Confronting Infectious Diseases in an Interconnected World:

People, Animals, and the Environment

The National Center for Zoonotic, Vector-Borne, and Enteric Diseases
Strategic Framework 2009-2014

U.S. Department of Health and Human Services • Centers for Disease Control and Prevention
The National Center for Zoonotic, Vector-Borne, and Enteric Diseases

Involvement of Partners is Essential

Partnerships are essential for addressing the connectedness of human, animal, and environmental health. Achieving the vision of this framework will require improved communication, cooperation, and collaboration across disciplines, institutions, and countries. It will require valuing our existing partnerships while building new ones. It will require bringing a wide range of disciplines together to address infectious disease problems. Besides epidemiologists and laboratorians from a range of fields, we need social scientists, communications specialists, information technology experts, and people with a host of other skills and experiences, working together to address infectious disease threats. We also need to work closely with those who address failures in prevention --- including health-care providers.

Partnerships within the U.S. government will be critical to achieving this plan. This includes enhancing partnerships and building on successful collaborations with other CDC components, such as other CDC Centers that address infectious diseases and environmental health and partnerships across federal agencies. For example, moving upstream to reduce deaths and illnesses from foodborne diseases will require closer relationships, including enhanced data sharing, between NCZVED and the United States Department of Agriculture and the Food and Drug Administration on food and drug safety issues and the Department of the Interior on wildlife issues.

NCZVED has longstanding relationships with many types of global and national organizations. These include multilateral organizations like the World Health Organization and the Food and Agriculture Organization; national and international membership organizations for professionals and for agencies like the American Association of Veterinary Medical Colleges and the Association of State and Territorial Health Officials; and nonprofit organizations and donors.

State and local health and other agencies are also important partners of NCZVED. We commit to working with them to share data and information, increase collaborations, and improve efficiency of data collection and analysis systems.

Achieving the vision of this Framework will also require that we help build the capacity of our partners both in the United States and globally to detect and respond to environmental, animal, and human health changes and threats. This includes training, moving new laboratory tests into the field more quickly, and enhancing and developing interdisciplinary platforms that provide an armature for the collaborative work of many parties. It also includes supporting the efforts of other government agencies, universities and colleges, and partner organizations to encourage interdisciplinary training and education of the next generations of scientists, practitioners, and leaders.

NCZVED Commitment to our Partners

First and foremost, we are a science-led organization.
We support, conduct, and use the best science possible.
We continuously seek ways to be excellent in our science and service delivery.
We bring value to our partnerships.
We value our partners.
We are transparent in our dealings with partners and the public.
We share our data, information, and knowledge.

Dear Reader,

Two years after the creation of the National Center for Zoonotic, Vector-Borne, & Enteric Diseases (NCZVED) at the Centers for Disease Control and Prevention (CDC), I am delighted to share a bold strategic framework that articulates our vision, mission, action, and, ultimately, the intended impact that we desire to achieve. We live in a world where people, animals, and environments are interconnected. That interconnectedness creates new challenges for preventing and controlling infectious diseases. Our vision is to improve health by reducing the impact of infectious diseases using a comprehensive and holistic approach focused on the human-animal-environment interface.

This framework puts ZVED in a leadership role in infectious disease ecology (which connects these domains) with commitments for us to:

— Innovate in all aspects of our scientific and programmatic endeavors
— Integrate systems, services, and multi-disciplinary perspectives and approaches
— Impact the health of people in the U.S. and around the world by preventing and controlling infectious diseases.

But we don't do this work alone. We are interconnected to the larger CDC community and to the larger public health community as well. We commit ourselves to being intentional and consistent in inviting and involving partners to collaborate in the work of preventing and controlling infectious diseases – because it's a shared vision and mission. In fact, the framework described in this document was co-created from a series of meetings with ZVED staff and many governmental and non-governmental partners so that diverse perspectives and ideas could shape it. I found the process very engaging and am very pleased with the insights we received. This document truly represents a process and a plan that emulates the big idea of the framework: interconnectedness.

I personally invite you to read this document with a mind-set of looking for how you or your organization connects with the exciting work of preventing and controlling infectious diseases that result from the interaction of people, animals, and the environment. And then share your ideas about how we can work together.

Sincerely,

RADM Ali S. Khan
Acting Director and Assistant Surgeon General
National Center for Zoonotic, Vector-borne, & Enteric Diseases
Centers for Disease Control and Prevention
Department of Health & Human Services

EXECUTIVE SUMMARY

Infectious diseases remain a major contributor to illness, death, and suffering throughout the world, both from their acute and chronic effects. The potential for epidemics and pandemics is a concern for all countries.

The title of this document, "Confronting Infectious Diseases in an Interconnected World: People, Animals, and the Environment," emphasizes that greater progress in prevention and control of infectious diseases will require us to address human health as interconnected to the health of animals and the environment. This concept has implications for how we conduct our public health work, the focus of our work, and who our partners are and how we work together.

In 2007, in recognition of new opportunities for addressing infectious diseases and the need to take a broader approach to disease prevention and control, the Centers for Disease Control and Prevention (CDC) reorganized, including creation of a Coordinating Center for Infectious Diseases that includes four Centers, each with a different yet complimentary focus. One of these Centers --- the National Center for Zoonotic, Vector-Borne, and Enteric Diseases (NCZVED) — has made a particular commitment to embracing a "one health" approach to its work in disease prevention and control. This approach requires emphasizing the interconnectedness of human health with the health of animals and the environment. While NCZVED's sister infectious disease centers also embrace and address these issues as part of their public health missions, this document particularly describes the vision and priorities of NCZVED for the next 5 years. NCZVED will rely on ongoing collaborations with CDC colleagues in the National Center for HIV, Viral Hepatitis, STD, and TB Prevention; the National Center for Immunization and Respiratory Diseases; and the National Center for Preparedness, Detection, and Control of Infectious Diseases to address these issues.

The three themes of this framework are:

— **Innovate:** Respond to the challenges of an interconnected world with new and creative approaches.

— **Integrate:** Link systems and people across locations and disciplines to enhance early detection of problems, create synergistic opportunities for research, and increase the likelihood that systems solutions can be found.

— **Impact:** Transfer and share knowledge and capacities for prevention and control.

Each theme includes specific priorities for research, surveillance, and programs related to zoonotic, vectorborne, and enteric diseases.

As a result of the implementation of this framework, we believe we will make substantive contributions to the ability of individuals to protect their health and that of their families from infectious disease threats, the ability of communities and state and local governments to develop and implement plans and programs that reduce the risk of infectious diseases, and make improvements in the health of people in the United States and throughout the world. We call on our partners to join with us as we use our new perspectives and tools to confront the challenge of infectious diseases.

BACKGROUND

Infectious diseases remain a major contributor to illness, death, and suffering throughout the world, both from their acute and chronic effects. The potential for epidemics and pandemics is a concern for all countries.

In the 1990s, the term "Emerging Infectious Diseases (EIDs)" captured the concept that pathogenic organisms were posing new threats to human health. The growing problems of antimicrobial resistance, emergence of H5N1 avian influenza as a possible pandemic agent, and the spread of vector-borne diseases like West Nile virus (WNV) provided vivid proof that infectious diseases posed potentially catastrophic threats.

While progress has been made in specific areas, the factors that contribute to disease emergence remain and may be increasing. The reasons for this lie not only in changes in humans and organisms, but also in changes in animal hosts, vectors, and the environment. The increasing recognition that human health protection requires attention to the broader ecology in which we dwell is transforming our approach to infectious disease prevention.

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Why we need a new Framework now

Continued threats

Infectious diseases continue to be major causes of death, suffering, and economic loss, and we continue to confront new and potentially devastating infectious disease threats. Not surprisingly, the threat of pandemic influenza or a new outbreak like severe acute respiratory syndrome (SARS) is as high as before. Waterborne disease outbreaks are increasing in the United States, and in 2008 the United States experienced the largest recorded foodborne outbreak in the past decade. Rates of diseases like dengue fever are rising worldwide. Outbreaks of diseases like chikungunya fever are occurring in locations quite distant from previously recognized foci and pose a threat to the United States, which has competent mosquito vectors. Familiar pathogens are becoming more virulent or difficult to treat; for example, a new form of *Clostridium difficile*, which can cause life-threatening diarrhea, is both more lethal than previous strains and more resistant to treatment, leading to higher death rates, more severe illnesses, and higher healthcare costs. Longstanding endemic infections, like those now termed "neglected tropical diseases," continue to have enormous impact on the health and well-being of billions of people throughout the world.

New tools and technologies

We have new tools and technologies available for understanding and preventing disease and illness. These range from cheaper and faster methods for genetic analysis, to computer programs capable of integrating huge amounts of data, to hand-held devices for conducting surveillance, even from the most remote parts of the world. They allow us to track and respond to diseases that are occurring, as well as to predict and prevent diseases that pose a threat to human health. This framework calls for harnessing existing technologies and taking advantage of new technologies as they develop.

Economic impacts

The economic impact of infectious diseases includes not only direct health care costs, but also impacts on productivity (for example, when people are unable to work or contribute to the economy because of illness or death), as well as on trade and commerce.

The impacts of infectious diseases on health and productivity are very large, especially in developing countries. High disease burdens strain the health care system, reduce economic activity, and potentially lead to political instability.

In an ever-more interconnected world, infectious disease outbreaks that start in one country can have global economic impact. For example, worldwide there were around 9,000 cases of SARS in the 2002-2003 outbreak, but it had devastating effects on global travel and tourism. Disruption of trade from contaminated food and products are common, including trade embargoes and other costly responses to infectious agents.

Interconnectedness of human, animal, and environmental health

Based on our growing understanding of the interconnectedness of human, animal, and environmental health, we need to broaden and refocus our efforts. We need a plan that promotes more integrated, more interdisciplinary relationships among scientists and public health practitioners focused on humans, animals and vectors, and environment.

In addition to attention to humans and their interactions with disease-causing organisms, we must focus on the interplay among humans, including behavior and host factors; animals, including food animals, wildlife, companion animals, and insect and other vectors; and the environment, including soil, plants, climate, and practices and processes in food and other industries.

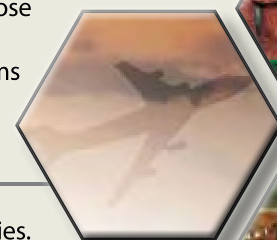
Connecting to "One Health" and other initiatives

"Confronting Infectious Diseases" builds on movements like the "One Health Initiative," which grew out of efforts by the American Veterinary Medical Association (AVMA) to strengthen communication and collaboration with colleagues in human medicine. One Health was launched in 2007 by the AVMA, with the American Medical Association House of Delegates approving a resolution in support of One Health just two months later. It has garnered support from other organizations, such as the CDC, the American Society for Microbiology, and the American Society of Tropical Medicine and Hygiene. The One Health Initiative recognizes the interrelationships among human, animal, and environmental health and seeks to enhance communication, cooperation, and collaboration in integrating these areas for the health and well-being of all species.

The Great Convergence: People, Animals, and the Environment

Human health, animal health, and environmental conditions are inextricably connected. This framework largely focuses on foodborne diseases, waterborne diseases, vectorborne diseases, and zoonoses, all of which illustrate this convergence.

People Although human behaviors can reduce the risk of infection, we remain vulnerable. Outbreaks of foodborne illness have occurred despite excellent food preparation practices, and even people who take precautions like applying insect repellents can get sick from vectorborne diseases. People with immune problems or other underlying chronic conditions are at particular risk from infectious diseases. Those who are poor are not only at higher risk for infectious diseases, but they are also less likely to receive effective care when they get sick.

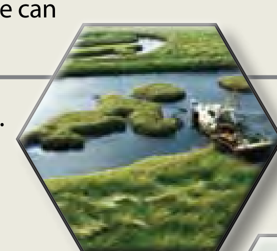


Travel and population movements are important factors in disease spread. Travelers, immigrants, and refugees can bring new organisms and diseases into relatively naïve populations, whose health-care professionals lack necessary diagnostic and treatment skills for these conditions. They can also impact local ecosystems, for example, introducing organisms into areas with competent vectors (like mosquitoes), with potentially significant impacts on human health.

Animals Humans can get illnesses directly from sick animals, as illustrated by rabies. Although the United States has few rabies cases, worldwide there are an estimated 50,000 deaths a year, over 90% of these deaths from exposure to rabid dogs. In the United States, more than 7,000 rabid animals are reported and at least 20,000 to 40,000 people are exposed to rabies each year and require prophylaxis.

Sometimes, animals that appear healthy can spread disease. Escherichia coli 0157:H7 can be present in the gut of a cow without causing the cow any harm. However, feces or gut contents from the cow can contaminate meat during slaughter, and if the meat is not cooked enough to kill the bacteria, people eating the meat can become very ill.

Diseases can also be spread by vectors, when insects, snails, or other members of the animal kingdom carry infectious agents from one animal or human to another. For example, mosquitoes in the United States can carry viruses such as West Nile and eastern equine encephalitis to humans from birds, and ticks from deer mice can transmit Lyme disease to humans.



Environment Environmental changes can result in the spread of infectious agents. For example, *Vibrio parahaemolyticus* is a bacterium that grows in warm salt water. In 2004, a large outbreak of *V. parahaemolyticus* infection occurred on an Alaskan cruise ship after people on the ship ate raw oysters harvested in Alaska, which was at least 1,000 km further north than sites of previously documented *V. parahaemolyticus* contamination. This extension northward of the range of *V. parahaemolyticus* follows higher water temperatures, which permit this organism to flourish in oyster beds that had previously been too cold to support its growth.

Changing land use patterns and urbanization have contributed to the dramatic rise in dengue fever in the last 40 years. Unplanned urbanization, with standing water in waste and other receptacles, has created mosquito breeding sites, and movement of people and goods has spread both mosquito vectors and infections. In Latin America, dengue increased from 66,000 reported cases in 1980 to more than 900,000 reported cases in 2007; the emergence of dengue and dengue hemorrhagic fever has been most dramatic in the American region. In the United States, the numbers of dengue patients may be expected to increase as travel between the United States and endemic areas continues to rise.

Patterns of human infection due to fungi are also changing. For example, rates of coccidioidomycosis in the American southwest have increased dramatically in recent years, probably reflecting increasingly warm, dry conditions; the older, vulnerable population; and other factors. *Cryptococcus gattii* is a fungus that was rarely reported as a pathogen and not thought to cause outbreaks until 1999, when increasing numbers of people and animals becoming sick from this organism were reported on Vancouver Island in British Columbia; new cases of infection continue to be identified today. In addition, in the past three years there have been cases of infection with the outbreak strain in humans and companion animals from the northwestern United States.

Benefits of a multidisciplinary, collaborative approach

Increased efficiency

By linking human, animal, and environmental surveillance, research, and prevention, we will increase efficiency and decrease duplication of efforts. We will create synergies, as researchers and practitioners from different fields come together to solve critical problems and share ideas and approaches. We have high-priority opportunities to integrate surveillance, research, and prevention efforts in well-defined areas such as vectorborne diseases and food safety.

Systems solutions

Linking efforts will also increase the likelihood of finding systems solutions. For example, linkages will facilitate the shift from addressing problems that arise in humans (such as foodborne outbreaks) to anticipating and preventing problems in the first place (as through predicting the implications of changes in food production practices on human health). The concept that integration will result in systems solutions can be visualized with the metaphor of moving upstream --- for example, protecting the watershed of the river that supplies drinking water to a town instead of relying on water treatment plants to kill contaminant organisms. For many human health problems, upstream solutions mean addressing issues related to animal health and the environment.

Upstream prevention

We are proposing to increase our ability to answer not only the question, "What happened?", but also the question: "Why did it happen?" We will focus not only on human illnesses, but also on the sources of pathogens and factors that influence them. By working with our partners to integrate systems that identify, respond to, and prevent human health problems with those that address animal health and the environment, we will be able to move further upstream towards predicting risks for human health problems before they occur and putting prevention in place.

Prevention: Upstream, Midstream, and Downstream Examples			
	Upstream	**Midstream**	**Downstream**
Examples			
Foodborne diseases *(Salmonella* Enteriditis, *for example)*	Removing infected flocks from the breeding supply, preventing infection in egg-laying flocks through hygiene and vaccination, and pasteurizing eggs for institutional use.	Good food preparation practices, like cooking eggs thoroughly, using pasteurized eggs for high-risk populations, keeping eggs refrigerated, and not using cracked eggs	Supportive care for sick individuals, antibiotics if needed, education and work restriction to prevent secondary cases (transmission of the illness to family, friends, and others)
Waterborne diseases *(cryptosporidiosis, for example)*	Protecting watersheds through farming practices, like fencing to keep animals from the water and separating calves from cows to reduce cryptosporidiosis among calves and consequent shedding of organisms	Chlorination and filtration of drinking water in municipal water plants	Supportive care for sick individuals, prevention of secondary cases
Vectorborne diseases *(malaria, for example)*	Draining breeding areas, controlling larval mosquitoes with insecticides, genetic engineering to create mosquitoes that do not transmit malaria	Insecticide-treated bednets to prevent mosquito bites	Drug treatment and supportive care for sick people
Zoonoses *(rabies, for example)*	Rabies vaccination of dogs	Teaching people how to reduce the risk of getting bitten	Post-exposure rabies immunizations

CONFRONTING INFECTIOUS DISEASES: THE FRAMEWORK

This document is a framework for our work over the next five years, with a focus on foodborne, waterborne, vectorborne, and zoonotic diseases. "Confronting Infectious Diseases" calls for us to be more effective with the tools we already have, while building towards the future for infectious diseases prevention --- a future that addresses the convergence of human, animal, and environmental health. We will use our existing tools, and we will also try approaches for which there are few precedents or roadmaps.

The three themes of this framework are:

- **Innovate:** Respond to the challenges of an interconnected world with new and creative approaches.
- **Integrate:** Link systems and people across locations and disciplines to enhance early detection of problems, create synergistic opportunities for research, and increase the likelihood that systems solutions can be found.
- **Impact:** Transfer and share knowledge and capacities for prevention and control.

Innovate

To innovate means to solve problems or add value with new and creative approaches. This theme emphasizes research to create new knowledge and development of tools that will lead to upstream solutions to infectious disease problems. It involves creative use of laboratory tools, epidemiology and surveillance tools, and data. It also includes taking steps to ensure that the knowledge and information generated through our research is widely shared.

Pathogen identification, characterization, and diagnostic test development

New pathogen identification is important both to understand unexplained illnesses and to solve outbreaks. In some cases, such as in the investigation of well-defined specimens from outbreaks without an identified cause, the work can be very targeted. For example, in the case of outbreaks like SARS, rapid laboratory work led to the discovery of the causative agent --- a previously unknown coronavirus. When organisms undergo major changes, such as the development of greater virulence by *C. difficile*, characterizing the altered organism and the mechanisms that result in its changed behavior is a step toward developing new and more effective interventions.

SARS

In 2002-2003, outbreaks of unusually severe respiratory illness were recognized in Asia. While public health officials, epidemiologists, infection control specialists, clinicians, and many others worked to identify cases and limit the spread of infection, laboratorians, including many at CDC, worked to identify the cause of the illness. Through a combination of classic microbiology techniques and state-of-the-art molecular biologic techniques, the causative agent was identified as a previously unrecognized coronavirus, designated SARS-CoV.

Within weeks, diagnostic tests were developed at CDC and distributed to detect the virus in clinical samples like respiratory secretions and to detect antibody responses in patient sera. These assays and others were rapidly distributed so that people with SARS-CoV could be accurately diagnosed and their contacts could be followed and provided appropriate care. Meanwhile, investigators searching for the origin of the outbreak found that civet cats in game markets in China carried a very similar coronavirus. Subsequent studies have documented that civet cats were the likely intermediate host for direct transmission of SARS-CoV to humans, but bats, or some other host, are likely the natural reservoir.

Many lessons were learned from this outbreak, including the importance of: early detection, effective communication to the public, the need for increased research and development and for linking zoonoses research with biomedical research, strategies for containment that include attention to ecology and animals, and approaches to multinational collaboration and collaboration across disciplines and professions.

Once a new organism is identified, its role in disease and the risk factors for infection and settings in which contamination occurs must be characterized to help us understand options for control. This is best done through collaborations among those who study human health and those who study animal and environmental health issues, with a goal of determining the options for prevention, especially those that are upstream. To understand the factors that lead to an organism causing human disease involves not only creativity and innovation in laboratory work, but also creative use of tools from epidemiology and other disciplines.

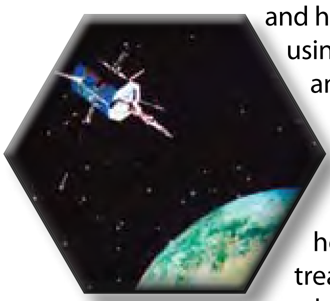
The laboratory tests used to identify new organisms are often complex and are not standardized. They are seldom appropriate for widespread use. Once an organism is identified, especially if it is known or believed to be pathogenic, protecting the public's health may require developing screening or diagnostic laboratory tests that can be used on a routine basis. We will address this need through a comprehensive program for pathogen identification and development of diagnostic tests for organisms of public health significance.

Also critical is the development of better tests for routine diagnosis of known pathogens. For example, a study in Minnesota showed that enterotoxigenic *E. coli*, for which a routine test is not available, is an important cause of diarrhea. It is currently as common a cause of diarrhea in Minnesota as are other pathogens for which laboratory testing is routine. Diarrheal disease rates from this pathogen in the U.S. may be increasing as a result of increased travel and consumption of imported produce. Until a clinically useful test is developed, this pathogen will continue to be underdiagnosed and prevention will be limited.

In addition, laboratories that focus on testing of human samples for infection are typically not linked closely with laboratories that test environmental samples. We propose emphasizing environmental microbiology. This will enable us to support field work and research, leading to a better understanding of diseases that are strongly influenced by environmental and ecological factors. It includes research on how the environment influences pathogen and vector activity and survival; how organisms adapt to environmental changes; and how air, water, and soil contribute to human and animal disease. An important component of this new approach will be the application of new technology toward organisms that cannot be cultured and the discovery of fungal agents of disease whose ecologic niche is often the environment.

<u>Predictive modeling to guide planning and prevention</u>

We will develop and test predictive models that will lead to prevention or detection strategies. This includes modeling the transmission dynamics of infectious disease agents and vectors and their interactions with animals and humans. It also includes evaluating the impact of changes in climate and commerce, and using the results to guide prevention. This work will take advantage of new technologies and skill sets such as analytic techniques for geographic information systems, molecular techniques that can track the geographic distribution and movement of specific pathogens, and satellite-based remote sensing of ecological conditions.



Modeling can also be used to predict how best to combine proven strategies or how to time interventions to have maximal impact. For example, use of insecticide-treated bednets has been shown to reduce overall mortality by 20% in malaria-endemic areas by forming a protective barrier. Indoor residual spraying --- coating the walls of homes with insecticides --- has also been shown to markedly reduce malaria cases. Modeling could be used to predict whether combining these approaches is likely to be synergistic, and what the optimal strategy is for combining them, for example, whether they should be done simultaneously or whether their initiation should be temporally offset.

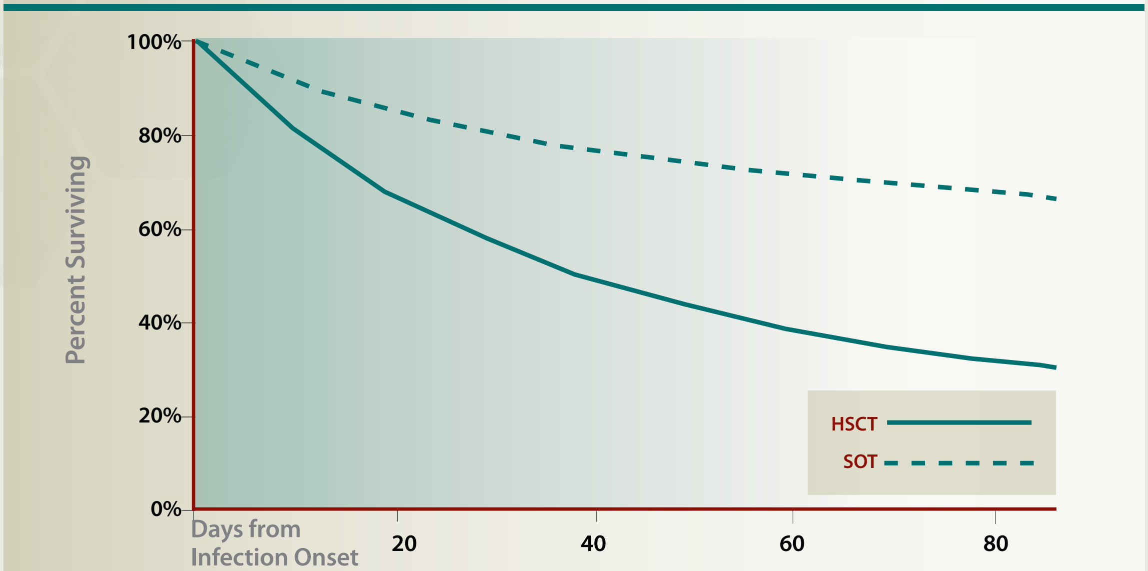
<u>Understanding the role of host factors</u>

Understanding human factors that result in disease susceptibility or protection from disease may lead to new and targeted prevention and treatment approaches. The growing number of people with increased susceptibility to disease --- whether from HIV/AIDS or diabetes, use of drugs to suppress the immune system, advanced age, or other conditions --- is also a critical input to our research, surveillance, and prevention agendas. Temporary perturbations, such as changes in intestinal flora from antibiotics, can have significant impacts on susceptibility and response to infection, for example, increased susceptibility to *C. difficile* or yeast infections after antibiotic treatment. Host factors are also important predictors of the outcome of infection, such as the development of neuro-invasive disease following WNV infection or the hemorrhagic form of dengue fever.

Vulnerable Populations: Transplant Recipients

The number of persons in the United States receiving hematopoietic stem cell transplants (HSCT) and solid organ transplants (SOT) continues to increase. In 2006, almost 30,000 SOTs and more than 18,000 HSCTs were performed in the United States. Because people who receive transplants are immunosuppressed, they are particularly vulnerable to severe infections and infections caused by organisms that do not usually cause disease in healthy persons. Invasive fungal infections are a common problem among transplant recipients. For example, more than 8% of patients receiving HSCTs from unrelated donors or mismatched related donors will develop invasive fungal infections within a year of transplant, most of these within the first 6 months. These infections are often fatal. Twenty-five percent of SOT recipients and nearly 52% of HSCT recipients die within 3 months of being diagnosed with invasive fungal disease. Recognizing these risks and the potential for similar issues with viral and bacterial pathogens, NCZVED collaborates with NCPDCID, NCIRD, and 6 organ transplant centers to conduct the Organ Transplant Infection Project to explore improved diagnostic methods.

Survival Curves for Hematopoietic Stem Cell Transplant (HSCT) and Solid Organ (SOT) Recipients Who Develop Invasive Fungal Infections



New technologies are creating an explosion of knowledge about possible relationships between human genes and disease. In some cases, genetic variants protect against infection (for example, people with sickle cell trait are less likely to get malaria); in others, they affect the expression of clinical illness. Better understanding of the relationship between human genetics and susceptibility and response to infection may provide a basis for development and testing of vaccines for diseases like malaria. Genetic variability has also been shown to affect response to medication; causes of treatment failure or adverse reactions may include genetic characteristics of the organism or the human. NCZVED's laboratories work with NCPDCID's Biotechnology Core Facility, which is poised to broaden CDC's host genomic lab capability.

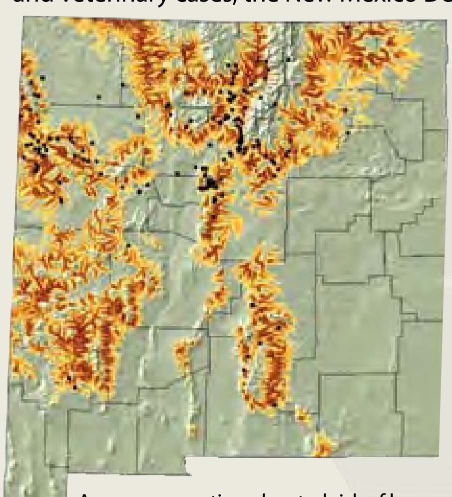
Social factors are major determinants of health, and their impact can be measured both in comparisons between countries (for example, life expectancy at birth ranges from 32 years in Swaziland to 84 years in Macau) and among groups within a given country. Income is among the important determinants. Both country economic status and individual income can affect the likelihood an individual receives information and has knowledge about disease prevention and control. They affect access to prevention tools (ranging from clean drinking water to soap to vaccinations) and disease treatments. Social factors may also result in lifetime stressors that can affect immune and endocrine responses to acute stresses like infections.

In some cases, the outcome of infection is a chronic disease. Infectious agents cause chronic diseases through a variety of pathways, including direct effects of the infection and from the body's immune response. Although in some cases age or other measured factors have been shown to put infected individuals at risk for long-term sequelae --- for example, age at infection, alcohol use, and sex are known to affect the risk of hepatocellular carcinoma following hepatitis B infection --- the understanding of the role of host factors in development of chronic diseases following infection is in its infancy. For instance, chronic fatiguing illnesses that sometimes follow infections like Lyme disease or Q fever are poorly understood, but may be influenced by the interaction of the cumulative stress an individual has experienced over his or her lifetime and the response of the hypothalamic-pituitary-adrenal axis.

Predictive models are used to identify when and where humans are at greatest risk of exposure to disease agents. Typically, the probability of rodent- and vector-borne disease occurrence is strongly correlated with environmental or geographical factors such as elevation, vegetation, rainfall, soil type and agricultural practices that can be assessed remotely. As a result of these strong associations, surveillance data from small but ecologically diverse areas can be used to identify ecological correlates of risk and then extrapolate these predictions to ecologically-similar areas where surveillance activities are inadequate or non-existent.

Predictive Modeling Guides Plague Prevention and Planning

Plague, a severe, primarily flea-borne bacterial zoonosis caused by *Yersinia pestis*, is characterized by long inactive periods punctuated by rapidly-spreading outbreaks. Humans are at greatest risk of exposure to *Y. pestis* during epizootic periods when infectious fleas abandon their dying rodent hosts and occasionally bite humans. The disease is often fatal if appropriate antibiotic treatment is delayed or inadequate. Improved assessments of when and where humans are at highest risk of exposure to *Y. pestis* may aid in targeting limited public health resources and ultimately reduce the burden of disease. Within the United States, the majority of human infections are reported from New Mexico. Following reports of human and veterinary cases, the New Mexico Department of Health (NM DOH) conducts field investigations to determine locations of probable exposure. Capitalizing on more than 40 years of epidemiological surveillance data, researchers in DVBID and the NM DOH developed a spatial risk model that identified approximately 17% of the state as high risk (figure 1), suggesting that resource requirements for regular surveillance and control could be effectively targeted on less than 20% of the state. Similar spatial and temporal predictive models are currently under development for plague in East Africa, a region of the world that in recent decades has reported the largest number of human plague cases world-wide. Although our example focuses on plague, these predictive tools are applicable to other disease systems.



Areas representing elevated risk of human exposure to *Y. pestis* on privately owned or tribal land in New Mexico based on a non-linear relationship with elevation and Euclidian distance to piñon-juniper ecotones and water. Locations of residence-linked human cases (black) are shown. (Figure from Eisen, R.J., et al. (2007) Am J Trop Med Hyg, 77: 121-125.)

Integrate

Connections and interrelationships are both part of the problem of infectious diseases and critical to the solution. Inherent in the concept of EIDs, and echoed in this framework, is an acknowledgement of global interconnectedness. Travel, production and distribution of food and other products, movement of animals and vectors, and climate and other environmental modulators all affect the spread of infectious diseases.

Also inherent in this framework is the recognition that increased effectiveness in addressing EIDs will require new and enhanced collaboration and coordination and an integration of our efforts. This framework calls for an even wider circle of disciplines to engage together for surveillance and prediction, and to find upstream solutions to infectious disease problems. It recognizes the need for changes in relationships between scientists and regulators, researchers and industry, government, and the private sector to achieve disease prevention and control.

Integrated Research and Development Centers

We propose to fund integrated centers—some in the United States and some in critical regions of the world — that will bring together researchers in infectious diseases of humans, infectious diseases of animals, and environmental health sciences, along with other critical disciplines, such as engineering, economics, and social sciences. These centers will provide regional and country support as they conduct and integrate surveillance, conduct research and development, and integrate multidisciplinary approaches to identify opportunities for prevention and test interventions. A high priority will be having centers in places where conditions increase the threat of devastating emerging infectious diseases or where conditions are such that findings will have broad applicability. Ideally, these centers will be linked to or even co-located with other centers and networks conducting critical public health research throughout the world.

Integrating information to create action

Current surveillance systems are often fragmented. Systems that address different human pathogens are disconnected from each other, if they even exist, and there is very little linkage among systems for human and animal diseases and environmental conditions. We propose linking and integrating existing surveillance systems into a coordinated system --- a network of networks — using innovative approaches to extract maximum benefit from the samples and data, improving the use of these data by decision-makers, and building communications networks so that we can rapidly alert appropriate people working in human, animal, or environmental health when actions should be taken. Our vision is a global network of information about human, animal, vector, and environmental pathogens for rapid detection and response, with information available at every level of the public health system — from national and international leadership to the front-line provider.

A component of this effort is biosurveillance, the monitoring of information from a range of sources, from prescription drug purchases to animal surveillance to media reports to blogs, to detect an emerging epidemic or major health event, whether naturally occurring or the result of bioterrorism. Efforts are underway across CDC to develop real-time systems that would use continuous data collection and analysis to ensure the prompt detection of unusual events.

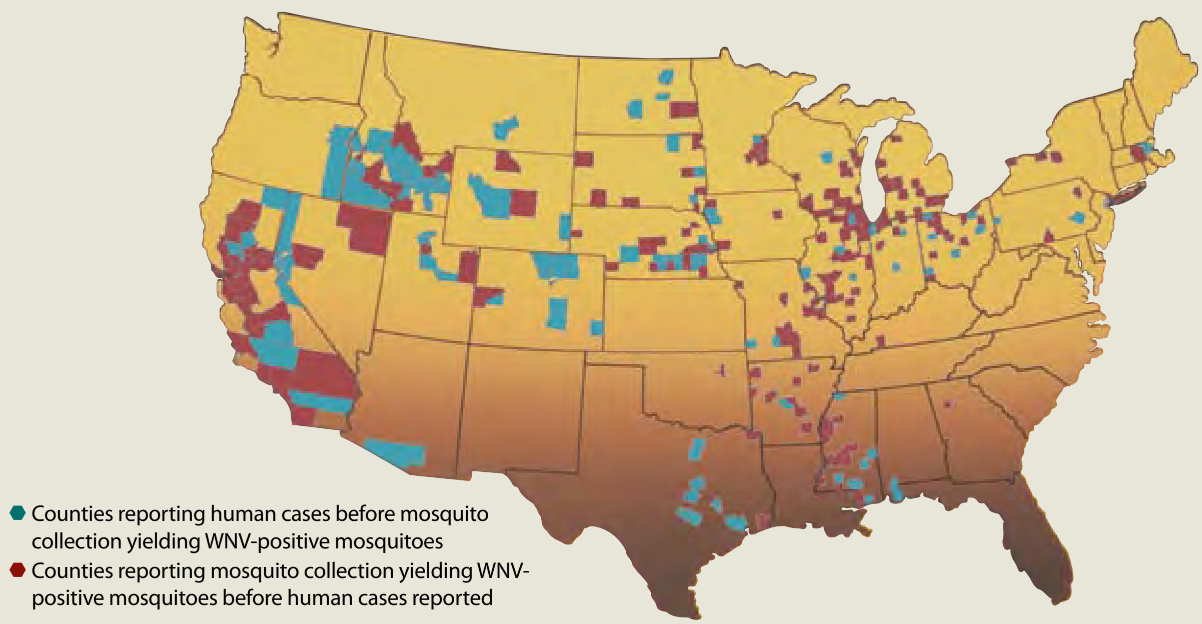
Clear, accurate, and consistent messaging is also critical for ensuring that information is turned into action. One aspect of this is the bundling of related and complementary messages, so that people get the information they need organized in a way that makes it maximally useful.

Vectorborne Zoonosis Surveillance

Vectorborne zoonoses like West Nile virus (WNV), plague, and Rocky Mountain spotted fever (RMSF) exemplify the complex ecologies that impact public health. Surveillance programs intended to predict risk of these diseases must monitor zoonotic as well as human epidemiology. ArboNET is an example of such an integrated surveillance system. It captures human case data, blood donor data, as well as environmental surveillance indicators (virus identified in mosquitoes, dead birds, horses, sentinel chickens) for WNV and other domestic arboviruses (such as St. Louis encephalitis and eastern equine encephalitis). It can also capture information about imported zoonoses, such as chikungunya and Japanese encephalitis. By including environmental data, the system could identify places where people may be at particular risk for exposure before people become sick, providing opportunities for prevention.

A potential next step in developing an integrated vectorborne zoonosis surveillance system is to expand the scope of ArboNET to include case report and environmental surveillance data for other vectorborne pathogens, such as Lyme disease, plague, and RMSF. As effective risk prediction models are developed, weather data, land use patterns, and other factors that affect vectorborne zoonotic diseases could be added to the system to provide better targeting and implementation of upstream interventions.

Timing of WNV-Positive Mosquito Pool Collection and Human WNV Case Onset, By County, United States, 2006



In 2006, WNV-positive mosquitoes were collected in 180 counties before reports of human cases, raising the possibility that enhanced control measures and encouragement for people to use personal protection could have prevented illnesses. Over 50% of counties that have positive mosquito pools report at least one human case, so the finding of WNV-positive mosquitoes may serve as an early warning indicator.

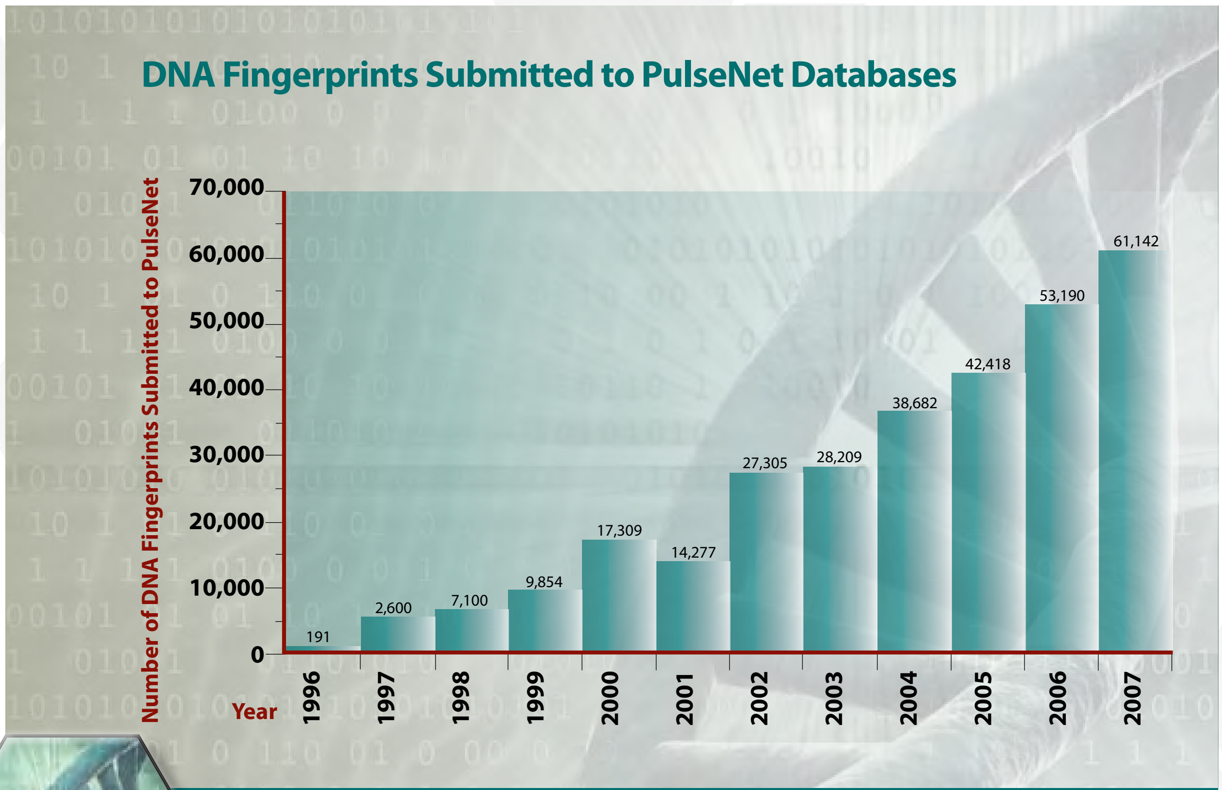
Genomic surveillance of pathogens

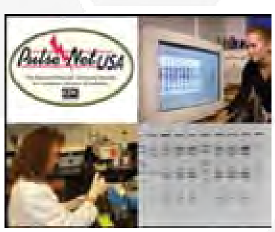
The benefits of surveillance based on molecular subtyping for foodborne organisms in humans has been demonstrated by PulseNet, the award-winning program that identifies outbreaks that would otherwise go undetected and results in faster and more effective outbreak responses. We propose to expand this platform to include subtyping based directly on gene sequencing of other pathogens from humans, animals, and the environment. This will further enhance outbreak detection and help us determine the sources and reservoirs of infection with even greater speed and accuracy and for a greater range of organisms. High priorities for organisms to include are *Salmonella, Escherichia coli O157:H7, Listeria monocytogenes, norovirus, Cryptosporidium*, and organisms isolated from sterile sites like blood and the central nervous system.

DNA "Fingerprinting" and Investigation of Organisms to Detect Outbreaks

In 1996, scientists at CDC, collaborating with the Association of Public Health Laboratories, launched PulseNet, a national network that uses DNA "fingerprinting" to rapidly identify outbreaks of bacterial infections that are often spread through the food supply. Strains of bacteria with the same pattern are likely to have the same source, so detecting a cluster of infections caused by bacteria of a single pattern can trigger an investigation to see if they have a common source, like a particular food item, that can be identified and controlled. Each investigation is also an opportunity to learn how to prevent future similar ones. Through fingerprinting of organisms in humans, animals, and the environment, we are learning about the ecologies and connections that lead to outbreaks, which will help us develop long-term prevention strategies.

By 2001, all 50 states and some large cities were participating. PulseNet also receives isolates from the U.S. Department of Agriculture and the Food and Drug Administration, and is linked to the VetNet system for animals and foods and to PulseNet Canada. Not only does PulseNet find outbreaks more quickly than traditional surveillance approaches, it can even detect outbreaks that would have been missed altogether in the past, like finding "needles in a haystack."


DNA Fingerprints Submitted to PulseNet Databases
Number of DNA Fingerprints Submitted to PulseNet
70,000
60,000
50,000
40,000
30,000
20,000
10,000
0
Year
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
191
2,600
7,100
9,854
17,309
14,277
27,305
28,209
38,682
42,418
53,190
61,142



Impact

The returns on our investments in innovations and connections will grow over the years. The focus in this theme is on increasing our impact now. We will do this by working towards widespread implementation of proven interventions, earlier identification and upstream prevention of outbreaks, completing eradication and elimination of select diseases, providing expert services, and disseminating tools and knowledge. This framework calls for a renewed orientation to building toward widespread adoption of techniques and practices that will reduce the toll of infectious diseases. Inherent in this is a commitment to using our experience, tools, and knowledge to reduce health disparities.

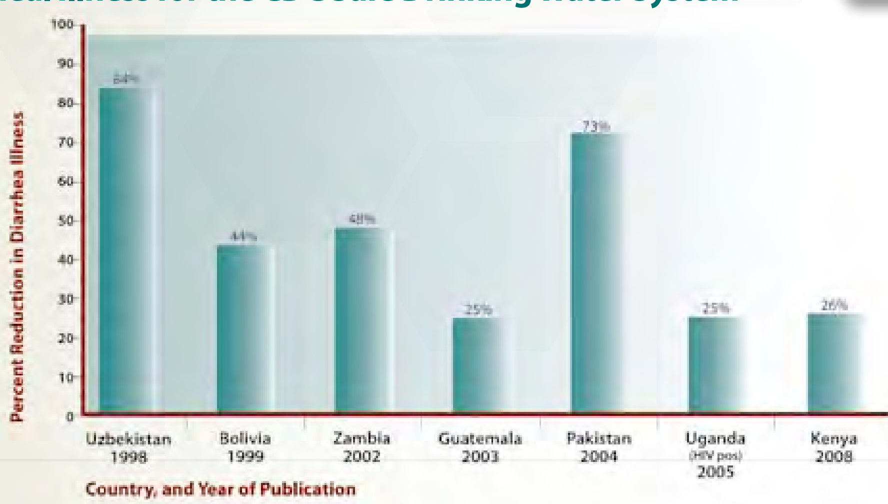
Widespread implementation of interventions that work

CDC studies have shown the effectiveness of a host of interventions, from point-of-use treatment to provide safe drinking water to use of insecticide-treated bednets to prevent malaria to policies related to pasteurization. Once a program is shown to be effective, we will mount concerted efforts to increase adoption. This includes evaluation of policies that can result in change, implementation research, monitoring and evaluation when interventions are implemented, building on lessons learned, and development of business plans.

Many of our current efforts in prevention focus on trying to change behavior of individuals, for example, through education. This approach is not always effective, especially if a person has to choose to perform the healthy behavior over and over again (for example, handwashing) or if people perceive a risk to performing the behavior (for example, that the risk of insecticides outweighs the benefits of preventing insect bites). The power of *policies* to change behavior and disease risk is evident for such diverse interventions as requiring childhood immunizations for school entry, routinely pasteurizing milk, and presumptively treating pregnant women in malaria-endemic areas. We will evaluate policies as vehicles for preventing infectious diseases, including evaluating costs and benefits, and then work with partners to increase use of policies that can make a difference. In all of our research and interventions, we are more interested in what works best.

Reductions in Diarrheal Illness for the CDC Safe Drinking Water System

The CDC Safe Water System consists of a solution of dilute sodium hypochlorite, often distributed with a narrow-mouthed, lidded water vessel that is designed to discourage hands and other objects from being put in the water. The sodium hypochlorite, which can be produced locally, works as a disinfectant. The cheap, easy-to-use system has been shown to reduce diarrheal illness in randomized controlled trials.



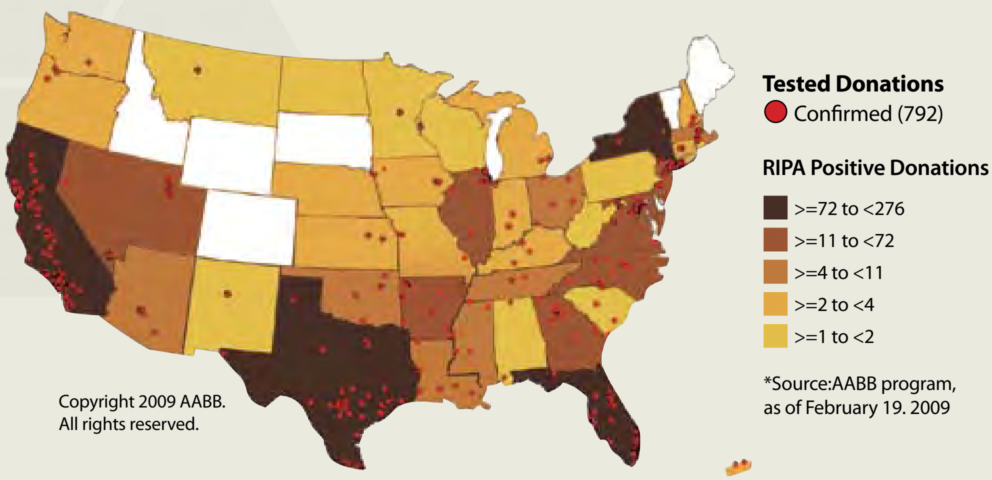
Translation research is needed to ensure that interventions that have been shown to work are successfully institutionalized. This includes research to ensure that interventions proven in small-scale studies or in specific settings are effective when applied broadly and what factors need to be addressed to encourage widespread use. Also important are economic analyses that help make the case for prevention and control measures, as well as providing useful information for making choices among effective interventions.

Another aspect of ensuring that interventions continue to be effective when widely implemented is monitoring and evaluation. Not only do evaluation data indicate if an intervention is having an impact, they also can be used as a basis for continuously improving the intervention and its implementation. For example, concern about unpasteurized juice as a source for outbreaks began in the 1990s, with eight outbreaks between 1995 and 1998. Between 1999 and 2001, seven more outbreaks occurred. In 2001, the Food and Drug Administration published a new regulation requiring that commercial fruit juice be treated to kill 99.999% of microbes, with implementation to occur over a 3-year period. Since then, outbreaks related to commercial fruit juice have virtually disappeared, indicating the success of this approach.

Migration and the movement of infectious diseases: Chagas disease

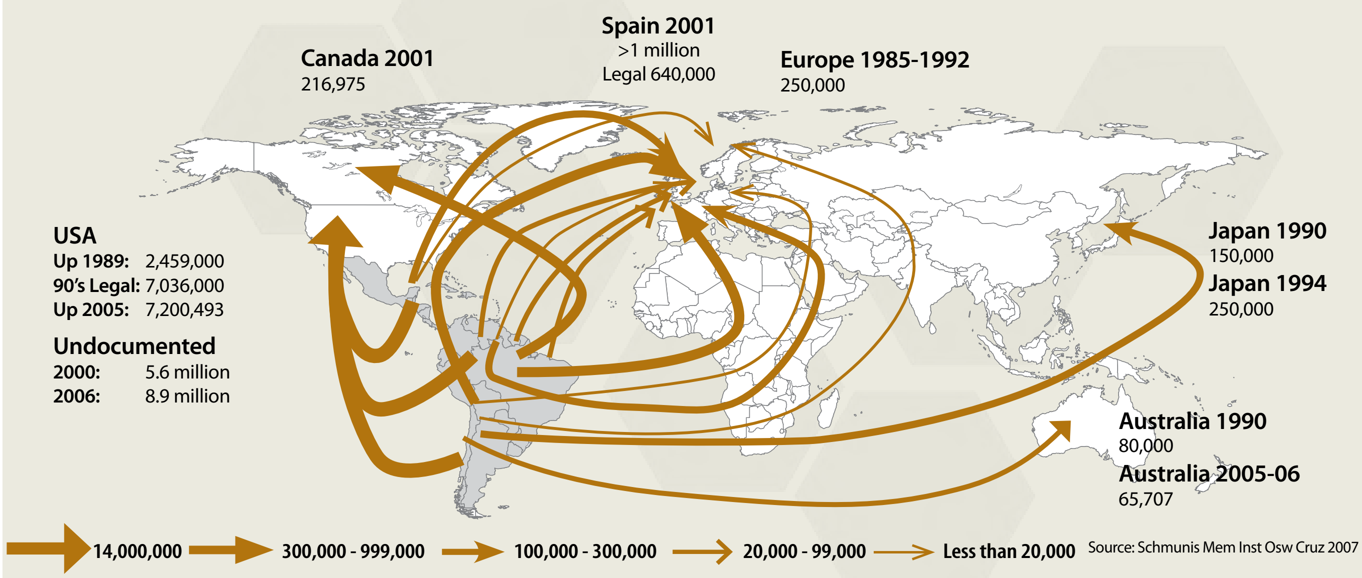
Since initiation of voluntary blood screening for Chagas disease in 2007, nearly 800 cases of confirmed Chagas disease have been detected at United States blood centers. The greatest numbers of positive donors, now deferred from donation, have been identified in those states with the largest populations of Latin American immigrants, but this map illustrates that positive cases can occur anywhere. NCZVED works with NCPDCID's Office of Blood, Organ, and other Tissue Safety and external partners to monitor Chagas disease and to implement programs for preventing transfusion/ transplant-associated cases.

Blood donors confirmed positive for Chagas Disease, 2007-2009*, n=792



Population migration can have a profound impact on movement of infectious diseases. This map illustrates the relative magnitude of movement of persons from Chagas endemic countries, including an estimated 18 million to the United States.

18 million people in the U.S. born in Mexico, Central and South America



Outbreaks of illness occur on a daily basis. At any given time, staff from throughout CDC are providing consultation, assisting with laboratory work, and working in the field to help investigate outbreaks and develop control strategies. Each outbreak represents an opportunity to learn how to identify outbreaks more quickly, understand the causes of the outbreak faster, and intervene to stop the outbreak and prevent future ones. We must develop and test new approaches to gathering information, such as having banks of volunteers who have already agreed to serve as healthy controls during outbreaks, and to sharing information, such as having surveillance data available in publicly searchable web formats. Particularly as we link human, animal, and environmental investigative efforts, we anticipate that outbreak investigations will more often lead to the identification of upstream prevention strategies.

As much as possible, we will use organized, creative, multifaceted approaches to increase support for and implementation of programs. For example, business plans could include such approaches as social marketing, microfinance programs, and innovative partnerships. In some cases, it will make sense to bundle programs together to increase their appeal and decrease costs. This is currently being done with mass drug administration programs for several neglected tropical diseases. Research and planning to ensure sustainability are also part of implementation.

<u>Eradication and elimination</u>

Successful eradication and elimination programs save lives, reduce suffering, and save money. For example, smallpox eradication required a one-time investment of $100 million. It is estimated to save the world $1.35 billion per year.

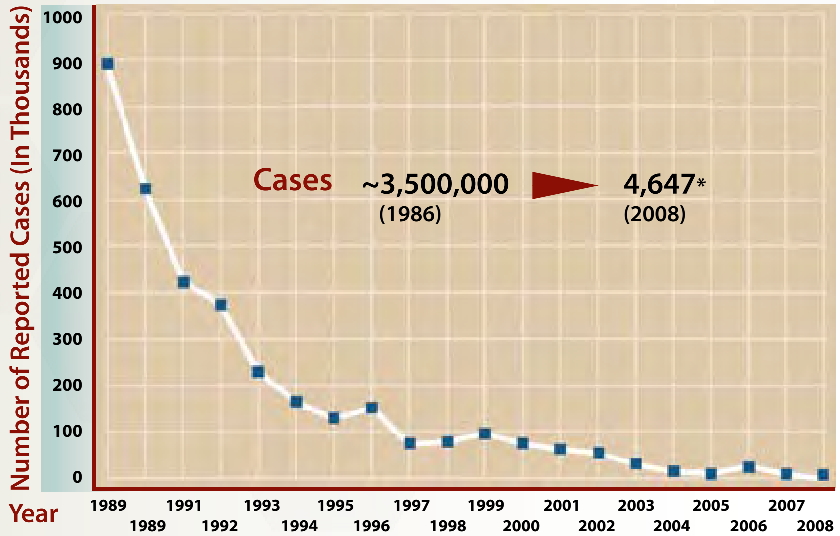
Several parasitic diseases --- diseases that epitomize interconnectedness of humans, animals, and the environment --- are ripe for eradication or elimination. For example, Guinea worm disease is contracted when a person drinks stagnant water that is contaminated with microscopic water fleas carrying infective larvae. Inside a person's body, the larvae grow for a year, becoming thin thread-like worms, up to 3-feet-long. These worms create agonizingly painful blisters in the skin, through which they slowly exit the body. People with emerging worms deposit millions of larvae when they walk in water --- eggs that infect water fleas that can then enter more people, perpetuating the cycle.

In 1986, when CDC began the campaign to eradicate Guinea worm disease, there were more than 3.5 million cases of the disease. Today, with the leadership of the Carter Center and participation of CDC and other partners, there are fewer than 10,000 cases in only five African countries—Sudan, Ghana, Nigeria, Niger, and Mali. Guinea worm is poised to be the next organism eradicated.

Other diseases that are also a high priority for eradication include lymphatic filariasis and, from the Americas, onchocerciasis. We believe that malaria can be eliminated from many parts of the world. Even in Africa, which is the continent most affected by malaria, remarkable success is being achieved by treating people who contract malaria, reducing transmission with bednets and insecticides, and preventive treatment of pregnant women. We believe that the goal of the President's Malaria Initiative of a 50% reduction in malaria deaths in at least 15 countries in Africa by 2010-11 can be achieved.

Number of Reported Cases of Guinea Worm, by Year, 1989 - 2008*

Since the start of the campaign to eradicate Guinea worm disease, we have made great progress. A concerted effort could eradicate this disease. Because people can only become infected by drinking contaminated water, educating people to follow simple control measures and either treating water with larvicides or providing new water sources can completely prevent illness from this disease and stop transmission.



*Data for 2008 are provisional, based on reports through November. The Carter Center, 2009

Expert services, tools, and knowledge

When a state laboratory, a private laboratory, or a laboratory in another country is having difficulty making a diagnosis, they can depend on the CDC for assistance. Assistance ranges from telediagnosis of parasitic diseases (laboratories send images over the internet and rapidly receive assistance) to identifying and characterizing unusual pathogens to specialized tests on biologic samples. CDC is the only source in the world of malaria parasites of many strains in all stages of their life cycle; these are critical for vaccine development. CDC also provides clinical management advice, which is especially important for diseases rarely seen by medical practitioners, and provides medicines to treat specific parasitic diseases.

An important need in outbreak investigations, especially those that extend across many states, is for investigators to choose approaches that are likely to yield valid results and use the same methods and tools for investigating the outbreak in different sites. CDC and its partners have achieved great success in standardizing laboratory methods for identification of pathogens; perhaps the best example of this is PulseNet, with the standardization allowing for comparisons of strains among PulseNet participants and the earlier and more comprehensive identification of multistate outbreaks. A similar standardization in epidemiologic methods and innovative ways of interviewing case patients and healthy controls would lead to quicker and faster identification, investigation, and control of outbreaks.

In addition, to continuing its reference laboratory work, CDC is committed to enhancing capacity among state and local laboratories and in clinical laboratories. Priorities in this framework include not only developing tests for new organisms, but increasing the numbers of tests that can be made available for routine use by other organizations.

CDC will also increase opportunities for training of partners. This will include the use of distance learning approaches. The integrated research and development centers will also provide opportunities for training of people in developing countries. Given the rapid increase in the number of biosafety level-4 (BSL4) laboratories, a high priority is to establish a BSL4 Center of Excellence, which can train people from throughout the world in safe, effective BSL4 techniques.

OUTCOMES FROM IMPLEMENTING THIS FRAMEWORK

We believe that implementing this framework is essential for preventing deaths and suffering from emerging infectious diseases. It will be an important contribution to achieving CDC's Health Protection Goals of Healthy People in Every Stage of Life, Healthy People in Healthy Places, People Prepared for Emerging Health Threats, and Healthy People in a Healthy World.

As a result of implementing this framework, NCZVED will contribute substantially to the following outcomes.

For individuals:

- Information that people can use to keep themselves and their families safer from microbial threats
- Security in knowing that their food and water will not make them sick from infectious organisms

For communities, local governments, and state governments

- Evidence-based guidance, data, and predictive modeling to help in developing policies and programs for prevention of infectious diseases
- Increased capacity to protect people from infectious diseases

For the United States

- Improved health through prevention and control of infectious diseases
- Fewer infectious diseases and outbreaks from domestically produced and imported foods and products, resulting in benefits for industry and consumers

For the world

- Improved health through prevention and control of infectious diseases
- Fewer disruptions in commerce as a result of infectious diseases
- Increased prosperity and political stability of countries through improved health status through improved health status of their populations

We look forward to working with our partners to usher in a new era in confronting infectious diseases.

NCZVED's
Strategic Framework

Vision

To improve health by reducing the impact of infectious diseases using a comprehensive and holistic approach focused on the human-animal-environment interface.

Infrastructure

- Quality leadership
- World-class workforce
- Well-equipped laboratories
- Commitment to innovation
- Healthy workplace
- Productive relationships
- Excellent stewardship of resources
- Transparent and pro-active communications
- Effective operational support
- Technology development
- Alignment with CDC goals and strategies

Our Values

Strong Partnerships • Excellent Science • Multidisciplinary Perspectives
Outstanding Strategies & Services • Effective Systems

Innovate

- Pathogen identification, characterization, and diagnostic test development
- Predictive modeling to guide planning and prevention
- Understanding the role of host factors

Integrate

- Integrated Research and Development Centers
- Integrating information to create action
- Genomic surveillance of pathogens

Impact

- Widespread implementation of interventions that work
- Eradication and elimination
- Expert services, tools, and knowledge

National Center for Zoonotic,
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