diseases in a timely manner, and whereby individual health authorities can access regional centers.

4. Identifying regional and international resources that can provide diagnostic reagents for low incidence diseases and help identify rare and unusual diseases.
5. Assisting WHO to establish global surveillance of antibiotic resistance and drug use, as a first-step toward the development of international agreements on antibiotic usage.
6. Encouraging and assisting other countries to make infectious disease detection and control a national priority.
7. Preserving existing U.S. Government activities that enhance other countries' abilities to prevent and control emerging and re-emerging health threats.
8. Identifying and strengthening WHO Collaborating Centers that serve as unique reference centers for diseases whose re-emergence is feared.
9. Establishing the authority of relevant U.S. Government agencies to make the most effective use of their expertise in building a worldwide disease surveillance and response network.

Strengthen the U.S. capacity to combat emerging infectious diseases by

10. Enhancing collaborations among U.S. agencies to ensure maximum use of existing resources for domestic and international surveillance and response activities. Supporting the G7-initiated project on public health applications of the Global Information Infrastructure, entitled "Toward a Global Public Health Network."
11. Rebuilding the U.S. infectious disease surveillance public health infrastructure at the local, state, and federal levels.
12. Working with the private and public sectors to improve U.S. capacity for the emergency production of diagnostic tests, drugs, and vaccines.
13. Supporting an active community of epidemiologists, clinical investigators, laboratory scientists, health experts, and behavioral scientists ready and able to seek new solutions for new disease threats.
14. Strengthening technical training programs in disciplines related to infectious disease surveillance and response.
15. Providing accurate and timely health information to private citizens and health providers, both in the United States and abroad, when a disease outbreak occurs.
16. Strengthening infectious disease screening and quarantine efforts at ports of entry into the United States.
17. Strengthening the training of American physicians and microbiologists in the recognition of "tropical diseases" and in travel medicine in general.
18. Establishing an Interagency Task Force to coordinate the implementation of these recommendations.
19. Establishing a private sector subcommittee of the Interagency Task Force that includes representatives of the U.S. pharmaceutical industry, medical practitioners and educators, and biomedical scientists.

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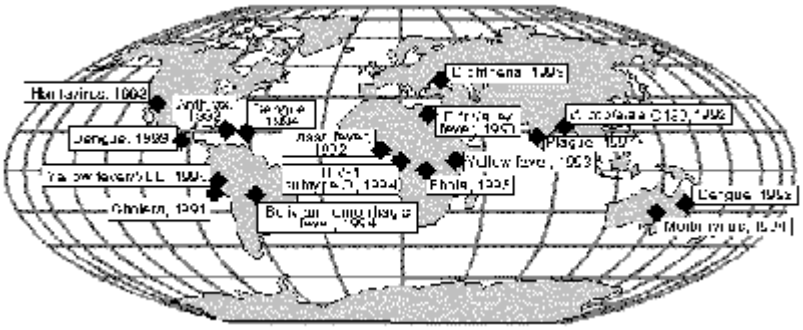


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## II. What actions are taken by the U.S. Government when an infectious disease outbreak occurs?

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For the U.S. Government to help in controlling an incipient - or raging - epidemic in another country, three things must occur. First, reliable information must reach the United States. Second, U.S. scientists and public health officials must evaluate the information and decide what measures should be taken. Third, U.S. officials must help the affected country implement those measures. However, U.S. participation in an epidemiologic investigation within another nation is dependent upon a formal request for assistance from the foreign government. This was the pattern of events during the Ebola virus investigation (see "Lessons Learned From the Ebola Virus Outbreak in Zaire"). If no request is received, our Government may still take action to minimize the risk of disease importation into the United States (see "Plague in India").

### The informal global surveillance network

When a cluster of cases of an emerging infectious disease occurs in a remote part of Africa, Asia, Eastern Europe, or the Americas, the international community may or may not learn about it. In some cases, an American company or Government agency overseas (the Army, Peace Corps, USAID, a U.S. embassy) or an WHO official may report an unusual illness to the CDC and seek assistance in testing specimens for diagnosis. Occasionally, a colleague from another industrialized country who is working in a developing area will provide the first notification of an emerging disease. Through international conferences and scientific collaborations, U.S. infectious disease experts have made contacts with colleagues all over the world. As a consequence, these experts receive informal calls from foreign colleagues requesting advice and assistance when an unusual outbreak occurs.

In some cases -- if the notification arrives quickly enough -- this informal surveillance system works. When international resources are successfully mobilized, assistance in diagnosis, disease control and prevention can be made available to local health authorities. Clinical specimens can be sent to a diagnostic reference laboratory to rule out known disease agents (see "The Informal Global Network"). Epidemiologists can be sent into the field to investigate the source of the new infection and determine how it is transmitted. Public health officials can use this information to implement appropriate control measures. Once the infectious agent has been identified, which is often a difficult task, experimental scientists can start to develop diagnostic tools and treatments if the agent is a newly recognized one.

However, a new infectious disease can be easily overlooked, especially when the disease originates in a part of the world that lacks effective domestic disease surveillance and modern communications. Left unchecked, the disease may spread far and wide before it is recognized and reported.

### Evaluation of disease surveillance information

When reports of a potential epidemic and requests for assistance reach the United States, scientists evaluate the

information and provide advice on further investigations, the availability of diagnostic tests, and treatment. Within the United States, CDC takes the lead in evaluating surveillance information. In many instances CDC and USAID will offer to send diagnostics, drugs, or vaccines to the affected area.

## Response to international disease outbreaks

When the U.S. Government learns of an epidemic in another country, agencies consult with each other on what the United States response should be. Among the Government agencies with relevant expertise in this area are CDC, FDA, NIH, DoD, and USAID.

**Lack of an executive function for response to epidemics.** The U.S.Government response to international epidemics occurs on an ad hoc basis. As described below (and in the inventory that accompanies this report), many Government agencies and departments have resources that can facilitate an effective response to epidemics of infectious diseases.

The authority of CDC, for instance, does not cover international disease control and prevention, and USAID has limited technical and financial resources in this area. In practice, individual Government workers who become aware of outbreaks do what they can to coordinate agency efforts and provide aid to affected countries. But there is no formal structure or designated resources for this activity.

**Resources for emergency responses.** ***At present, the U.S. Government has no funds set aside for responses to international disease outbreaks.*** Government disaster assistance groups such as the Federal Emergency Management Administration and USAID's Office of Foreign Disaster Assistance (OFDA) do not take responsibility for infectious disease emergencies. At CDC although approximately 65% of the budget is dedicated to the prevention and control of infectious diseases, about 95% of these funds are earmarked for AIDS, TB, and sexually transmitted diseases and vaccine preventable diseases. Moreover, USAID has limited resources available for international outbreak investigations. Thus, when a new or re-emerging disease is suspected in another country, there is very little flexibility in any U.S. Government agency's budget to provide for an investigation.

**Importation of infectious diseases into the United States.** Each time an infected person (or a contaminated food or sick animal) enters the United States, an opportunity arises for a contagious microbe to spread to the American people. CDC strives to prevent this in two ways. One protective measure is to issue advisories that caution against travel to or from the site of an epidemic. CDC also provides information on travelers' health, including information on recommended vaccinations and on regimens for drug prophylaxis. A more comprehensive line of defense relies on local surveillance systems, at the state, county, and city levels. Unfortunately, our local public health surveillance systems are no longer adequate because of our past complacency about infectious diseases, poor planning, and lack of resources.

***Screening of travelers at U.S. ports of entry.*** Under the Public Health Service Act and the Foreign Quarantine Regulations, all aircraft and ships captains are required to radio the nearest CDC quarantine station at their port of arrival when they have an ill person or when a passenger has died. CDC has the authority to detain, isolate, or conditionally release any person believed to be infected or exposed to a communicable disease. CDC staffs quarantine stations at seven ports of entry at major airports in New York, Miami, Chicago, Seattle, San Francisco, Los Angeles, and Honolulu. Each station provides backup for other ports in their geographic area of responsibility. At ports of entry where CDC does not have staff, the gap is filled by airline workers, by physicians on contract with CDC, and by officials of the Immigration and Naturalization Service (INS). U.S. civilians, foreign nationals (including tourists, business travelers, long-term visitors), and immigrants can enter at any of these airports, as well as seaports and land border areas. There are approximately 50 international airports in the United States and more than 150 other legal entry points.

The identification of persons carrying pathogens capable of causing serious disease outbreaks is made difficult by the very large number of people entering the United States from increasingly remote locations. Most American cities can be reached within 36 hours from anywhere in the world, either by direct or by connecting flights. The incubation periods of most infectious diseases (the time between infection and the appearance of symptoms) is considerably longer than 36 hours. Because only obviously ill patients are identified by screening at ports of entry, routine state and local surveillance efforts are relied on to identify infected travelers who become ill some time after entry into the United States.

***Screening of soldiers.*** Military personnel who return to the United States are not routinely quarantined. Military personnel who become ill overseas are evacuated to DoD medical facilities in the United States. Military personnel who are not sick return to their unit bases. Deployed reservists are more apt to re-enter civilian health-care channels than active duty personnel. The medical tracking of all deployed military personnel after they return home is being improved by DoD to facilitate the recognition and diagnosis of latent infections.

***Food-borne and animal-borne diseases.*** CDC's quarantine program also coordinates with the U.S. Department of Agriculture (USDA), U.S. Fish and Wildlife Services, Department of Interior, and FDA to ensure that other possible carriers of human disease (food and animals) are managed appropriately.

USDA's Food Safety and Inspection Service (FSIS) plays an important role in disease control and eradication. FSIS samples food products for a number of pathogens and protects the food supply by retaining or recalling products. FSIS inspects for conditions and collects samples to test for many diseases such as rabies, tuberculosis, brucellosis, and pseudorabies which can be transmitted to humans. This inspection is crucial for the surveillance and monitoring system of the USDA-APHIS.

The Animal and Plant Health Inspection Service (APHIS) of the USDA is responsible for protecting American livestock and poultry from foreign and domestic diseases. Many diseases of humans are carried by and transmitted from animals or animal products (Ebola, anthrax, cryptosporidium, hantavirus, Rift Valley fever, Lyme disease, *E. coli*, tuberculosis, brucellosis, rabies, pseudorabies, to name to few). APHIS carries out this responsibility through several activities:

1) exclusion of foreign animal diseases,
2) disease exclusion through import testing,
3) domestic animal disease control and eradication, and
4) national animal health monitoring.

The USDA's animal health infrastructure and mission is, in part, built on the important task of excluding and rapidly responding to the introduction of these pests and diseases. APHIS inspects animals entering the United States from foreign countries at the border or port of entry. APHIS establishes quarantine and testing requirements for imported animals to reduce the risk of diseases and operates several USDA quarantine facilities.

In addition to exclusion activities, APHIS operates programs to control and eliminate diseases in domestic livestock, including those that also affect humans. Interstate movement and transport of infected and exposed animals are regulated in an effort to stop further spread of the diseases. Monitoring of animal diseases is maintained through APHIS' National Animal Health Monitoring System.

## Conclusion

Three steps are involved in responding to a disease outbreak -- *surveillance, evaluation, and implementation of control measures.* Surveillance begins with accurate diagnosis and requires open lines of communication among doctors, scientists, and government officials. Evaluation requires epidemiologic and laboratory based investigations. Disease control requires that public health infrastructures are in place and that resources are available to procure and distribute medical supplies, such as drugs and vaccines. Significant improvements can be made in surveillance and response to international epidemics, if U.S. agencies are granted mandates and authority to make the most effective use of U.S. expertise in public health.

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## The Informal Global Network

Sometimes the informal global surveillance and response system for infectious diseases works very well, however, sometimes it does not - as the following examples illustrate.

**Successful Surveillance to Prevent Disease Transmission: Venezuelan Equine Encephalitis in Peru**
During 1994 and early 1995, the U. S. Naval Medical Research Institute Detachment (NAMRID) in Lima, Peru,

detected several cases of dengue fever, oropouche, and Venezuelan equine encephalitis (VEE) in northern Peru. These diseases are caused by arboviruses, which are carried by insect vectors, and vaccines against several arboviral illnesses are available. CDC followed up on the NAMRID reports and determined that VEE had occurred among Peruvian soldiers stationed in the area of the border dispute with Ecuador. The health authorities in Peru and Ecuador were notified and control measures were implemented.

After these occurrences, it came to the attention of CDC that the U.S. Army was planning to deploy troops in this area to mediate the border dispute. CDC notified the U.S. Army at Fort Detrick, Maryland, and the Southern Command in Panama, and advised that all troops be immunized against VEE before deployment.

**An Epidemic Spreads from Continent to Continent: Dengue Fever in Asia**
In recent years several Caribbean countries have experienced epidemics of dengue fever but have failed to report them, fearing that the news would have a negative impact on their tourist industries. The outbreaks became known only after tourists returning to their home countries became ill.

Although CDC and WHO received rumors of outbreaks of dengue and dengue hemorrhagic fever (DHF) in Asia during the late 1980s, CDC did not receive official information about them, and no diagnostic samples were sent for confirmation. (DHF and dengue fever are different clinical manifestations of the same viral infection.) Eventually, CDC's WHO Collaborating Centre for Reference and Research on Dengue and DHF received blood samples from a pediatrician in the area of Asia, and the presence of a specific strain of dengue virus was confirmed. In 1994, when dengue fever broke out in Central America, scientists isolated the same strain of virus from the Central American blood samples, indicating that the virus that caused DHF in Asia had spread to the Americas.

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## Plague in India

In August 1994, CDC received informal reports of bubonic plague in Maharashtra state, India. Bubonic plague is carried by fleas that live on rodents. That summer, many flea-infected rats had died because of a drought, and some of the fleas had apparently moved to human hosts. In September, reports were also received of pneumonic plague (a different clinical manifestation of the same infection) in Gujarat state, India. Pneumonic plague spreads more quickly than bubonic plague, because it is transmitted from one person to another by coughing. CDC sent diagnostic reagents to India and offered technical assistance, but the Indian Government did not request on-site assistance.

The U.S. Government took several steps to ensure that plague would not be imported into the United States. The State Department invited two American epidemiologists to New Delhi to assist the U.S. embassy and to be available if Indian doctors or political authorities requested help. In addition, CDC issued advisories to international travelers, notified state health authorities, and increased surveillance at U.S. airports. FDA worked with pharmaceutical manufacturers to accelerate efforts to increase supplies of plague vaccine. In October, CDC participated in a WHO-led investigation, and by October 27 determined that no infectious disease emergency existed. Effective surveillance, followed by prompt diagnosis and treatment, could have reduced the magnitude of the crisis and saved India much of the estimated $2 billion in revenues lost from tourism, exports, and shipping. The U.S. agencies which participated in the Government response to the plague in India included the Departments of State, Justice (Immigration and Naturalization Service), Agriculture, and Transportation; the Public Health Service (including CDC and FDA) of the Department of Health and Human Services; USAID; and state and local health departments. Despite the cooperation of these agencies, the U.S. Government had domestic obstacles to overcome in responding to this international health emergency. At present, CDC has the only laboratory in the world that serves as a reference laboratory for plague. Unfortunately, support for that laboratory has decreased to the point where there is only one full-time employee with experience and training in plague epidemiology and treatment. To respond effectively, CDC had to pull staff and resources from other programs.

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## Public Health Terms

**Reference Laboratory:** A specialized laboratory to which clinical specimens (such as sputum, stool, spinal fluid, or blood samples, or organisms isolated from them) can be sent (from a primary care laboratory) for diagnosis, identification, or confirmation. Many WHO Collaborating Centres function as reference laboratories.

**Sentinel Surveillance System:** A network of individuals, facilities, or laboratories that monitors changes in the incidence of disease in a systematic way. Such networks usually include many strategically located outposts and are designed to serve as early warning systems for disease outbreaks.

**Epidemic or Outbreak:** The occurrence of cases of a disease above the expected number or baseline level, usually over a given period of time, in a geographic area, or in a specific population group.

**Emerging Infection:** A new or newly identified pathogen or syndrome which has been recognized over the last two decades, or which has resulted in new manifestations of disease.

**Re-emerging Infection:** A known or previously identified pathogen or syndrome which is increasing in incidence, expanding into new geographic areas, affecting new population groups, or which threatens to increase in the near future.

**Zoonosis:** A disease that can be transmitted from animals to humans.

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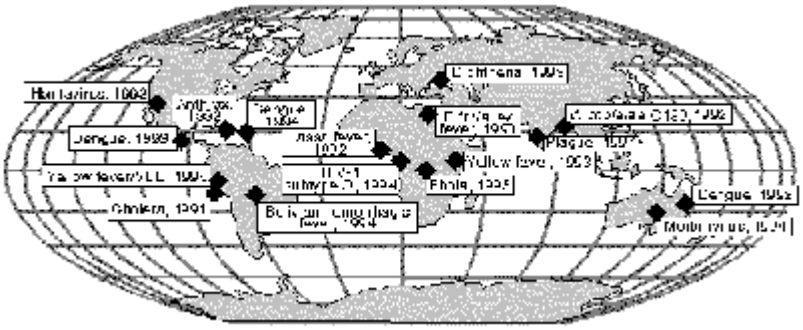
# *Global Microbial Threats in the 1990s*




## III. How can we help build a global network for infectious disease reporting and response?

To avert the threat of emerging infections and prevent their spread into the United States, or into any other countries, health officials must be aware when epidemics occur anywhere in the world. However, reliable information can only be secured through clinical and laboratory-based surveillance that links medical and public health workers into a cooperative worldwide network. "Laboratory-based surveillance" implies that diagnostic tools and technicians are available to analyze blood, sputum, or stool samples from sick people or animals. The public health workers in the network must include epidemiologists who can investigate the nature and extent of microbial threats. Moreover, the global network should also incorporate prevention efforts by coordinating investigations into the environmental and human factors that promote the evolution and emergence of infectious microbes.

Many elements of a potential global network do exist - but need to be linked, coordinated, and strengthened, working in partnership with other countries and with WHO. Many U.S. Government department and agencies - including DoD, CDC, USAID, NIH, USDA, NASA, and NOAA - maintain field stations and laboratories in Africa, Asia, and the Americas. The introduction of inexpensive communications linkages among these facilities - by fax, by phone, by Internet - could provide an initial framework for global infectious disease reporting. This skeletal network could be expanded over time to include many other national and international resources. For instance, the U.S. State Department and the Peace Corps maintain medical facilities in remote areas that could be brought into the network as important sentinel outposts. Internationally, the network would include links with national health ministries, with hospitals and laboratories operated by other nations, with foreign research centers such as the French Pasteur Institutes, with American and foreign non-governmental organizations (NGOs), and with WHO Collaborating Centres around the world.

### A Network for Global Disease Surveillance

Four strategic objectives are necessary to establish a global system for disease surveillance and response:

**Surveillance.** Strengthen existing surveillance systems so that changes in the incidence of known illnesses are routinely reported, and information on the emergence of new or unusual diseases is readily available to the ministries of health in other nations, WHO, and CDC. Reliable lines of communication must be established to ensure that surveillance information is received promptly enough to control outbreaks before they spread.

**Diagnostic Tests.** Work with WHO, national public health authorities, universities, and research centers to implement WHO's country-level objectives. This entails determining which "common" diseases should be diagnosed within a country and which "uncommon" ones should be referred to reference laboratories. It also requires that diagnostic tests be made available through a regional laboratory referral and distribution system.

Develop simpler, more cost-effective procedures to determine the causes of disease. Ideally, these procedures should be

simple enough for use in the field when laboratory facilities are not available.

Support basic and applied research on infectious microbes, especially on pathogens for which there are no reliable diagnostic tests. The new tools of biotechnology should be exploited to speed these efforts.

**Response**. Enhance the capabilities of U.S. Government agencies and existing disease-specific networks (see "International Resources Related to Infectious Diseases") to respond to recognized outbreaks identified through improved surveillance. Also, rebuild and coordinate the relevant technical resources of U.S. Government agencies such as CDC, DoD, USAID, and FDA.

Diseases that are transmitted by different routes will necessarily require different control strategies. Types of response may include sanitation and hygiene measures, controlling populations of disease vectors (for example, malaria-carrying mosquitoes or rabid raccoons), drug treatment, vaccination or post-exposure prophylaxis, or education to decrease human behaviors that cause spread.

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## Surveillance to Detect New Diseases

Unexplained disease symptoms or clinical circumstances that may suggest a need for further investigation when clusters of cases occur include:

- Acute respiratory disease
- Encephalitis and aseptic meningitis
- Hemorrhagic fever
- Acute diarrhea
- Fever and rash
- Acute flaccid paralysis
- Resistance to common treatment drugs
- Unusual clusterings of deaths
- Outbreaks of disease in domestic or wild animals (epizootics)

Each nation should be encouraged to report, as early as possible, new events or trends in human or animal, diseases that are affecting its own population.

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## Interdisciplinary Research to support Control and Prevention.

Form linkages between

- Experimental biologists and epidemiologists both here and abroad.
- The global infectious disease network and environmental and climatic research programs.

Encourage collaborative research to determine the causes of epidemics, devise strategies for control and prevention, and identify environmental and climatic conditions that favor the emergence of pathogenic microbes.

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## Prevention Through Immunization: The Search for an Effective Pneumonia Vaccine

The largest killer of infants and young children in developing countries are acute respiratory infections, mainly pneumonia, which claim the lives of an estimate 3.8 million children under age 5 every year. While appropriate case-management, using common antibiotics, has been very successful in treating these diseases, the emergence of antimicrobial resistant strains suggest that this success may be relatively short-lived. One way to avoid problems with resistance is to prevent the infection from occurring, using safe and effective vaccines.

Through its Children's Vaccine Initiative Project, USAID is initiating a major new program to evaluate newly developed vaccines that may protect children in underdeveloped countries. These vaccines are aimed against major bacterial and viral causes of pneumonia, including *Streptococcus pneumoniae* and *Haemophilus influenzae* b. Studies in the industrialized world and preliminary studies in developing countries suggest that these vaccines, especially new "conjugated" versions, hold great promise.

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## RECOMMENDATIONS OF THE CISET WORK GROUP

### How can the United States Accomplish These Surveillance Objectives?

To build an effective international surveillance and response network, a U.S. Government Interagency Task Force should be established and granted the authority and resources to implement the following actions:

Work in partnership with other countries, with WHO, and with other international organizations to improve worldwide disease surveillance, reporting, and response by

**1. Establishing regional disease surveillance and response networks linking national health ministries, WHO regional offices, U.S. Government laboratories and field stations abroad, foreign laboratories and medical centers, and WHO Collaborating Centers.**

These activities can be closely linked with our domestic surveillance networks through CDC, which is responsible for infectious disease surveillance within the United States. In addition, several "vertical" (disease-specific) networks that are currently sponsored by WHO (see WHO) can be integrated into these regional networks.

Model surveillance and response projects can be established in such regions as the Middle East, Sub-Saharan Africa, Southeast Asia, South America, and Eastern Europe and the Newly Independent States of the former Soviet Union. An example of a proposed regional network in the Middle East is shown on map .

Over time, the functions of these regional "hubs" may be expanded to include

- Surveillance of antibiotic resistance
- Surveillance of zoonoses
- Surveillance of insecticide resistance in parasite vectors
- Warnings of potential increases in disease incidence predicted by environmental and climatic monitoring systems

**2. Ensuring that reliable communications links are available (by post, telephone, facsimile, and Internet) between local and national medical centers and between national and regional (or international) reference facilities.**

Some vulnerable areas of the world (such as rain forest communities in South America, Africa, and the South Pacific) are relatively isolated. An assessment of gaps in the global communications network should be undertaken to avoid excluding such communities. While WHO should initiate and support this survey, U.S. agencies such as CDC, DoD, and USAID can supply the technical advice and expertise to help ensure its success.

**3. Developing a global alert system whereby national governments inform appropriate worldwide health authorities of outbreaks of infectious diseases in a timely manner.** This recommendation entails a concerted diplomatic effort to develop a sense of shared responsibility and mutual confidence in the international effort to combat infectious diseases.

**4. Identifying regional and international resources that can provide diagnostic reagents for low-incidence diseases, and help identify rare and unusual diseases.**

To identify and control unusual diseases such as those caused by hantaviruses or Ebola virus, clinical diagnoses must be confirmed using diagnostic tests. For example, to stem the spread of Ebola virus in Zaire in May 1995 (see Lessons

Learned From the Ebola Virus Outbreak in Zaire), the international team of epidemiologists needed to distinguish between fever patients infected with Ebola virus and febrile patients infected by other microbes. The team shipped blood samples to CDC biohazard laboratories in Atlanta, which had the necessary diagnostic capability.

Many countries, both industrialized and developing, have medical and research institutions which can serve as significant resources in combating emerging diseases.

> **5. Assisting WHO to establish surveillance of antibiotic resistance and drug use, as a first-step towards the development of international agreements on antibiotic usage.** WHONET, an international reporting system for antibiotic resistance, provides WHO with a starting point for this significant work. Taking advantage of its overseas networks USAID can provide support for surveillance of drug resistance that hinders the treatment of internationally important diseases. In addition, CDC can contribute technical support and data management resources.

It is also crucial to develop and implement strategies that extend the useful life span of antibiotics and other drugs by retarding the development of resistance. This entails behavioral research on how to ensure correct drug use and biomedical research on the development of alternative drugs and drug regimens.

> **6. Encouraging and assisting other countries to make infectious disease detection and control a national priority.**

Although international efforts must be coordinated to prevent global pandemics, disease surveillance must be the responsibility of each sovereign nation. To ensure that the United States is notified when an unusual outbreak occurs, we must encourage and support other countries' efforts in national disease surveillance and respond when asked for assistance. It is especially important to engage in information-sharing and dialogue with less developed countries. The improvement of domestic disease surveillance and response capabilities in other countries and regions is discussed in Section VI.

> **7. Preserving existing U.S. Government activities that enhance other countries' abilities to prevent and control emerging and re-emerging health threats.**

Helping other countries to help themselves by improving domestic disease surveillance and response capabilities in other countries and regions is discussed in Section VI. It is also important to identify those individuals and offices in each country who have responsibility for participating in international infectious disease surveillance efforts.

> **8. Identifying and strengthening WHO Collaborating Centres that serve as unique reference centers for diseases whose re-emergence is feared.**

WHO Collaborating Centres operated in the United States by Government agencies or by American universities require support to build or rebuild their capacity to serve as reference laboratories within a larger and more active global infectious disease network. A list of the relevant WHO Collaborating Centres is included in an inventory of resources compiled by the CISET working group.

> **9. Establishing the authority of relevant U.S. Government agencies to make the most effective use of U.S. expertise in helping to build a worldwide disease surveillance and response network.**

Proposed legislative changes for the implementation of this recommendation are discussed in Section V. First, CDC's mandate to protect the health of U.S. citizens should be expanded to include outbreak investigations and selected responses to epidemics overseas in coordination with appropriate U.S. agencies, including state and local health departments, USAID, DoD, etc. In disaster relief operations involving infectious diseases where USAID/OFDA has the lead, CDC will operate as part of the U.S. effort as appropriate. Second, a responsible lead agency or agencies should be provided with the authority, emergency procurement powers, and financial resources to coordinate interagency responses to foreign disease outbreaks that have the potential to spread globally.

Strengthen the U.S. capacity to combat emerging infectious diseases by

**10. Enhancing collaborations among U.S. agencies to ensure maximum use of existing resources for domestic and international surveillance and response activities.**

A U.S. Government inventory compiled by the CISET Working Group on Emerging and Re-emerging Diseases is available as a guide for this activity.

**11. Rebuilding the U.S. public health infrastructure that protects American citizens against infectious diseases, including those that are imported into the United States from other countries. This includes strengthening domestic surveillance and response activities.**

State and local health departments require support to restore the surveillance and response capacity that has eroded over the past two decades. This recommendation is discussed in detail in Section VI of this report.

**12. Working with the private and public sectors to improve U.S. capacity for the emergency production of diagnostic tests, drugs, antisera, and vaccines.**

The U.S. Government and private sector should work together to establish a better investment environment for the production of urgently needed medical products. This can be accomplished by combining the resources of national and international government institutions with the technical expertise in the U.S. pharmaceutical industry and in other sectors of the private health-care industry. Improvement of the U.S. capacity for emergency production or procurement of diagnostic tests, drugs, antisera, and vaccines is discussed in Section IV.

**13. Supporting an active community of epidemiologists, clinical investigators and experimental scientists ready and able to seek new solutions for new disease threats.**

Research and training are the foundation of an effective disease surveillance and response system. Scientific studies provide the fundamental knowledge base used to develop diagnostic tests to identify diseases, drugs to treat them, and vaccines to prevent them. At the present time, many of the brightest young American microbiologists are leaving the field, discouraged by the lack of jobs and research funds.

Specific recommendations to strengthen the infectious disease research infrastructure in the United States are provided in Section VII.

**14. Strengthening technical training programs in disciplines related to infectious disease surveillance and response.** In addition to laboratory research instruction, specialized training programs are needed in the handling of hazardous microbes, in public health management, in patient education and management, and in field epidemiology. Recommendations concerned with training are discussed further in Section VII.

**15. Providing accurate and timely health information to private citizens and health providers, both in the United States and abroad, when a disease outbreak occurs.**

As much as possible, individuals should be armed with the practical knowledge to protect themselves and their families from infectious diseases. U.S. agencies should work with foreign governments, multilateral organizations, NGO's, and the news media to improve public communication and avoid misinformation and panic. NGO's that might participate in this effort include women's groups, international organizations concerned with children's health, medical missionary organizations, U.S. corporations, and medical and public health associations.

**16. Strengthening screening and quarantine efforts at ports of entry into the United States.**

The likelihood of the importation of infectious diseases can be decreased by: expanding screening and quarantine facilities at U.S. ports of entry; making information about ill passengers more accessible to health authorities; encouraging greater cooperation in this area between local, state, and federal health departments; and strengthening the training of American physicians and microbiologists in the recognition of "tropical" diseases and in travel medicine.

**17. Strengthening the training of American physicians and microbiologists in the recognition of "tropical**

**diseases" and in travel medicine in general.**

**18. Establishing an Interagency Task Force to coordinate the implementation of these recommendations.**

No single U.S. agency has the authority and resources to investigate epidemics in other countries. However, each agency can and does respond within its own disciplines. It is strongly recommended that the disease surveillance efforts of U.S. agencies be coordinated through an interagency task force chaired by one or more lead agencies, as discussed in Section V.

**19. Establishing a private sector Interagency Task Force subcommittee that includes representatives of the U.S. pharmaceutical industry, medical practitioners and educators, and biomedical scientists.**

The role of the Task Force in fostering a dialogue with private industry and with academic and private sector researchers is discussed in Section IV.

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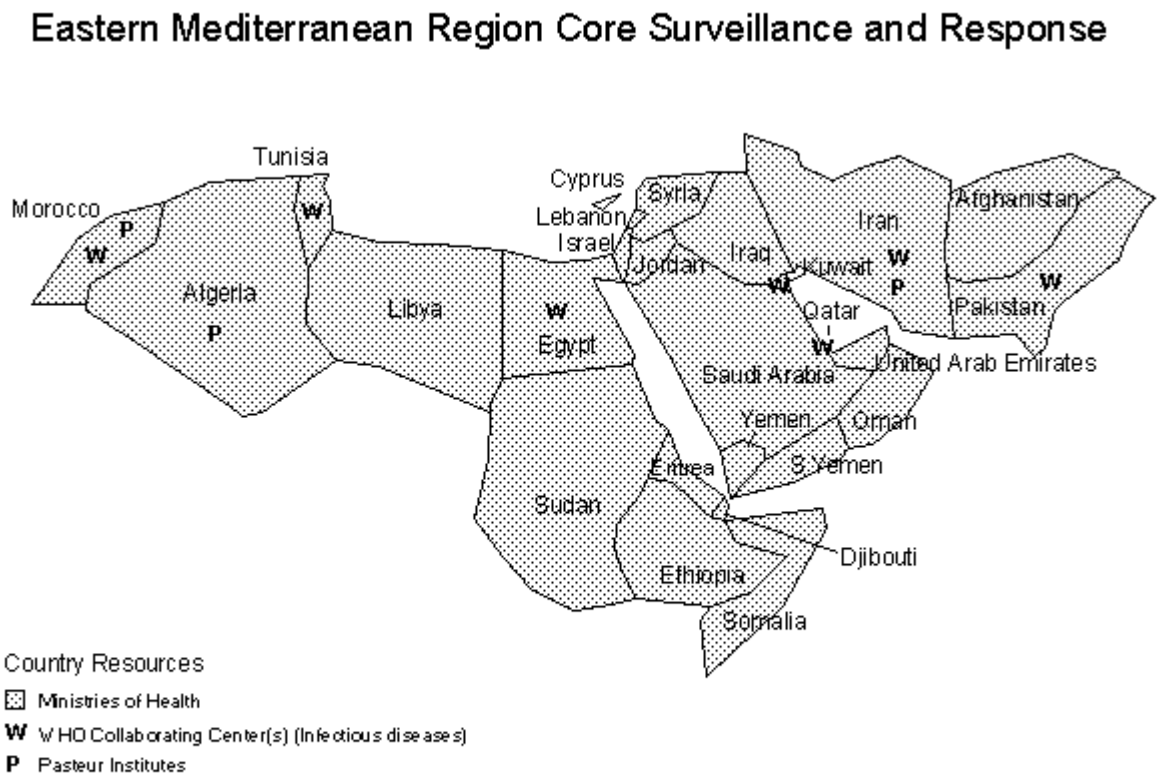
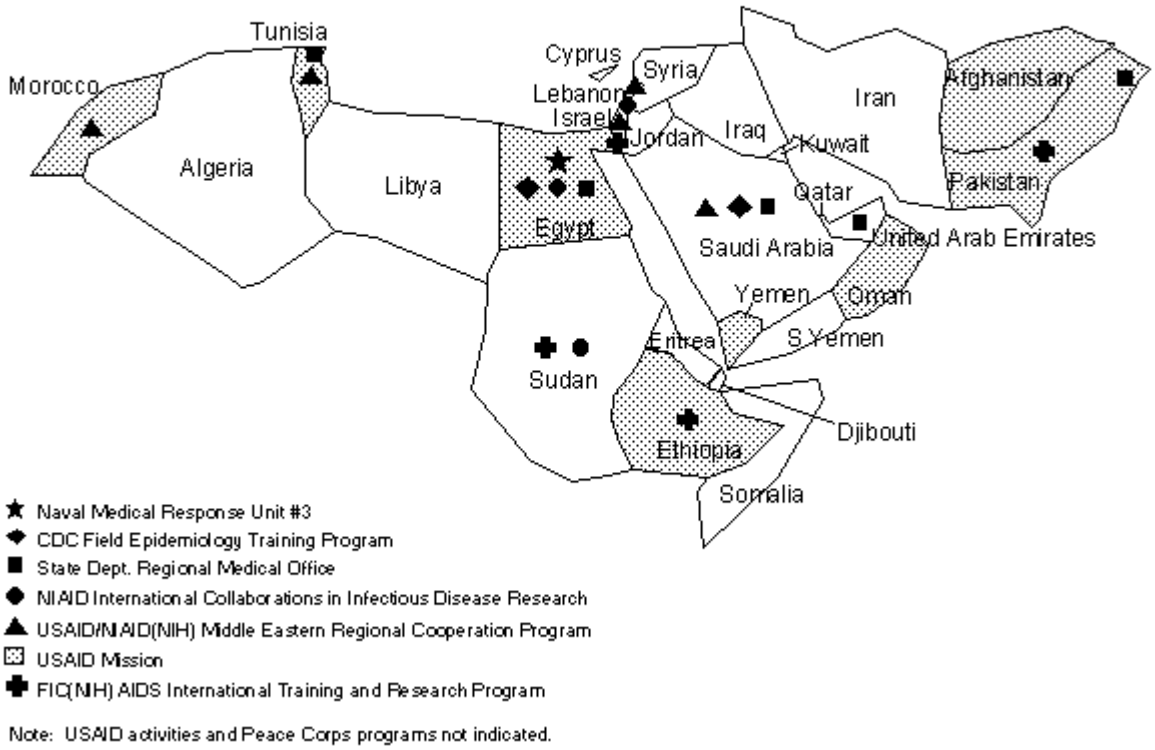


## U.S. Contribution to the Eastern Mediterranean Region Surveillance and Response Capacity




Note: USAID activities and Peace Corps programs not indicated.

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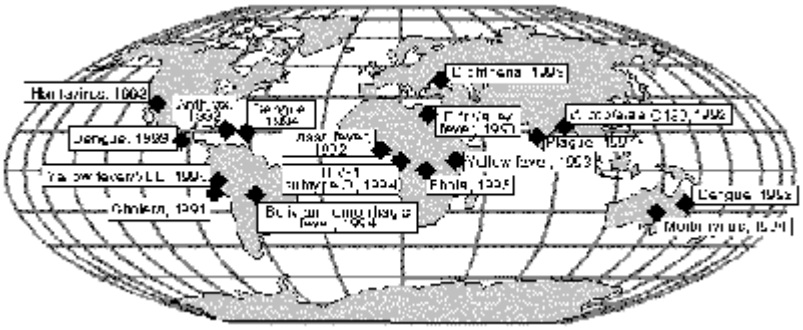


# IV. How can we ensure the availability of drugs, vaccines, and diagnostic tests when they are needed to combat infectious disease emergencies?

An improved global surveillance and response system will supply U.S. Government agencies with timely, reliable information on outbreaks of infectious disease that occur anywhere in the world. To control the spread of these outbreaks, that information must be evaluated and acted on as quickly and effectively as possible. This section concerns responses that are made on an emergency basis to control incipient epidemics.

## U.S. Government role in response to epidemics overseas

At the present time there is no Government agency or interagency group that has the mandate, the flexibility, or the funds necessary to respond to international infectious disease emergencies. Therefore, the capacity of the U.S. Government to provide assistance to control epidemics overseas is limited, at best. Concerned individuals in different Government agencies scramble to find resources and solutions on an ad hoc basis. Response is made even more difficult by the occasional occurrence of widespread shortages of drugs, vaccines, and antisera. Moreover, there is virtually no surge capacity for producing many of the unique medical supplies needed on an emergency basis.

Nevertheless, the international public health community relies heavily on U.S. expertise and on U.S.-supported institutions overseas. CDC, NIH, DoD, and USAID may provide technical assistance to WHO when a disease outbreak occurs, and USAID often provides communications facilities as well as financial and logistical support. However, CDC, DoD, and USAID (as well as other U.S. agencies) all face legal, financial, or jurisdictional obstacles when they strive to respond to international infectious disease emergencies. Our ability to respond ensures that we learn of outbreaks quickly. Thus, it is critical to retain that capability.

## Supply, production, and distribution of emergency medical supplies

Medical supplies that are frequently required during an epidemic include the following.

**Diagnostics**
If a country suspects an outbreak of a re-emerging disease (such as Venezuelan equine encephalitis in Peru, plague in India, or cholera in Brazil), health practitioners may lack the diagnostic reagents to confirm the nature of the threat. Without timely confirmation, it is not possible to institute effective control measures or to rule out known diagnoses if a new, or re-emerging disease is suspected. In many cases, diagnostic reagents are available as research tools, but not as standardized commercial products. In such cases, training may be needed to use these research tools appropriately.

**Vaccines**
If a disease is reliably diagnosed as one that is preventable by vaccine (e.g., diphtheria and yellow fever), vaccinating people in the surrounding area represents the most cost-effective way to protect those people and prevent the disease from spreading. Indeed, smallpox has been eradicated worldwide using a vaccine, saving millions of dollars (see

"Savings Due to Vaccination,"). By the year 2000, polio is targeted for eradication as well. Logistical considerations may prevent delivery of doses of a vaccine in time to stop transmission promptly. Where a vaccine is appropriate, a coordinated response network can help gain rapid access to an adequate supply of quality products that meet local requirements. However, if supply needs are greater than can be met by redistribution, the time required for additional production can be lengthy. In such cases, a coordinating infrastructure may be able to mobilize the industrial surge capacity required to meet increased production needs.

**Immunoglobulins and Antisera**

Individuals who recover from certain infections produce protective antibodies that are present in the bloodstream. When commercially prepared serum from the plasma of former patients is transferred by injection to another person, these antibodies (or immunoglobulins) can provide temporary protection from that disease when a vaccine is not available. Antisera can be made by immunizing animals, such as horses, and the resulting high-titered animal antisera can be used for treatment. Immunoglobulins and antisera can be very important in some situations, but are of limited use for long-term control. In addition, available supplies are generally limited.

**Drugs**

Many infectious diseases are caused by microorganisms that are susceptible to antibiotic drugs. However, there are occasional regional shortages of antibiotics and in some cases, there may be only a single manufacturer of the material from which the finished product is made. These shortages may worsen as more microbes become drug-resistant and fewer antibiotics remain effective. Antiviral drugs may be of value in some situations, and appropriate studies may be needed to determine their effectiveness.

When an epidemic occurs, diagnostics, drugs, vaccines, and/or antisera are often needed in considerable quantities. However, in many cases they may not be available in sufficient quantities or at the necessary site, and there may be no company or agency with the surge capacity to produce more of them. The supply of medical products is driven by multiple factors, including international market forces; the needs anticipated by U.S. agencies, foreign governments, and international organizations; and the needs stimulated by Government incentives, such as the Orphan Drug Act and national vaccine plans. Some supplies may be available from other countries. However, most countries have national quality control requirements that need to be met. Harmonization of standards internationally along with strengthened local enforcement may enhance the acceptance of emergency medical supplies.

When a drug or vaccine shortage is extensive, the best solution may be to initiate production of additional supplies. However, emergency production is often hampered by insufficient manufacturing facilities, the complexity of production methods, the length of time needed for production and quality control testing, licensure requirements, concerns over liability issues, distribution problems, and/or lack of funds. These difficulties can cause significant delays, giving diseases time to spread. Early detection and rapid coordination should shorten the response time.

Moreover, if the disease is newly emergent, and no treatments or vaccines are available, it is necessary to mobilize the research and public health communities to begin seeking new solutions.

In times of need, interagency Government groups and ad hoc committees try to find remedies as best they can. FDA, CDC, and pharmaceutical manufacturers have successfully worked to redistribute available supplies of drugs, vaccines, immunoglobulins, and antisera, and to accelerate the production, testing, and release of new supplies to meet shortfalls. In certain emergencies they have resorted to modifying immunization schedules. When necessary, ad hoc coordination of activities of the NIH, CDC, FDA, DoD, and USAID has redirected resources to research and development efforts. In the vaccine area, coordination activities have been assigned by legislation to the Director of the National Vaccine Program Office. The FDA has limited authority under the Public Health Service Act to prepare biologic products for FDA or other agencies' use, although resources are required to utilize this authority. Both the National Vaccine Plan and the draft Pandemic Influenza Plan contain provisions that authorize payment for some production of vaccines against influenza and childhood diseases, for use in the United States. However, in most cases there is no U.S. Government mechanism to oversee procurement or production of emergency medical supplies.

There is a critical need for coordination and strategic planning to rethink and upgrade efforts for emergency preparedness for responding to disease outbreaks. Many groups are needed to participate in this effort, including CDC, NIH, and FDA; the DoD, the Department of State, and USAID; state and local health departments; and the private sector, including pharmaceutical trade organizations and research universities.

## Steps Involved in Emergency Production of Medical Supplies

Shortages of drugs or vaccines can hinder attempts to control disease outbreaks of influenza, diphtheria, TB, and other diseases. The CISET Working Group on Emerging and Re-emerging Infectious Diseases recommends that a U.S. Government agency or interagency group be granted the necessary mandate and authority to procure emergency medical supplies when a disease outbreak occurs, as is currently granted to USAID for disaster assistance.

To fulfill this function, a designated U.S. Government group might identify potential suppliers of the drug or vaccine and enter into production agreements with one or more of them who might require

- Financial support to expand, re-establish, or setup a new production system;
- A commitment to use or purchase the product, once it is made and tested;
- Human and financial resources to conduct pre-clinical and clinical trials, if needed;
- Indemnification against liability;
- Government or contractual support to ensure that appropriate regulations were followed;
- Assistance and support in working with the governments of the countries where the problem exists to enable cooperation in development efforts and in the design and conduct of clinical trials.

In addition, the designated group might need

- Access to emergency funding sources;
- The flexibility to by-pass the usual rules, such as Government contracting procedures;
- The ability to seek emergency legislative provisions, such as waivers or exemptions from export rules, or liability indemnification for the producer; and
- The cooperation and commitment of all relevant government agencies.

## Shortages of Drugs Effective Against Tuberculosis

Once thought under control, TB is now spreading throughout Asia, Africa, and the Americas, and it is once again common in some U.S. cities. Left untreated, TB spreads from person to person, and when treated inadequately, drug resistance emerges. Recently, many of the drugs most commonly used to treat TB were in short supply. These included streptomycin, para-amino salicylic acid and isoniazid. Although these shortages have been resolved, they point out the weaknesses in the system for responding to emerging diseases.

## Strategic planning

As described in Section V, it is strongly suggested that an Interagency Task Force be established to coordinate the implementation of the recommendations in this report. One of the functions of that Task Force (or its subcommittee) will be to analyze the gaps in U.S. emergency response capacity and to determine which gaps may be filled by improved interagency or public/private sector coordination. The Task Force will be encouraged to draw on industrial, academic, and other non-governmental expertise, as needed. The Task Force should also coordinate U.S. efforts with those of United Nations agencies including WHO, UNHCR, UNDP, and UNICEF.

To aid in this work, it is recommended that the Task Force

1. Determine which Governmental or non-governmental organizations participate in mobilizing emergency production of medical supplies by producing drugs, diagnostics, vaccines, or antisera, "stockpiling" nonperishable supplies, research, recommending where necessary and development of relevant medical products, providing

capacity for emergency responses ("surge" capacity), anticipating the need for emergency production

2. Determine which known diseases are of highest concern, based on their likelihood of occurrence and potential impact, and consider whether vaccines, drugs, or diagnostic reagents are presently available to treat them, and if so, whether surge capacity exists for their production, distribution, and use.

    - Using this information, the Task Force may consider how to

    - Develop a coordinated Government mechanism for responding to infectious disease emergencies in other countries,
    - Maintain an on-going dialogue with the private sector, and with researchers in industry as well as in academia, through a private sector subcommittee that includes representatives of the U.S.
    - Prepare for outbreaks of "high priority" diseases by
        - evaluating U.S. and foreign capacity for production of existing drugs and vaccines,
        - recommending research to develop and evaluate new drugs, vaccines, and diagnostic reagents, where existing products are inadequate,
        - anticipating the likelihood of occurrence through predictions based upon epidemiologic, environmental, climatic, and social data.
    - Develop a program to promote the rapid development of standardized diagnostic tests for new and re-emergent diseases.
    - Assess existing strategic plans for producing vaccines, drugs, and diagnostics for targeted diseases.
    - Strengthen the capacity to produce medical supplies of limited market value, such as vaccines for Argentinian hemorrhagic fever and drugs for Lassa fever.
    - Consider the utility of stockpiling certain priority vaccines, drugs, and diagnostics, based upon estimates of the likelihood of occurrence and potential impact. Recently, the NOAA has developed the capacity to forecast changes in climate due to El Nino currents, which can increase the incidence of infectious diseases. Predictive tools like this one may be useful in guiding stockpiling decisions.

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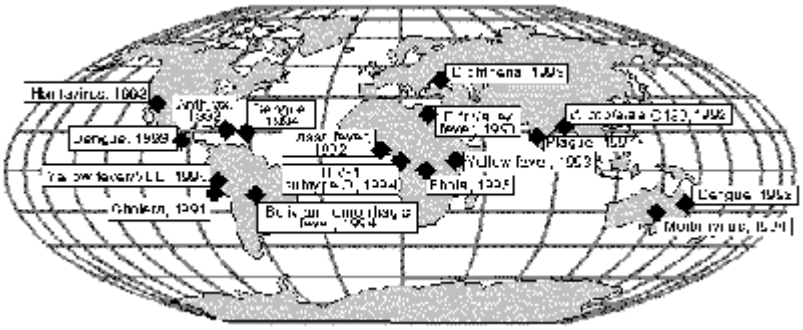
# *Global Microbial Threats in the 1990s*

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## V. What mandates and authority should be granted to U.S. Government agencies to enable them to strengthen global disease surveillance and response?

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The U.S. Government has many existing resources that may be coordinated with those of foreign countries, WHO, and other international agencies to build a global international system for infectious disease surveillance and response. To make the best possible use of U.S. expertise and resources, the efforts of U.S. Government agencies should be well-coordinated. In those instances in which a disease outbreak occurs in the midst of a major disaster, USAID's OFDA has a clear mandate to facilitate a coordinated U.S. response. However, when an outbreak occurs in the absence of a disaster, no U.S. Government agency has the authority to take the lead in coordinating U.S. efforts, and no government structure exists to oversee the development of a surveillance network, to mobilize a concerted response when a disease outbreak occurs, or to coordinate preventive measures aimed at anticipated health threats. It is strongly recommended that some lead agency or agencies be given the authority and resources to fulfill these functions.

### Establishment of an Interagency Task Force

Further strategic planning is required to help build an international network for infectious disease surveillance and response. To carry on this work, it is recommended that an Interagency Task Force be established that meets on a regular basis to

- Oversee the coordination, strengthening, and geographical widening of existing global communications networks for use in the surveillance and control of infectious diseases.
- Determine how gaps in U.S. capacity to respond to infectious disease outbreaks abroad may be filled by improved interagency or public/private sector coordination

Participation in the Task Force should include, but not be limited to, CDC, FDA, NIH, State, DoD, and USAID. These six agencies should form a core group for facilitating U.S. Government responses to infectious disease outbreaks in other countries.

### Activities of individual U.S. Government agencies with regard to disease surveillance and control

As a matter of U.S. Government policy, all U.S. laboratories, field stations, and offices abroad should be encouraged to participate in infectious diseases surveillance, as far as it is within their resources and mandate to do so. Listed below are current activities performed by U.S. Government agencies which contribute to infectious disease surveillance and response throughout the world. In some cases, recommendations are made on how to overcome the gaps in authority and structure described in this report.

## Department of State

The Department of State coordinates interagency policy on international issues and should take a lead role in the Interagency Task Force's strategic planning efforts.

- As with other natural disasters, like earthquakes or hurricanes, U.S. ambassadors should be granted the authority to make the determination that an outbreak of infectious disease requires U.S. attention and/or assistance.
- When a U.S. Ambassador makes such a determination, State should facilitate a rapid U.S. Government response by
    - Contacting the Interagency Task Force, and
    - Coordinating U.S. action with that of other nations and WHO.
- U.S. ambassadors should be encouraged to support the efforts of other agencies, including the DoD, USAID, NIH, and CDC, in strengthening the global disease surveillance and response network. The DoD's infectious disease laboratories abroad are aligned with and dependent on close interaction with the embassies. U.S. ambassadors should ensure that personnel ceilings in the DoD laboratories are adequate to allow global disease surveillance to proceed.
- The Department of State and USAID should take a lead role in encouraging and assisting other countries to make infectious disease detection and control a national priority.
- Diplomatic resources should be made available as needed to encourage foreign governments to cooperate with international efforts to contain epidemics that occur within their borders.
- The Department of State's Office of Medical Services employs 24,000 doctors and nurse practitioners in 260 locations, some of which are located in remote areas. Medical information gathered from these locations should be supplied to the global disease surveillance network.

## Department of Health and Human Services: Public Health Service

### Centers for Disease Control and Prevention

CDC is the lead U.S. agency in matters of domestic disease surveillance, control, and prevention. However, CDC does not have direct authority to support the development of international health programs. Because it lacks direct authority in this area, CDC cannot receive appropriations in support of international infectious disease surveillance, except for AIDS surveillance.

- In view of the international nature of emerging infectious diseases, and of the increasing mobility of infectious microbes, CDC's mandate to protect the health of U.S. citizens should be extended by legislation to include outbreak investigations and responses to epidemics overseas in coordination with appropriate U.S. agencies, including state and local health departments, USAID, DoD, etc, when they occur outside the context of disaster assistance.
- CDC should assist in formulating and implementing the US Government international surveillance, response, and prevention strategies. They should provide epidemiology and laboratory personnel and direction for epidemic response. They should also provide assistance with diagnostic referrals.
- CDC should serve as the primary link with the global network of Field Epidemiology Training Programs (FETPs), providing for improved communications and sharing of epidemiologic and laboratory information among the FETP network (including CDC), and identifying epidemiologic and laboratory expertise in the global FETP network that could assist in emerging disease and disaster assistance in partnership with the U.S. Government.
- Along with the USAID and the Office of International Health of the Department of Health and Human Services, CDC should coordinate the disease surveillance initiatives of the U.S. Interagency Task Force with those of WHO.

### Food and Drug Administration

The FDA has a broad mandate to ensure the safety of foods and the safety and efficacy of a variety of other products it regulates including drugs, biologics, blood and blood components, diagnostics and medical devices.

- As a member of the Interagency Task Force, the FDA should make its expertise available to the Task Force to the extent resources allow, to ensure adequate supplies and to assist others in the emergency development and production of vaccines, drugs and diagnostics. The FDA should serve as the focal point for coordination between the Interagency Task Force and U.S. or multinational private companies, trade associations or other suppliers that may be called upon to assist in the emergency manufacture or development of medical supplies.
- The FDA should collaborate with CDC and USDA in establishing an active surveillance system for foodborne diseases.
- The FDA should continue its emergency response efforts in cooperation with CDC and USDA to investigate sources of food-borne pathogens and to respond to outbreaks by taking appropriate measures.

**National Institutes of Health**

The mandate of NIH includes the support of research and training related to infectious disease. In accordance with this mandate, the National Institute of Allergy and Infectious Diseases (NIAID) and the Fogarty International Center should take the lead in supporting research and training that will provide information relevant to the development of vaccines, therapeutics, and diagnostics. These research and training activities should support the global disease surveillance network and response efforts.

**National Institute of Allergy and Infectious Diseases**

The NIAID funds multiple research grants and contracts with clinical research and epidemiologic component. These include 11 International Collaborations in Infectious Disease Research (ICIDR) and three Tropical Medicine Research Centers (TMRC), in several countries. The purpose of these centers is clinical research, including population-based studies and epidemiologic research. In addition, NIAID supports nine HIVNET projects overseas and eight in the United States, which monitor the incidence of AIDS in populations likely to participate in future vaccine trials and help create an infrastructure for future vaccine efficacy trials by training technicians and supporting the development of laboratories.

- Workers at NIAID-supported units should be encouraged to report any infectious disease outbreaks that come to their attention. Overseas centers may also be able to facilitate communication with their local ministries of health.
- Many of NIAID's projects involved in research on parasitic, enteric and respiratory diseases are linked in a network of international centers for tropical disease research, which includes academic institutions in over 15 countries and meets regularly with federal agencies and international organizations involved in international research. This network could form an effective base for expanded international collaboration on emerging disease issues, and should be encouraged to take a leadership role in this area.
- In accordance with their mandates, the NIAID, Fogarty, and other NIH-supported facilities should participate in research and training in support of the global disease surveillance network.

**Fogarty International Center**

The Fogarty International Center should support research and training efforts and bilateral and multilateral scientific collaborations that enhance the capabilities of developing countries to address emerging and re-emerging disease, including epidemiology and surveillance and the conduct of research. The current FIC AIDS International Training and Research Program (AITRP) has linked 11 U.S. universities with institutions in 65 countries. This network will provide a model for expansion into other emerging diseases.

**Office of International Health**

The Office of International Health of the Department of Health and Human Services should work with the Interagency Task Force to coordinate U.S. global surveillance initiatives with those of WHO.

## U.S. Agency for International Development

USAID is the lead U.S. agency in support of international health. As such, USAID provides assistance in health research and health care delivery in over 40 developing countries. This support is provided to national governments,

non-governmental organizations, universities, research institutes, and private sector entities. USAID has resident technical staff managing bilateral and regional health programs in most of these countries. In accordance with its mandate and its current role in strengthening the capacity of developing countries to identify and solve health problems, USAID will:

- Help to strengthen developing country capacity to address emerging health threats such as AIDS and drug resistant malaria;
- Develop and improve methods for detecting and responding to antimicrobial resistance to drugs used for the treatment of pneumonia, malaria, diarrhea, and TB;
- Assist, together with other donors in efforts to strengthen health information systems;
- Support and expand existing programs to strengthen developing countries' capacities in epidemiology and laboratory and clinical diagnosis;
- Continue to play a leadership role with WHO and international donors in addressing emerging health issues of major importance to developing countries.

Although USAID has the legislative mandate to implement international health programs, current and anticipated budget constraints will limit USAID activities that address emerging and re-emerging health threats. On-going health programs have already been cutback substantially due to lack of resources. Current activities in child survival, AIDS, and environmental health address many issues related to the prevention and control of new and re-emerging diseases. Additional health funds would have to be appropriated to enable the USAID to initiate new or expanded activities in this area.

## Department of Defense

The DoD operates research laboratories in the United States for studying infectious diseases that threaten military personnel. The emphasis is on insect-borne parasitic and viral diseases and diarrheal diseases of travelers. Work focuses on improved diagnosis and development of better preventive measures. DoD operates a U.S. research laboratory and treatment unit with the highest level of biocontainment. DoD has the capability of transporting patients infected with hazardous agents from anywhere in the world for care.

DoD operates overseas infectious disease laboratories in Brazil, Egypt, Indonesia, Kenya, Peru, and Thailand. These laboratories conduct research on diseases of mutual interest to the host country and the United States. Each laboratory has a capability for evaluating new problems through epidemiologic investigation, for diagnosing diseases, and for recommending control measures.

DoD has a limited capability to produce prototype vaccines for human testing. Vaccines produced are for diseases uncommon in the United States. Large-scale vaccine manufacture depends on contracts with commercial facilities. Emergency scale-up of vaccine production by contractors is available for a select group of highly hazardous agents.

- DoD should strengthen communication among its laboratories to create a communication network for global surveillance.
- DoD should work with USAID, CDC, and host nations to provide diagnostic, logistical, and communication assistance for responding to epidemics.

## U.S. Department of Agriculture

USDA cooperates with the Centers for Disease Control and Prevention, the Food and Drug Administration, and the Department of Defense on international disease issues, as well as with international organizations such as the World Health Organization and Food and Agriculture Organization. A permit and health certificates must be obtained from APHIS by people intending to import animals into the United States. APHIS then arranges the supervision of testing and examinations of animals by licensed and accredited veterinarians in that country.

- Rapid detection and diagnostic capabilities need to be developed and made available for many zoonotic diseases.
- Innovative risk management approaches are needed, especially with increasing travel and trade.

## The Peace Corps

The Peace Corps' Epidemiologic Surveillance System receives reports on the medical status of volunteers in 92 developing countries, and thus, can serve as a valuable component in the global surveillance network. Possibly this surveillance system could be expanded to include wider reporting of illnesses in the villages where the volunteers work.

## Department of Veterans Affairs

One of the Department of Veterans Affairs' (DVA) four missions is emergency preparedness. DVA's experience in tracking the illnesses of soldiers who return from abroad, as well as in investigating disease transmission, should help the Interagency Task Force detect and respond to infectious diseases.

## U.S. Department of Commerce

### National Oceanic and Atmospheric Administration

The NOAA ability to forecast El Nino currents has yielded useful predictions of climate variability up to one year in advance in certain parts of the world, particularly in the tropics. This activity offers the opportunity to provide a predictive dimension to the global disease surveillance system.

Climate variability affects the distribution and number of insect and rodent disease vectors, as well as of other animals that serve as reservoirs for human diseases. Climate variability also affects the distribution and quality of fresh water and therefore affects the incidence of waterborne diseases. Climate monitoring and forecasting should be integrated with global disease surveillance to enhance U.S. predictive and preventive capacities.

### National Institute of Standards and Technology

The National Institute of Standards and Technology (NIST) laboratories are responsible for the standardization of many products used in measurement and testing, including some diagnostic reagents. NIST's Advanced Technologies Program (ATP) currently supports research and development on diagnostic tests for infectious diseases based on DNA probes. NIST should be encouraged to continue work on the standardization of products for the diagnosis of infectious diseases.

## Environmental Protection Agency

The Environmental Protection Agency (EPA) is studying the effects of long-term climate change on vector-borne diseases, which can be especially sensitive to subtle changes in temperature, precipitation, and weather variability. Ecological perturbations resulting from either climate change or human land use patterns may alter the environment in such a way as to promote disease emergence.

EPA should have the capacity to provide to the Interagency Task Force results from the monitoring of environmental changes which may relate to shifting disease distribution or emergence. As environmental factors involved in disease systems become better understood, the EPA could be encouraged to improve monitoring, surveillance, and reporting of such potential indicators to provide the opportunity for earlier pubic health intervention.

EPA personnel working in the environmental health offices of WHO could further serve to help link relevant environmental data to the international disease surveillance efforts of WHO.

## Cooperation with the World Health Organization

The WHO is often in the best position for early recognition of infectious disease outbreaks through its interactions with the various networks of WHO Collaborating Centres, and is also often best suited to coordinate response activities. The Interagency Task Force should therefore maintain close communications with the WHO.

During the 1995 World Health Assembly, a resolution was passed that deals specifically with emerging and re-emerging infectious diseases. The resolution defines a global leadership role for WHO in addressing emerging infectious diseases,

and its endorsement by member states will facilitate implementation activities. The U.S. Government strongly supported both the acceptance and implementation of the resolution.

As the WHO has no laboratory resources of its own, it relies upon an international network of Collaborating Centres for technical guidance. Many of these WHO Collaborating Centres are located in the United States, but most of them do not receive funds from WHO to offset the costs they incur in providing this critical service. The Interagency Task Force should identify WHO Collaborating Centres within the United States that are essential to address emerging and re-emerging infectious diseases and should ensure their core funding through a combination of U.S. Government (CDC, NIH, USAID, and others) and international resources (WHO and others).

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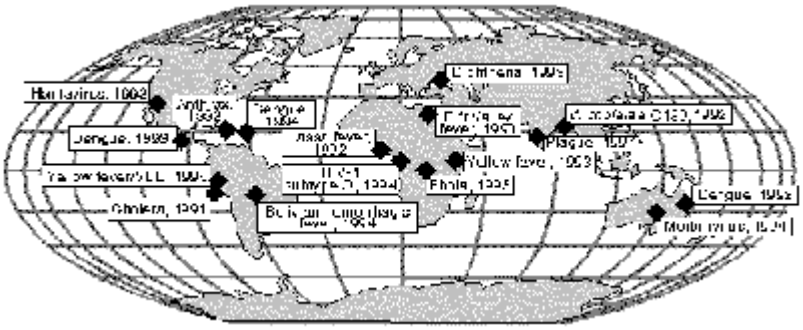
# *Global Microbial Threats in the 1990s*




## VI. Capacity Building: What actions are taken by the U.S. Government to prevent and prepare for emerging and re-emerging diseases?

Forward-looking, sustained efforts to control and ultimately prevent major disease threats form the essential foundation for any plan to successfully address new and re-emerging diseases. The process of responding to international microbial threats encompasses a multitude of activities, including diagnosis of the disease; research to understand its modes of transmission; research to develop adequate means to treat it or prevent its spread; and production and dissemination of the necessary drugs and vaccines. Effective response to outbreaks of infectious disease includes both immediate responses to disease emergencies (discussed in Section II) and on-going activities to develop and maintain the tools to control outbreaks, or, better yet, to predict and/or prevent them before they happen.

**Preparation**

To be ready to respond effectively to infectious disease outbreaks, whenever and wherever they occur, requires international preparation and planning. The response component of a global infectious disease network must rest on a complex foundation that includes skilled public health workers, national and regional laboratories for diagnosis and research, communications systems, and the commitment of national health ministries. A current goal of WHO is to assist each country to develop its ability to provide laboratory diagnosis of diseases endemic to its area and to refer specimens from suspected newly emergent diseases to an appropriate regional reference laboratory. To reach this goal, each country must train medical workers and laboratory technicians and supply them with appropriate equipment and diagnostic resources.

Several additional international elements must be in place to provide the wherewithal for effective and timely disease control and prevention efforts. First, regional reference laboratories must be maintained to provide diagnostic expertise and distribute diagnostic tests. Second, an international communications mechanism should be made available to receive and analyze global disease surveillance information. Third, regional procedures should be instituted to facilitate the production, procurement, and distribution of medical supplies, including vaccines for disease eradication programs. Fourth, enhanced public education in simple health measures in developing countries must be instituted.

**Prevention**

Disease prevention is an investment in the young people of the world and in our collective future. Every year, an estimated four million infant and child deaths are prevented by vaccination and other preventive health measures, due to multilateral efforts. The elimination of smallpox would not have been possible without a truly global effort. Similarly, multilateral leadership and resources propel the international program to eradicate polio. Both examples demonstrate the value to American citizens of resources invested in global disease prevention.

In recent years, many countries have dramatically strengthened their health-care delivery systems, even in the face of

economic stagnation. Prevention efforts - vaccination, education to change unsafe human behaviors, and other public health measures - are the most cost-effective and beneficial of all measures that address the problem of new and re-emerging infectious diseases. In recent years, a few countries have dramatically strengthened their public health systems even in the face of economic stagnation. However, even these gains are fragile and subject to eclipse by shorter term economic and political pressures.

## 1. Public health infrastructure in the United States

As a nation, our first-line of defense against infectious diseases is our national system for notifying health authorities of individual cases of infectious diseases. The legal authority for disease reporting rests with the states, which determine which diseases or conditions must be reported by doctors and medical laboratories. In turn, the states voluntarily report cases of more than 40 infectious diseases to CDC. To be effective, our national surveillance system must be comprehensive, including not only reporting and investigation of cases, but also submission of clinical specimens for testing at local, state, or federal public health laboratories. The surveillance system breaks down if any one step - diagnostic testing, case reporting, or follow-up investigation - is not accomplished.

### Neglect of the U.S. public health infrastructure

In the past, our national surveillance system for "notifiable" diseases has provided the basis for public health decisions concerning communicable disease prevention and control. However, during the past decade or more, state and local support for infectious disease surveillance has diminished, largely as a result of budget restrictions. In 12 states, for example, no personnel were dedicated to the surveillance of food-borne disease, which is believed to be on the rise (see "Food-borne and Waterborne Infectious Diseases"). In addition, the notifiable disease surveillance system is understaffed in many states. As a result, many of the currently reportable diseases are in fact significantly underreported, and in many areas there is limited followup of the cases that are reported. Moreover, public health agencies are reluctant to add new diseases to the list of notifiable diseases because their capacity to support the surveillance system is already limited by lack of funds and personnel.

Because of this breakdown, targeted federal programs concerned with AIDS, TB, sexually transmitted diseases, and vaccine-preventable childhood diseases have been unable to rely on data from our crippled surveillance network and have developed independent, federally supported parallel surveillance systems to obtain data for their prevention and control activities. Thus, at the same time that AIDS surveillance was being established, other parts of the surveillance system for communicable diseases were failing. A 1993 nationwide survey of public health agencies revealed that -- except for the targeted disease programs noted above -- only skeletal surveillance staff exist in many state and local health departments. At the current level of disease surveillance, it may take hundreds of cases before an outbreak of a non-targeted disease in a large urban area will be detected.

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### Food-borne and Waterborne Infectious Diseases: Communities at Risk

In 1993, a municipal water supply contaminated with the intestinal parasite Cryptosporidium caused the largest recognized outbreak of waterborne illness in the history of the United States. Over 400,000 people in Milwaukee, Wisconsin, had prolonged diarrhea, and approximately 4,400 were hospitalized. Also in 1993, hamburgers contaminated with the bacteria *E. coli* 0157:H7 and served at a fast-food restaurant chain caused a multistate outbreak of bloody diarrhea and serious kidney disease. More than 600 people got sick; 56 people had kidney failure, and 4 children died. Other outbreaks of food-borne illness in recent years have included cholera from coconut milk from Thailand, Shigella diarrhea linked to green onions from Mexico, and Salmonella diarrhea from an Israeli snack food. These diseases were emerging at the same time that domestic surveillance of infectious diseases was diminishing. A number of factors were associated with the occurrence of the outbreaks of *E. coli* 0157:H7 and *Cryptosporidium*. However, the lack of prompt diagnosis and reporting likely contributed to morbidity, mortality, and economic costs.

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### Three ways to improve domestic surveillance of infectious diseases

1. Strengthen the national notifiable disease system.

For acute infectious diseases that require prompt reporting and investigation of every case (such as botulism and meningococcal meningitis), a national notifiable system works best. Local health departments must be made stronger and more flexible, so that disease-reporting can be modified to include new illnesses as they arise. State, local, and federal public health offices must work in partnership to achieve these goals.

2. Establish sentinel surveillance networks.

For many other diseases, reporting of all cases is unnecessary. Instead, sentinel networks linking groups of health care providers and laboratories to a central data processing center may be particularly helpful in observing rises in the incidence of particular diseases. For instance, such networks can be used to monitor unexplained adult respiratory distress syndrome and childhood illnesses characterized by fever and rash. A good example of a sentinel network is the one established for influenza (see "Sentinel Surveillance for Influenza").

3. Establish public health centers for emerging diseases to prevent future AIDS-like epidemics in the United States.

A different type of sentinel system is required to detect and investigate newly emergent diseases, which by definition are not on any reportable list. A sentinel system for this purpose would perform comprehensive surveillance within several well-defined sites that offer access to various population groups. Such centers could be developed through cooperative agreements with local and state health departments in collaboration with local academic institutions and other governmental or private-sector organizations. Strategically located epidemiology and prevention centers for emerging infections could also be used to monitor antimicrobial drug resistance, foodborne diseases, and opportunistic infections. Each center would conduct population-based surveillance projects, evaluate new diagnostic tests, and implement pilot projects for disease prevention and intervention.

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### Sentinel Surveillance for Influenza

The influenza sentinel surveillance network was established through the American Academy of Family Physicians and includes approximately 150 primary care physicians located throughout the United States. These physicians submit weekly reports of the number of patients seen with influenza-like illnesses by age group, per number of patent visits, as well as the number of hospitalizations among patients with influenza-like illness. A subgroup also collects nasopharyngeal specimens that are sent to a central laboratory for influenza virus identification.

The international component of influenza surveillance involves a network of collaborating laboratories, established in 1947, which now includes over 100 WHO National Collaborating Laboratories. The primary purpose of the network is to detect the emergence and spread of new strains of influenza that may signal a need to update the strains contained in the influenza vaccine. To augment the WHO network, CDC supports a surveillance system for influenza virus isolation at six sites in China, where many pandemic and epidemic strains have first appeared.

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## 2. Public health infrastructure in other nations

The United States is usually informed about disease outbreaks in other countries because we are widely respected as the world's foremost authority on infectious disease recognition and control. Individuals, laboratories, and ministries of health seek to collaborate with CDC, either formally or informally, when they are confronted with an infectious disease problem that they cannot resolve. To ensure that we continue to be notified, we must ensure that we remain ready to assist in national capacity building for disease surveillance, and to respond when asked for assistance.

The effectiveness of a global disease surveillance and response system depends on each nation's capacity to detect and control infectious diseases. Some industrialized countries have become sufficiently concerned about the resurgence of infectious diseases to devote substantial resources to a surveillance effort. In addition, the Executive Board of the World

Health Assembly recently passed a resolution that focuses on capacity building related to emerging infectious diseases.

In many developing countries, however, health resources are extremely scarce, and U.S. health experts agree that WHO has not been able to fill the existing gaps in global surveillance and response. Furthermore, major U.S. funding for this purpose is not a likely prospect during this period of federal deficit reduction and downsizing. However, there are several inexpensive, cost-effective actions that can and should be taken.

First, we can encourage and assist other countries to make disease prevention, surveillance, and preparedness a national priority.

Second, we can build new efforts onto long- standing programs and relationships that help other countries to strengthen disease prevention efforts and preparedness by improving their public health infrastructures such as their systems for treating waste water and disinfecting drinking water.

Third, we can identify and preserve existing projects that enhance other countries' capacities to detect and control infectious diseases.

The goal of enhancing other nations' capabilities to monitor and control infectious diseases is in accord with the security and foreign policy aims of the United States. In the post-cold war period, a major objective of U.S. foreign policy is the promotion of sustainable economic development around the globe. Helping other countries to help themselves - to improve the lives of their citizens, develop their economies, and find niches in the global economy - is a major guide for U.S. foreign assistance and aid. Support for international health initiatives is a valuable part of the U.S. effort to promote economic development and political stability.

## The U.S. Government's role in international prevention and control efforts

As mentioned above, the U.S. Government has contributed money, time, and expertise to the successful effort to eradicate smallpox and to the continuing effort to eradicate polio and other childhood diseases. This was accomplished through a sustained interagency and private sector effort. Many or most of the vaccines used in the disease eradication programs were developed in the United States, building on many years of basic research by American scientists.

Many other U.S. Government activities assist developing countries to lay the foundation for effective disease prevention and control, surveillance and response. Most of these programs are supported and organized by USAID, which is the U.S. agency responsible for international sustainable development, humanitarian assistance, and disaster response. Disease control efforts are often thwarted and microbes given fertile breeding grounds by political and economic instability and civil strife. Worldwide efforts to promote good governance, economic development and resolution of conflicts are not out of place in a discussion of how to deal with new and re-emerging diseases. To neglect such efforts is to potentially doom us to costly crisis response making long-term prevention and control difficult or impossible. Thus, activities targeted at improving less developed countries" abilities to conduct surveillance, prevent and control diseases, and prepare for epidemics are integral to sustainable development efforts.

## Helping countries to help themselves: U.S. Government activities in public health capacity building

The United States, through USAID, provides technical assistance to health programs in over 40 countries. The agency's country missions supply the on-the-ground support, information, local capacity-building, and networking that are so important to other government and non-government health programs. They also frequently provide emergency support during disease outbreaks. Many USAID activities are carried out in collaboration with other donor nations and take advantage of U.S. technical leadership in health research and public health planning. These activities also rely on the expertise of American research institutions, universities, and non-governmental organizations.

Several specific activities supported by USAID and other U.S. agencies are described in boxes in this section. The overall objectives of these activities are:

- Helping to strengthen developing country capacity to address emerging health threats such as AIDS and drug-resistant malaria;

- Developing and improving methods for detecting and responding to microbial resistance to drugs used to treat diseases as pneumonia, malaria, diarrhea, and TB; facilitating the introduction of these methodologies into country control programs; and improving drug management and local drug prescription patterns to reduce the development and spread of antimicrobial resistance.
- Strengthening communication about infectious disease-related health issues;
- Supporting applied research relevant to emerging and re-emerging heath threats in developing countries.
- Supporting and expanding existing programs to strengthen developing countries' capacities in epidemiology and laboratory and clinical diagnosis;
- Continuing to play a leadership role with WHO and international donors in addressing emerging health issues of major importance to developing countries.

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## The Center for Health and Population Research

The International Center for Diarrheal Disease Research, Bangladesh (ICDDR,B; now known as the Centre for Health and Population Research), is a leading international health research institute in the developing world. USAID has supported the ICDDR,B for over 25 years, dating back to the landmark clinical trials of oral rehydration therapy for cholera. Other scientific achievements include the characterization of new cholera strains; the demonstration of cholera vaccine efficacy in field trials; the development of inexpensive, simple diagnostics for diarrheal diseases; and the development of successful integrated family planning and health services delivery programs through operations research. The ICDDR,B also provides training to scientists from around the world and essential medical care for thousands of Bangladeshis. The ICDDR,B has also provided technical assistance to humanitarian relief efforts in Peru, Zaire, and Rwanda.

Although the United States made the initial investments, the success of the ICDDR/B over the years has attracted multi-donor support from the governments of Switzerland, Canada, and Japan; from multilateral organizations such as the UNDP, the WHO, and UNICEF; and from private foundations such as the Sasakawa and Ford Foundations.

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## Research and Capacity Building: The Applied Diarrheal Disease Research (ADDR) Project

The Applied Diarrheal Disease Research (ADDR) Project, developed by USAID and the Harvard Institute for International Development, has pioneered research capacity building through innovative workshops, consultancies, and research grants. ADDR provides assistance in proposal development and implementation, data collection and analysis in developing countries. ADDR works with collaborating groups of local scientists and policy makers (an effective combination for policy change) to set the research agenda and to develop national networks of investigators. ADDR-sponsored research, which emphasizes social science research, provides new health interventions, better tools for epidemiologic studies, and better case management in priority countries. All of the research is conducted in developing countries.

ADDR has developed a network in 12 developing countries of over 300 scientists who are collaborating successfully in the search for new ways to prevent and control infectious disease outbreaks. The ADDR network in Mexico, for example, is demonstrating how one developing country can slow the evolution of antibiotic resistant microorganisms through appropriate antibiotic prescribing and compliance practices. In an initial study, ADDR scientists determined that educational and managerial interventions in a Mexican Social Security (IMSS) clinic significantly reduced the proportion of children who received antibiotics and anti-diarrheal drugs, and increased the use of oral rehydration therapy. These changes have lasted more than 18 months after the intervention ended. Medication compliance improved among patients in the intervention group even though improving such compliance was not an explicit objective of the intervention.

A second study undertaken by the IMSS extended the same methods to 17 clinics from both the IMSS and the Mexican Ministry of Health, and looked both at diarrheal and acute respiratory diseases. Results from this randomized controlled

trial of clinics were very successful; medication costs decreased by 36% and medication waste due to noncompliance and over-prescribing decreased by 51%. Mexico's Minister of Health took an active interest in the studies and, as a result, the IMSS is now implementing a new diarrheal disease treatment program in 12 Mexican states. If successful, this large scale intervention may lessen the likelihood that antibiotic resistant microorganisms will emerge from Mexico.

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## U.S. Foreign Aid for Health Technologies: Program for Appropriate Technology in Health (PATH)

**Saving money and lives through immunization programs.**

The success of the effort to immunize children throughout the world against common childhood diseases is dependent on the availability and quality of local immunization programs. Yet limited health budgets in many developing countries limit the number of children who are immunized. USAID has invested in identifying and developing cost-effective technical solutions that save money - and lives.

For example, with USAID assistance, the Program for Appropriate Technology in Health (PATH), has worked with a U.S. company to develop simple monitors for individual vaccine vials that indicate when a vaccine has been exposed to heat and needs to be discarded. Previously many vials were discarded unnecessarily. As much as $20 million will be saved each year on oral polio vaccine alone, a savings that can be used by countries to purchase more vaccine and immunize a far greater number of children.

**Diagnostics: Rapid and simple for surveillance and prevention.**

Rapid, easy to use diagnostic tests can be invaluable to track the spread of emerging infectious diseases. In the developing world, the capacity to locally manufacture high quality diagnostics has lagged behind pharmaceutical and vaccine production. Yet diagnostic tests manufactured in industrialized countries are often inappropriate for use in developing country health programs. They are too costly, too complex to use, or need supporting laboratory equipment and highly trained technicians. Through its agreement with PATH under the HealthTech Project, USAID has supported the development of a generic low-cost, rapid "dipstick" technology that is suitable for use under field conditions. The dipstick technology is currently used to detect antibodies to HIV-1,HIV-2, and hepatitis B viruses in blood samples, and shows extremely high sensitivity and specificity. The basic technology can be adapted to allow detection of other important diseases.

None of these disease prevention technologies were of interest to the commercial sector initially because they were primarily designed for developing country needs. By advancing the technology, USAID and PATH have been able to stimulate commercial sector interest and investment so that U.S. industry now is producing new products that directly contribute to slowing the spread of diseases in the developing world.

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## Strategic Objectives for Capacity Building

### Country-level Objectives

Comprehensive country-level objectives for capacity building have been concisely described by WHO in its January 12-13, 1995 report on emerging infectious diseases.

- All countries should have the ability to provide laboratory diagnosis of "common" diseases endemic in their areas and the ability to refer specimens from suspected "uncommon" diseases to an appropriate reference laboratory.
- All countries should have the epidemiologic capacity to investigate outbreaks, collect specimens, and analyze test results.

Implementation of the first country-level objective would be facilitated by the compilation of a country-by-country list

of "common" diseases for which each country should be able to provide laboratory diagnosis, and of "uncommon" diseases that can be referred for diagnosis at a reference laboratory. A list of appropriate diagnostic tests and reagents and a plan for distributing them could also be developed.

**Regional-level Objectives**

Regional-level objectives recommended by U.S. agencies include

- Provision of surveillance and response coverage at the regional level for countries that lack the resources to detect and control epidemics within their borders.
- Linkage of local hospitals and laboratories into a coordinated regional surveillance network that provides referrals in the areas of diagnosis and epidemiologic investigation.
- Provision of diagnostic reagents to regional surveillance centers by WHO, the United States, and other nations.
- Support of regional self-sufficiency in the production, quality control, and distribution of medical supplies.
- Provide regional climate forecasts and develop the capacity to identify areas that are vulnerable to outbreaks of infectious disease because of changes in weather.

Implementation of the recommendations for establishing regional surveillance and response networks will provide significant steps toward the fulfillment of the first three regional level objectives.

## Four Target Areas for Capacity Building

Capacity building in support of a national surveillance and response system encompasses a complex set of skills and resources, many of which are readily available in industrialized countries but not in underdeveloped ones. The components of a public health infrastructure include human resources, physical resources, systems for laboratory referral and information exchange, and a favorable policy environment to encourage disease surveillance and permit disease reporting and cooperation with other countries. Recognizing, reporting, and responding to new disease threats involves each of these target areas.

**1. Human resources for capacity building**

- Individuals trained in disease surveillance, who anticipate the unusual
- Doctors, nurses, and other health practitioners who recognize and report the unusual
- Laboratory technicians and microbiologists who diagnose the unusual
- Epidemiologists and laboratory scientists who investigate the unusual
- Social scientists who understand the human context of the unusual
- Public health managers who use surveillance and diagnostic information to determine how to control and prevent the unusual

**2. Physical resources for capacity building**

- Laboratories that are safe and clean and accommodate appropriate equipment and supplies.
- Communications equipment. Depending on resources of the country, communications can be based on telephones and fax machines or on computers and satellite technology.
- Systems for treating waste water and disinfecting drinking water.

Both categories require people who are trained in the operation, quality control, and maintenance of the equipment.

**3. National systems for disease reporting**

- Successful disease surveillance and control requires a hierarchical laboratory and communications system for
- Reporting common and unusual clinical events
- Collecting specimens for laboratory diagnosis
- Providing access to diagnostic tests
- Investigating the epidemiology of outbreaks

- Instituting control measures
- Providing feedback for preventing future outbreaks, with special attention to communication between the producers and users of surveillance data

**4. Building a policy environment conducive to participation in a global system**

When a serious disease outbreak is suspected, the political authorities of a given nation may be reluctant to report it, fearing loss of trade and/or tourism, or to seek technical assistance for the epidemiologic and laboratory investigation. In the past, this reluctance has had serious consequences. In many cases, diseases have spread unchecked. In some other cases, in which an outbreak was quickly brought under control, unnecessary restrictive measures were imposed by other countries, causing economic damage. Governments should encourage international communication among scientists and public health personnel regarding emerging infectious diseases and request international assistance through WHO when disease outbreaks occurs or when unusual infections are suspected.

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## Creating an International Community of Epidemiologists

Since 1980, the Field Epidemiology Training Programs (FETPs) have set the standard for training in applied epidemiology in many countries. Sponsorship of these programs has given CDC the opportunity to help strengthen the international public health network while reducing the risk that infectious diseases will be imported into the United States.

CDC established the first FETP in Thailand in collaboration with WHO and the Thai Ministry of Health, in answer to a Government of Thailand request for assistance in training in applied epidemiology. Since then, programs have been initiated in 14 countries including Australia, Colombia, Egypt, Hungary, Indonesia, Italy, Mexico, Peru, Philippines, Saudi Arabia, Spain, Taiwan, Uganda, and Zimbabwe. Programs are currently under development in South Africa and the Dominican Republic, and several additional programs are in the preliminary planning stages.

The FETPs are modeled on CDC's domestic Epidemic Intelligence Service (EIS), 2-year training course in applied epidemiology. The FETPs maintain the basic structure of EIS with modifications to suit the needs of the individual host country. The objectives of the program are to:

- Provide a continuous supply of field-oriented epidemiologists who are able to meet their country's disease prevention and control needs, and
- Provide epidemiologic services to public health programs at the national and local levels.

FETPs directly benefit the countries in which they operate and also provide public health partnership benefits to the United States. Empowering national programs to deal effectively with their own disease control and prevention problems diminishes the need for further direct U.S. involvement. Moreover, working with FETP colleagues throughout the world has yielded a wealth of experience, professional collaborations, and international infectious diseases surveillance connections. For example, because of CDC's participation in Peru's FETP, CDC staff were in place in 1991 to help control the first cholera epidemic in the Western Hemisphere in the 20th century.

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## Building Surveillance Capacity in Sub-Saharan Africa

During 1981-1993, USAID supported the Africa Child Survival Initiative, Combating Childhood Communicable Diseases (CCCD) project, which was implemented by CDC in 13 countries in sub-Saharan Africa. At the outset the CCCD project, epidemiologic surveillance systems remained fairly rudimentary, despite the advances that the smallpox eradication program had made in the region. There were few epidemiologists, minimal data management capabilities, and few programs that made use of current health data. The CCCD project developed health surveillance programs in a variety of Francophone and Anglophone countries. These included a national program for sentinel infectious diseases

surveillance in Zaire; a hospital-based malaria surveillance project in Kinshasa, Zaire; and surveillance of resistance to antimalarial drugs in Guinea, Nigeria, Togo, and Zaire. Several valuable lessons were learned from these projects.

- Surveillance systems require investment and support including equipment, supplies, personnel, training, and supervision if they are to function successfully.
- Surveillance systems are likely to be sustained only where they provide data that are useful in program planning and management.
- Efforts are needed to assure the quality of the data that are collected, reported, analyzed, and communicated, and which serve as the basis for decisions.
- New applications of epidemiologic surveillance will become increasingly important in the years to come.

Technical obstacles that had to be overcome included the standardization of case definitions and the lack of reliable clinical diagnostic algorithms for some targeted diseases. Structural obstacles included the lack of basic laboratory services such as microscopy and chest X-ray facilities.

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## International Clinical Epidemiology Units (INCLEN): The Essential Role of Training and Research in Surveillance and Prevention of Infectious Diseases

In 1980 a group of health specialists from the Rockefeller Foundation, concerned about the growing crisis in global health care, created INCLEN, a non-profit international program to train faculty from medical schools in developing nations in clinical epidemiology. Such training enables medical practitioners to evaluate the availability, effectiveness and efficacy of health-care practices in their home countries. In addition, the physician/epidemiologists extend their vision beyond the individual patient or hospital ward to better understand the total impact of disease on the public and the country (medical, personal, cultural, economic, etc.) and the importance of prevention strategies.

The multiplier effect of this training program is impressive. It started with five training centers in five countries, and has now (15 years later) trained more than 300 physicians, social scientists, and biostatisticians, who have formed adjunct units in over 40 medical schools in 16 developing countries. These INCLEN units form the backbone of an active research and surveillance network which attempts to identify and confront infectious diseases before they become unmanageable, costly crises. The physician/epidemiologists conduct high-quality research on critical topics such as the economic implications of clinical decisions, cultural factors influencing attitudes and practices toward sickness and health.

USAID supports seven INCLEN units in India. Recently, these units in India collaborated to study the bacterial agent most commonly associated with pneumonia in various locations throughout the country. This activity was built upon the surveillance and treatment capacities established by the INCLEN epidemiology training and research development program. The study showed the pneumococcal pneumonia, treatable with penicillin, was by far the most common cause of pneumonia in Indian children throughout the country. This finding changed the focus of vaccine development and caused the Ministry of health to change its policy for case management of pneumonia which had previously relied on expensive broad spectrum antibiotics rather than the far cheaper and readily available penicillin.

The INCLEN approach demonstrated that use of public health tools (including surveillance of disease patterns and research on the effect of drug treatment) coupled with health economic analyses can lead to efficient and cost-effective preventive and curative interventions.

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## USAID/Nepal Inaugurates Center for Surveillance and Control of Emerging Vector-Borne Diseases

Emerging vector-borne diseases are a serious problem in Nepal and surrounding countries, posing a continuous threat to maternal/child survival and economic development. For example, the Terai region in southern Nepal has been the focus of a pandemic of Kala-azar (visceral leishmaniasis), which has spread from neighboring areas of India and Bangladesh. This parasitic disease, spread by the bite of an infected sandfly, is rapidly fatal if undiagnosed and untreated and the

available chemotherapeutic treatment is costly and losing its' effectiveness. It is estimated that more than 1 million children and adults have been affected in this region alone since the mid-1980s. Sporadic but increasing outbreaks of another emerging disease, Japanese encephalitis (JE), also causes many deaths. Adequate diagnosis and treatment are lacking. Although a preventive vaccine for JE is available, significant cost reductions will be needed if it is to be made affordable for developing countries.

Over the past 40 years, USAID supported the control of malaria in Nepal, and move recently supported the development of a Vector-borne Disease Center for the Division of Epidemiology and Disease Control of the Ministry of Health (MOH) of Nepal. The Center is centrally located in the Terai region where the bulk of vector-borne diseases are found. Through its Environmental Health Project (EHP), USAID provided overall leadership and coordination of a multi-agency response to emerging vector-borne disease in Nepal. In addition, the Government of Japan agreed to provide funding for local use of insecticides in areas in which Kala-azar is endemic. Finally, CDC is providing support for technical training of key staff in surveillance and control methods for JE.

This leveraging of the resources of collaborating agencies and governments has proven to be an essential component in addressing emerging diseases as public health issues, and should be a prerequisite for mounting effective response strategies in the future. The Center in Nepal has also benefited from the environmental health approach of EHP as it plans to conduct operational research to improve understanding of the mechanisms of the diseases at the community level.

As a result of local commitment, hard work, and foreign aid, Nepal will have the local capacity and appropriate tools to monitor future outbreaks of these and other emerging/re-emerging regional vector-borne diseases including malaria, dengue hemorrhagic fever, and plague.

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## International Resources Related to Infectious Diseases

**WHO**

- Disease-Specific ("vertical") networks:
  - Global Polio Eradication Program
  - Global Program on AIDS (now UNAIDS)
    - Global Tuberculosis Program
    - Global Influenza Network
- Division of Communicable Diseases
- Control of Diarrheal Diseases and Acute Respiratory Infections
- Leprosy Elimination Program
- Arbovirus and Hemorrhagic Fever Collaborating Centres (AHFCC)
- Control of Tropical Diseases
- WHO/World Bank/UNDP Joint programme for the Strengthening of Tropical Diseases Research
- Children's Vaccine Initiative
- International Office of Epizootics Worldwide Information System
- Collaborating Centers and Laboratories

**PAHO (Pan American Health Organization)**

- WHO Regional Office for the Americas
- Caribbean Epidemiology Centre (CAREC) , Trinidad
- Instituto de Nutricion para Centro America y Panama (INCAP), Guatemala
- Division of Disease Control and Prevention, Washington, DC
- Special Program for Vaccines and Immunizations

**International Clinical Epidemiology Network (INCLEN), Inc.**

**Food and Agriculture Organization (FAO) Reference Centres**

**French Scientific Research institute (e.g., Senegal, Congo, Cote d'Ivoire)**

**Pasteur Institutes (e.g., in Algeria, Central African Republic, French Guiana, Iran, Madagascar, Morocco, New Caledonia, Senegal, Vietnam)**

**Research Institute for Tropical Medicine, Philippines**

**Institute of Medical Research, Papua, New Guinea**

**Noguchi Center, Ghana**

**EPA**

Office of Research and Development scientists and engineers develop and evaluate practical, effective techniques for disinfecting drinking water.

**CDC**

Infectious Disease Field Stations (Cote d'Ivoire, Guatemala, Kenya, Sierra Leone, Thailand, Botswana)
FETPs (Australia, Canada, Columbia, Egypt, Hungary, Indonesia, Italy, Mexico, Peru, Philippines, Saudi Arabia, Spain, Taiwan, Thailand, Uganda, United States, and Zimbabwe)

**DoD**

U.S. Army Research Facilities (Brazil, Kenya, Thailand) Naval Research Facilities (Egypt, Indonesia, Peru)
Armed Forces Medical Intelligence Center
U.S. Army Medical Institute of Infectious Diseases
Uniformed Services University of the Health Sciences
Armed Forces Institute of Pathology
Armed Forces Epidemiology Board
Armed Services Pest Management Board

**NIH**

National Institute of Allergy and Infectious Disease Supported Facilities (e.g. Brazil, Colombia, Israel, Mali, Mexico, Philippines, Sudan, Uganda, Venezuela, Zimbabwe)

The Fogarty International Center has established a network of investigators trained in HIV-related research and epidemiology and strengthened institutions in over 65 countries in Africa, Asia, and Latin America.

**USAID**

Collaborative programs with U.S. universities based in developing
Program in Worldwide Control of Sexually Transmitted Diseases (STD/AIDS)
Schistosomiasis Research Project, in collaboration with the
Ministry of Health in Egypt
Center for Population and Health Research, Bangladesh
International Clinical Epidemiology Network in India (INCLEN/India)
Program for Appropriate Technology in Health (PATH)
Disease control programs in over 40 countries and research institutions in over 30 countries

Other U.S. resources abroad

Peace Corps (medical surveillance system)
Department of State (medical facilities and numerous research and training programs administered collaboratively by American and foreign universities, with funding by Fogarty, other branches of the NIH, USAID, or private foundations.

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## Cholera in Peru: An Example of Prevention, Preparation, and Mitigation in a Health Emergency

The effective response to the cholera epidemic in Peru in 1991 was launched from a base of sustained research, education, training and institutional capacity building. Death rates in excess of 7% and as high as 20% were expected, based on mortality from recent cholera epidemics in other regions, such as Africa; but mortality was less than 1%.

***What made the difference?***

Between 1985 and 1991 USAID supported several epidemiologic surveillance systems and child survival programs, including diarrheal disease control programs involving oral rehydration therapy. Education in the use of diarrheal disease control measures, combined with a high level of political and technical coordination, made it possible to deal successfully with cholera when it re-emerged, after an absence of almost 100 years. As cholera spread in Peru, deaths were kept to a minimum through the aggressive use of diarrheal control measures. Such measures were already institutionalized in the public health infrastructure by the Ministry of Health.

A U.S. Government interagency effort (USAID, EPA, DOD, CDC and the FDA) assisted the Government of Peru in responding to the outbreak. Disease control was established in a relatively short period of time because of the programs already in place, including the human and institutional resources developed over time to address diarrheal diseases.

***What more can be done to prepare and prevent emerging infectious diseases?***

Cholera is spread when food and drinking water are contaminated with fecal waste. The first line in prevention, therefore, is adequate human waste disposal, clean drinking water, and sanitary preparation and storage of food. The technologies necessary to prevent contamination can be as simple and cheap as appropriately placed and maintained latrines, household disinfection of drinking water and frequent hand-washing. Thus education programs in simple but effective interventions may help minimize the potential for future cholera outbreaks.

New technologies and research may also contribute to preparing for and preventing future outbreaks. Research is being conducted to develop a more effective cholera vaccine and to identify useful forecasting tools. The expertise of such institutions as the Center for Health and Population Research is being tapped to provide guidelines and training for NGOs involved in responding to outbreaks of cholera and other diarrheal diseases.

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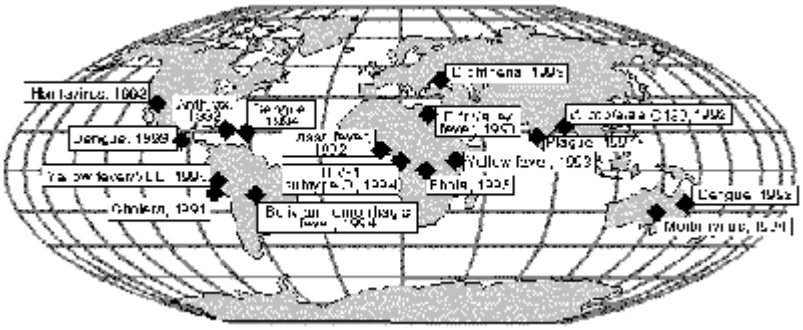


## VII. What research and training programs are required to support the nation's leadership role in global disease surveillance?

Laboratory and epidemiologic research are the essential foundation upon which a sound disease surveillance and response system is based. This is especially true in regard to emerging and unknown infectious diseases. To combat new diseases for which no treatments are known, it is essential to maintain an active community of epidemiologists and experimental scientists ready and able to seek new solutions for new disease threats. In addition, continued emphasis on effective social and behavioral science methods to enhance health promoting behavior should be maintained. To meet the challenge of emerging and re-emerging infectious diseases requires critical knowledge of the *fundamental biology* of infectious agents and the clinical disease processes they induce. Scientific studies of infectious agents and the diseases they cause provide the fundamental knowledge base used to develop diagnostic tests to identify diseases, drugs to treat them, and vaccines to prevent them. In addition, the ability to intervene effectively in an outbreak or epidemic, or to implement a successful prevention strategy, requires a thorough understanding of the **epidemiology** of the disease. An especially important research challenge that may require the combined efforts of epidemiologists, microbiologists, pharmacologists, and others is to find new ways to combat antibiotic resistance, either by preventing its development or by designing vaccines or new classes of drugs effective against bacteria, viruses, fungi, and parasites. Further, the establishment of an infrastructure of researchers trained in epidemiology and laboratory research provides a sound basis for a global network for surveillance and response.

At the present time, major gaps exist in U.S. research and training programs concerned with infectious diseases. The level of support for research on infectious diseases other than AIDS and TB is extremely limited. At NIH, funding for work related to infectious diseases, excluding AIDS and TB represents only about 5% of their total budgets. At CDC, although approximately 65% of the budget is dedicated to the prevention and control of infectious diseases, about 95% of these funds are earmarked for AIDS, TB, and sexually transmitted and vaccine preventable diseases. Furthermore, the number of individuals receiving infectious disease training at NIH and CDC is extremely low, and the number receiving field training overseas is even lower. The training capacity of the DoD in this area has also been eroded. Few individuals in the United States, for example, had the necessary expertise in the diagnosis and treatment of plague to provide assistance during the recent plague outbreak in India. For these reasons, it is imperative that an active scientific community focus on infectious diseases be maintained and supported.

It is likely that many new infectious diseases will emerge in other parts of the world. The earliest possible detection of such emerging problems is in our nations' best interest to anticipate them and respond in an effective manner. To develop effective prevention and control strategies for new and emerging pathogens, research is required on the complex interaction between humans and microbes and the evolutionary and genetic factors that cause epidemics.

Currently, there exist a number of international research and training programs funded by USAID, NIH, NIAID, Fogarty and CDC, that offer a base for studies of infectious diseases and are also well-situated to detect arising infectious diseases. These include the NIAID's TMRC and ICIDR and Fogarty's AIDS International Training and

Research Programs, and CDC's FETP. Optimal utilization of these research teams will strengthen recognition and identification of emerging infectious pathogens at their sites of origin. These teams are positioned to develop new prevention strategies through the discovery of those epidemiologic and biological principles that determine the emergence of new and re-emerging microbial diseases.

## Strategic objectives

- Strengthen or expand support for laboratory research related to infectious diseases.
- Increase support for epidemiologic research.
- Encourage linkages between epidemiologic and laboratory research training.
- Sustain support for international research and training.

## Recommendations for research

**Support laboratory research in these areas:**

- Fundamental aspects of microbial physiology, genetics, and biochemistry
- Pathogenesis of infectious diseases
- Human immune response to infectious diseases
- Development and standardization of diagnostic tests
- Development of drugs
- Development of vaccines
- Development of vector control interventions
- Improvement of surveillance tools, including computer programs for data management and reporting
- Methods for monitoring drug resistance
- Factors that accelerate the development of drug resistance and methods for limiting those factors
- Environmental and climatic factors that influence temperature, the quality and distribution of water, and the population biology of insect and rodent vectors

**Support epidemiologic research in these areas:**

- The transmission patterns and risk factors of infectious diseases
- The effectiveness of intervention strategies for limiting the spread of new diseases and preventing and controlling resurgent diseases
- New epidemiologic and statistical methods, including the development of predictive models for the occurrence and spread of epidemics, and the use of geographical information systems
- Environmental factors that influence the population biology of insect and rodent vectors
- Human behavior and human demographics as they relate to the epidemiology of infectious diseases

**Support social science research in these areas:**

- Human social behavior and demographics as they relate to the causes and control of infectious diseases
- Economic assessments of the cost-effectiveness of different surveillance and response strategies.

**Ensure that resources are available for studies of new microbial threats both here and abroad**. Maintaining diversity in infectious disease research will also allow us to retain expertise on types of bacteria, viruses, and parasites that may emerge and or re-emerge unexpectedly.

**Encourage the development of tools to monitor, investigate, and intervene in public health problems involving emerging or antibiotic resistant microbes.** Also, ensure that facilities are made available to test these products under field conditions.

## Recommendations for training

1. Strengthen interdisciplinary and interagency scientific exchanges and training programs within the United

States in the area of infectious diseases.

These interactions need to be fostered both between agencies and between scientific and public health disciplines. For example, CDC and NIH need to expand and strengthen exchange programs between the epidemiologic and laboratory based science, at the doctoral, post-doctoral, and mid-career levels. Maintaining a cadre of trained investigators who can deal with new disease problems is an essential part of U.S. preparedness. The establishment of an international training program on emerging infectious diseases as outlined by Fogarty in its long-range plan would help to maintain this cadre.

2. Coordinate U.S. agency efforts to enhance existing international research and training programs in infectious diseases.

- NIAID and DoD could work with CDC to strengthen laboratory based research at CDC's FETP units, whose primary focus is epidemiology.
- CDC could work with NIAID to strengthen epidemiology research training at ICIDR and TMRC, which emphasize clinical research.
- CDC's FETP units could collaborate with the USAID-supported INCLEN (see "International Clinical Epidemiology Units (INCLEN: The Essential Role of Training and Research in Surveillance and Prevention of Infectious Disease") to strengthen both programs. In general, enhanced communication among oversees infectious disease programs supported by CDC, DoD, Fogarty, NIAID, and USAID could have a synergistic effect on the global surveillance and response network.
- USAID, CDC and FDA could work with DoD to strengthen the in-country training components of DoD's overseas research laboratories.
- Capacity building at home and abroad could be enhanced by DoD and CDC collaborations with developing country research institutions supported by USAID, such as the ICDDR/B. In the past, U.S. Public Health Service workers were sent to the ICDDR/B for training, although no funds are presently available for this purpose.

***In addition,***

- All agencies could build upon the in-country research and training capacity established through Fogarty-supported programs.
- All agencies could benefit from USAID's experience with multi-disciplinary research and training projects in developing countries.
- More foreign nationals could be trained in epidemiology and experimental microbiology along with American students in U.S. academic centers funded by Government grants and contracts.
- International collaborations with NOAA's scientists could incorporate climate forecasting into disease surveillance training.

3. Encourage networking among the international research and public health communities that support the surveillance and response system for emerging diseases.

Several disease-specific "vertical" surveillance networks operated by WHO (see "International Resources Related to International Diseases,") receive technical assistance from CDC, NIH, DoD, USAID, WHO and various non-governmental organizations.

Connections can be encouraged among the participants in these networks and among participants in research training programs supported by Fogarty, all of whom are well-placed to share information on research and on public health, as well as among participants in research training programs supported by the NIH/Fogarty.

4. Strengthen the training of American physicians and microbiologists in the recognition of "tropical" diseases and travel medicine.

The identification of persons carrying pathogens capable of causing serious disease outbreaks is made difficult by the very large number of people entering the United States from increasingly remote locations. There is a constant influx of American civilians and solders, foreign nationals (including tourists, business travelers, long-term visitors), and immigrants. It is imperative that American medical students be trained to identify infectious diseases that are common

in other countries.

5. Strengthen resources for the education of laboratory and field-based scientists and physicians.

Current facilities operated or supported by CDC, NIH, DoD, and USAID overseas could serve as excellent training facilities for medical or graduate student rotations in laboratory research or field work, or for overseas training details for employees.

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## Scientific Research

Numerous examples illustrate the role that research plays in protecting the public against infectious diseases. In recent years, the techniques of modern molecular biology have been used to study new pathogens (e.g., the agents causing AIDS and Lyme disease) and to define their geographical spread (for example, hantavirus in the Southwest and other parts of the United States). Biomedical researchers have also uncovered new relationships between disease causing microbes and disease. For instance, a previously unrecognized herpesvirus has been detected in Kaposi's sarcoma, a tumor most often associated with AIDS in the United States. Scientists have also applied insights from basic research in physiology to devise life-saving therapies, such as oral rehydration therapy for the treatment of cholera.

In many areas, the lack of basic research has hampered our ability to cope effectively with disease threats. For example, the lack of adequate information about the *Cryptosporidium parvum*, an intestinal parasite, has made the development of new diagnostic reagents and therapies very difficult. Without reliable diagnostic tests, it has been difficult to assess the level of risk during a given outbreak and to design appropriate control measures.

Scientific research is also needed to guide public policy. For instance, scientific information is needed to formulate policy on the use of antibiotics in agriculture and aquaculture, as well as in the treatment of human illness. Similarly, research on the impact of environmental change and climatic variability on the emergence of microbes can inform policy discussions on land use, waste disposal, water resources management, and agricultural policy.

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## Final OMB/OSTP Caveat

The purpose of this report is to highlight ongoing Federal research efforts in this science and technology (S&T) field and to identify new and promising areas where there might be gaps in Federal Support. The report is intended for internal planning purposes within the Federal agencies and as a mechanism to convey to the S&T community the types of research and research priorities being sponsored and considered by the Federal agencies. The Administration is committed to a broad range of high priority investments (including science and technology), to deficit reduction, and to a smaller, more efficient Federal government. These commitments have created a very challenging budget environment-requiring difficult decisions and a well thought-out strategy to ensure the best return for the nation's taxpayer. As part of this strategy, this document does not represent the final determinant in an overall Administration budget decision making process. The research programs presented in this report will have to compete for resources against many other high priority Federal programs . If these programs compete successfully, they will be reflected in future Administration budgets.

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This document was prepared under the guidance of the National Science and Technology Council (NSTC). The NSTC, chaired by the President, is a cabinet-level council charged with coordinating science, space, and technology policies throughout the federal government. An important objective of the NSTC is to establish clear national goals for federal science and technology investments. The NSTC includes the Vice President, the Assistant to the President for Science and Technology, the Cabinet Secretaries and agency heads with responsibility for significant science and technology programs,and other key White House officials.