

# WORKING P A P E R

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## Improving Global Influenza Surveillance

### Strategies for the U.S. Government

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## PREFACE

Since 2003, the H5N1 avian influenza virus has been circulating in Asia and elsewhere leading to accelerated, intensified efforts by governments and international organizations to strengthen their public health systems to prepare for a possible human influenza pandemic arising from this virus, or another influenza virus strain. An important cornerstone of pandemic preparedness is the early detection of novel influenza viruses with pandemic potential. Such detection depends on effective public health surveillance, including laboratory diagnosis. U.S. (and global) preparedness is strengthened when surveillance systems in other countries are capable of detecting early cases of novel human influenza within their borders. Recognizing this, in September 2005, the Department of Health and Human Services (HHS) Office of the Assistant Secretary for Preparedness and Response (ASPR) asked the RAND Corporation to examine ways that HHS might strengthen its global influenza surveillance efforts. Subsequently, in May 2006, the U.S. government issued its comprehensive government-wide plan to prepare for the next influenza pandemic: the *National Strategy for Pandemic Influenza Implementation Plan*. This document lays out responsibilities for federal agency actions in the United States and internationally. One of the *Implementation Plan's* three pillars is Surveillance and Detection, which prominently focuses on international surveillance activities. The RAND study, conducted from October 2005 through November 2006, identifies strategies for improving global influenza surveillance and suggests practical steps that HHS might consider for implementing them. The study's systematic analytic approach also resulted in the development of an interactive tool that agencies can use to evaluate the effects of selected strategies.

Our report should be of direct and practical interest to HHS and other federal departments and to technical agencies in the United States and internationally that are responsible for pandemic influenza preparedness, in particular, and for public health preparedness more broadly. Our approach and the interactive tool should also be of interest to public administrators who routinely must determine strategies for a variety of public policy issues.

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## SUMMARY

Between December 2003 and November 2006, ten countries reported 258 confirmed human cases of illness caused by H5N1, a new strain of avian influenza. These H5N1 cases represent a clear warning that the world could face another human influenza pandemic if this virus—or another strain yet to emerge—mutates enough to pass easily from human to human. The stakes are high should an influenza pandemic materialize: In the United States alone, from 15 to 35 percent of the population could be affected, at an estimated cost of \$71 to \$167 billion.

The emergence of the H5N1 virus has led governments and international organizations to accelerate and intensify efforts to strengthen their public health systems to prepare for a possible human influenza pandemic. In May 2006, the U.S. government issued its comprehensive government-wide plan to prepare for the next influenza pandemic. This document, the *National Strategy for Pandemic Influenza Implementation Plan*, lays out responsibilities for federal agency actions in the United States and internationally. The *Implementation Plan* directs attention to the importance of international surveillance activities. To help address an important area of responsibility under the *Implementation Plan*, the Department of Health and Human Services (HHS) Office of the Assistant Secretary for Preparedness and Response (ASPR) asked the RAND Corporation to examine ways that HHS might strengthen its global influenza surveillance efforts. The RAND study team identified strategies for improving global influenza surveillance and suggested practical steps that HHS might consider for implementing them. The team also developed a prototype interactive tool that agencies can use to compare the relative merits of different strategies and thus potentially focus their program efforts.

### THE RAND STUDY

Key to pandemic preparedness is the early detection of novel influenza viruses with pandemic potential, especially those that are transmitted from person to person. Such detection depends on effective public health surveillance, including laboratory diagnosis. The earlier a novel virus strain against which humans have no natural immunity can be detected, the better the chances are that actions can be taken to limit the spread of the disease. Although disease surveillance is the responsibility of individual nations, the World Health Organization (WHO) is responsible for coordinating public health surveillance on a global level. Through its Member State status in the United Nations, and hence in WHO, the United States is part of this effort. HHS, mostly through the Centers for Disease Control and Prevention (CDC), has a lead role for human influenza surveillance, both domestically and as part of the global system coordinated by WHO.

From October 2005 through November 2006, a multi-disciplinary RAND team conducted a systematic examination of how to detect early cases of novel influenza illness. The overall aim of the study was to provide results that could be used to guide HHS policy and resource allocation to improve global influenza surveillance.

This study sought answers to four main policy questions:

- 1) *What strategies can HHS employ to improve global influenza surveillance, and how can these be implemented?*
- 2) *How can HHS quantitatively compare different strategies in order to select promising ones?*
- 3) *How can HHS identify strategic partners to extend global influenza surveillance?*
- 4) *How can HHS monitor its partnerships over time?*

In seeking answers to these questions, the RAND team examined surveillance in a much broader and more systematic way than has been done before, with particular interest in identifying new strategies unconstrained by traditional public health approaches. The orientation of this study is consistent with the CDC's new framework for evaluating surveillance systems aimed at early outbreak detection, although this framework is not specifically aimed at influenza surveillance.

## Conceptual Framework

Based on a review of the published literature related to public health surveillance systems and the *Implementation Plan*, as well as an iterative brainstorming process by the RAND study team to identify and then organize all important elements into a single logical structure, the team developed a conceptual framework suggesting a range of strategies and approaches to implementing them. The RAND team first synthesized surveillance system criteria recommended by CDC into four requirements, around which it could then identify specific surveillance improvement strategies:

- **Comprehensive surveillance coverage:** This encompasses a broad range of sources and signals for surveillance information.
- **High quality surveillance:** This requires accurate information based on standards, trained personnel, and quality-assured laboratory testing.
- **Timeliness:** This includes rapid data flow, analysis, and dissemination to trigger a timely investigation and response to limit or delay disease spread.
- **Transparency:** This necessitates open reporting and sharing of animal and human virus samples and virus genome information for purposes of global tracking and vaccine development.

Around these four requirements, the RAND team identified 16 strategies to improve surveillance: five strategies aimed at improving coverage; four strategies aimed at quality; six strategies aimed at timeliness; and a final strategy aimed at transparency. These strategies range from using new sources of disease information (e.g., the community, the electronic media, non-governmental organizations) to seeking new surveillance signals (e.g., disease events among persons who do not or cannot seek clinical services).

The RAND team then identified two major approaches to implementation: (1) direct actions that HHS can take itself and (2) leveraging strategic partners. The final conceptual framework ties together the improvement strategies and the approaches to their implementation by suggesting specific strategies that could be put into practice by HHS and by various illustrative partners (see Table S.1).



## **Process Model and Interactive Tool to Help Identify Promising Strategies**

The RAND team sought a way to show how surveillance improvement strategies from the conceptual framework can be evaluated for effectiveness and how this evaluation could be used for planning purposes. In doing so, the team identified nine paths that can lead to case detection, and used them to build a process model that traces the steps involved in going from a sick individual to laboratory confirmation of a novel influenza strain. In each path, information is passed from step to step covering actions by the sick individual, reports, investigations, and tests. These steps are complex with many uncertainties, all of which can block or slow the ultimate confirmation of a novel strain of influenza virus. In the process model, each step is described in terms of probabilities and delays. Probabilities reflect that each step in the model is a possible point of failure where the flow of information regarding a sick patient may terminate: a report is not filed, an investigation is not conducted, or a viral sample is not sent for further testing. Delays are associated with the time until a step occurs (e.g., a report may only be filed once a week) or the time needed to perform a task.

Starting with the process model and incorporating 12 of the 16 strategies for improving surveillance (those that directly influence the probabilities and/or delays associated with capturing and passing along information within a country), the RAND team developed an interactive tool that allows users to evaluate the effects of different strategies or combinations of strategies on improving influenza surveillance in terms of probability and timeliness of case detection. The goal of the process model and interactive tool is to help find ways to improve the chances that a case of disease caused by a novel influenza strain will be detected and ultimately confirmed by a reference laboratory, and to reduce the time it takes to do so. HHS can use this tool to select promising strategies and thus target its resources efficiently.

## **Strategic Partnerships to Extend Global Influenza Surveillance**

The RAND study identified the formation of strategic partnerships—with other U.S. government agencies, international organizations, foreign laboratory networks, foreign development agencies, and a range of nongovernmental organizations—as a key approach to improving global surveillance. Through strategic partnerships, HHS can extend its reach, potentially at little or no additional cost, and thus optimally direct its own resources while leveraging partners to help produce even greater improvements in surveillance globally.

The team analyzed the presence of a number of government agencies and nongovernmental organizations in more than 200 countries around the world, identifying agencies and organizations whose mandates, expertise, and mutual interests might lend themselves to potential partnership with HHS and/or other U.S. government agencies. These analyses included examples of practical applications of the information to identify potential partners to help address specific aspects of influenza surveillance in specific countries.

The team then suggested a possible approach to measuring relationships across a network of surveillance partners through an analytical approach called network analysis. The fundamental property of network analysis is the ability to measure the degree of interaction among organizations. As potentially applied to global influenza surveillance, this approach could quantify interactions among specific organizations related to coverage, quality, timeliness and transparency. Monitoring these over time helps identify both progress that has been made and gaps that should be addressed. Quantitative assessment of partnerships is a dimension that is not captured in traditional public health program monitoring and evaluation, but it is beginning to gain recognition in the public health community.

## **RECOMMENDATIONS**

The RAND study led to the following recommendations for improving global influenza surveillance:

1. Consider the different strategies proposed in terms of anticipated improvements in the probability and timeliness of case detection. The interactive tool developed by RAND may be one way to assess the relative merits of different strategies and select promising ones.
2. Pursue strategic partnerships that will complement HHS' own technical expertise and extend its reach within and across countries worldwide to improve influenza surveillance.
3. Plan to measure over time the strength of surveillance partnerships with an appropriate assessment method, such as network analysis.



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## ACRONYMS

<b>Acronym</b>	<b>Definition</b>
AFRIMS	Air Force Research Institute for Medical Sciences
AKHS	Aga Khan Health Services
APEC	Asia Pacific Economic Cooperation
APHL	Association of Public Health Laboratories
ASEAN	Association of Southeast Asian Nations
ASPH	Association of Schools of Public Health
AusAID	Australian Agency for International Development
CDC	Centers for Disease Control and Prevention
CIDA	Canadian International Development Agency
CNRL	Community Network of Reference Laboratories
CSTE	Council of State and Territorial Epidemiologists
DFID	Department for International Development
DoD-GEIS	Department of Defense Global Emerging Infections Surveillance and Response System
EIP	Emerging Infections Program
EIS	Epidemic Intelligence Service
EISS	European Influenza Surveillance Scheme
FAO	Food and Agriculture Organization of the United Nations
FAS	Foreign Agricultural Service
FETP	Field Epidemiology Training Programs
G-8	Group of Eight
GAO	Government Accountability Office
GAORN	Global Outbreak Alert and Response Network
GPHIN	Global Public Health Intelligence Network
GTZ	Deutsche Gesellschaft für Technische Zusammenarbeit
HHS	Health and Human Services
ICRC	International Committee of the Red Cross
IEIP	International Emerging Infections Programs
IHR	International Health Regulations
ILI	Influenza-like illness
IMC	International Medical Corps
JICA	Japan International Cooperation Agency
MSF	Médecins Sans Frontières
NAMRU-2	Naval Medical Research Unit-2

NAMRU-3	Naval Medical Research Unit-3
NBIS	National Biosurveillance Integration System
NGO	Nongovernmental organizations
NMRCDC	Naval Medical Research Center Detachment
NNDSS	National Notifiable Disease Surveillance System
NREVSS	National Respiratory and Enteric Virus Surveillance System
NSPI	National Strategy for Pandemic Influenza
NVSL	National Veterinary Service Laboratories
NVSN	New Vaccine Surveillance Network
OIE	Office International des Epizooties
PCMO	Peace Corps Medical Officer
PICNet	Pacific Regional Infection Control Network
PPHSN	Pacific Public Health Surveillance Network
SARS	Severe Acute Respiratory Syndrome
SIDA	Swedish International Development Cooperation Agency
SPC	Secretariat of Pacific Community
TEPHINET	Training Programs in Epidemiology and Public Health Interventions Network
UN	United Nations
USAID	U.S. Agency for International Development
USAMRU	U.S. Army Medical Research Unit
USDA	U.S. Department of Agriculture
WHO	World Health Organization
WHO CC	WHO Collaborating Centre
WHO NIC	WHO National Influenza Centre

## 1. INTRODUCTION

For the first time in history mankind has received ample warning to prepare for the possibility of the next human influenza pandemic. Unlike previous influenza pandemics in 1918, 1957, and 1968 that came with no warning, the discovery of a new strain of avian influenza that has also infected humans should serve as a catalyst to improve preparation, detection, and response to a potential influenza pandemic. Given that the pandemic of 1918 killed an estimated 40 million people in less than one year (WHO, 2005a), the pandemic of 1957 killed an estimated 2 million people, and the pandemic of 1968 killed an estimated 1 million people (WHO, 2005b), the stakes are high. In 2005, the Director of the General Accountability Office's Health Care division estimated that "from 15 to 35 percent of the U.S. population could be affected by an influenza pandemic" (Crosse, 2005), and the Centers for Disease Control and Prevention (CDC) estimated that associated costs would range from \$71 billion to \$167 billion (CDC, 2005).

The most recent concern regarding a potential influenza pandemic comes from the H5N1 avian influenza virus. As of November 29, 2006, ten countries had reported 258 confirmed human cases of H5N1 illness since 2003: Azerbaijan, Cambodia, China, Djibouti, Egypt, Indonesia, Iraq, Thailand, Turkey, and Viet Nam. Of these cases, 154 people died (WHO, 2006b). Furthermore, millions of birds have died from the virus or as a result of disease control efforts (OIE, 2006). While there is uncertainty about the possibility that the H5N1 virus will give rise to a human pandemic, most infectious disease experts agree that if the virus mutates so that it can be passed easily from human to human in sustained fashion, it could cause a devastating pandemic. In fact, more than half of the laboratory-confirmed H5N1 cases in humans have been fatal (WHO, 2006a). The question that looms large is whether the virus will mutate enough to enable it to cause sustainable human-to-human transmission.

Due to the potential for the H5N1 virus to cause a human pandemic, the U.S. government and international institutions have turned their attention to pandemic preparedness. In November 2005, the White House released the *National Strategy for Pandemic Influenza* (NSPI) (Homeland Security Council, 2005), and the Department of Health and Human Services released its *HHS Pandemic Influenza Plan* (HHS, 2005). In May 2006, the White House's Homeland Security Council released the *NSPI Implementation Plan* (Homeland Security Council, 2006). At the international level, the World Health Organization issued its *Global Influenza Preparedness Plan* in March 2005 (WHO, 2005a).

Disease surveillance has traditionally been the cornerstone of the public health detection and response to emerging diseases. Surveillance is particularly important when dealing with a novel virus like H5N1, for which humans have no natural immunity. The earlier a case of a novel virus strain can be detected, the better the chances are that precautions can be taken to limit the spread of the virus.

## THE RAND STUDY

In its review of a very early version on the HHS Pandemic Influenza Plan, RAND noted that many of the surveillance efforts did not seem as well integrated or robust as they could be. It also highlighted the need to further internationalize the plan, and pointed to the crucial role of global surveillance in delaying or possibly preventing a pandemic. As a result, HHS asked RAND to identify current global surveillance activities, examine their interrelationships, and propose additional steps that might be taken to strengthen global surveillance efforts by building on current activities.

The purpose of this study is to provide systematic analyses that could be used to guide HHS policy and resource allocation to improve international influenza surveillance.

This study is guided by four main policy questions:

- 1) What strategies can HHS employ to improve global influenza surveillance, and how can these be implemented?
- 2) How can HHS quantitatively compare different surveillance strategies in order to select promising ones?
- 3) How can HHS identify strategic partners to extend global influenza surveillance?
- 4) How can HHS monitor its partnerships over time?

This report addresses each of the questions above and is organized as follows:

- Chapter Two presents the relevant background on traditional public health surveillance as well as the rationale for our departure from a purely traditional approach.
- Chapter Three presents the conceptual framework that we developed to identify strategies to improve global influenza surveillance and approaches to implement them.
- Chapter Four presents the process model we developed to show how surveillance improvement strategies from the conceptual framework can be evaluated for effectiveness. The process model is the basis for an interactive tool that can be used to help select promising strategies that increase the probability and timeliness of detecting a case caused by a novel influenza strain.
- Chapter Five describes a number of agencies and organizations that could be considered for potential partnerships with HHS, presents maps depicting their current global programming, and analyzes opportunities for HHS.
- Chapter Six describes an approach to measuring relationships across a network of surveillance partners.
- Chapter Seven presents our conclusions and recommendations, including how our conceptual framework for improvement strategies, our process model and interactive tool for quantitatively comparing strategies, and our ideas regarding strategic partnerships can be of practical use to HHS decision makers to inform policy and guide resource allocations.

## 2. BACKGROUND

In this chapter, we set the stage for our examination of global influenza surveillance and how the Department of Health and Human Services (HHS) might frame its program policies and direct new resources to improve such surveillance. We begin with a brief description of traditional public health surveillance followed by a summary of how influenza surveillance is currently conducted in the United States and globally through the World Health Organization (WHO). We conclude with a description of how we approached our examination of opportunities for HHS to improve influenza surveillance in other countries.

### TRADITIONAL PUBLIC HEALTH SURVEILLANCE

Public health surveillance is defined as “the ongoing, systematic collection, analysis, interpretation, and dissemination of data about a health-related event for use in public health action to reduce morbidity and mortality and to improve health” (CDC, 2001). More simply stated, it is information for action. Surveillance answers the questions: “What is the problem, and where, when, and in whom is it occurring?” which is the first step in the classic four-step public health approach to address public health problems that begins with problem identification and ends with effective response.

Public health surveillance originally targeted communicable diseases but in recent decades has been expanded to include noncommunicable diseases, injuries, and behavioral risk factors, among others. As described by CDC, public health surveillance serves several important functions: estimate the magnitude of a problem, determine its distribution and spread, portray its natural history, detect excess occurrences (epidemics, in the case of communicable diseases), generate hypotheses, support public health interventions, evaluate control measures, detect changes in public health practice, and facilitate planning (CDC, 2006a).

A few key definitions and descriptions relevant to public health surveillance are important. For simplicity, we discuss these within the context of U.S. surveillance, but the principles also apply internationally.

*Passive surveillance* is the most common form of surveillance, in which CDC receives from U.S. state health departments standardized reports of clinical cases and/or laboratory test results for selected diseases and conditions. Virtually all routine communicable disease surveillance relies on passive data reporting. Passive surveillance is generally less costly and less burdensome than active surveillance (see below). However, because of such limitations as non-reporting or under-reporting, passive surveillance can easily miss timely detection and notification of disease outbreaks, and it can have an impact on the representativeness of the data collected.

*Active surveillance* involves outreach, for example, by health officials to laboratories, hospitals, and health care providers, in order to collect disease data. Active surveillance systems are intended to provide timely and

comprehensive detection and notification but are generally more resource intensive than passive data collection systems.

*Sentinel surveillance* is the monitoring of events through a selected subset of all sites, events, or providers. For example, CDC's domestic influenza surveillance program includes reports of disease from approximately 2,200 sentinel providers. Sentinel surveillance is appropriate for monitoring trends across people, place, and time. Inherent to its design, it does not include reporting of all cases of a disease and therefore may miss rare or early events.

*Notifiable disease surveillance* refers to mandatory reporting of all cases of specified communicable diseases. According to CDC, "A notifiable disease is one for which regular, frequent, and timely information regarding individual cases is considered necessary for the prevention and control of the disease" (CDC, 2006b). CDC's National Notifiable Disease Surveillance System (NNDSS) now includes approximately 60 reportable diseases. Reporting requirements vary by U.S. state; however, most state requirements are similar to a national list of notifiable diseases updated periodically by the Council of State and Territorial Epidemiologists (CSTE) in conjunction with CDC. State and local health departments require health care providers to report cases of notifiable diseases and then are responsible for conducting initial investigations into those reports. State public health departments then report those findings to CDC for aggregation to help monitor national trends. Of note, the only influenza cases included in the NNDSS are laboratory-confirmed pediatric hospital deaths.

*Syndromic surveillance* is a somewhat newer approach to public health surveillance. These systems "gather data on patient symptoms looking for anomalous increases in the frequency of these symptoms that may indicate the presence of an infectious disease outbreak" (GAO, 2004). An example of syndromic surveillance is the reporting of "influenza-like illness" (ILI). In this case, CDC collects information on outpatients meeting its case definition (fever > 100 °F AND cough or sore throat) from its sentinel provider network on a passive reporting basis. Another approach to syndromic surveillance uses data-mining techniques to review clinical data usually on a daily or near real-time basis, and applies mathematically defined algorithms to detect "signals" of excess occurrence of "syndromes" such as fever and rash, respiratory disease, or febrile diarrheal disease. Data mining, therefore, represents another approach to active surveillance. However, syndromic systems have not yet been thoroughly evaluated for their utility and effectiveness within an overall surveillance system (GAO, 2004; Crosse, 2005).

A growing body of literature exists on how to evaluate individual surveillance systems, and CDC has recently updated its guidelines for such evaluations (CDC, 2001). While our study does not rigorously evaluate individual surveillance systems, we have collapsed the metrics recommended by CDC into a smaller number of characteristics that can be examined within a larger systems model to help identify gaps and opportunities related to influenza surveillance in individual countries. These characteristics, which become our requirements for achieving the surveillance goals described in Chapter 3, include:

- 1) coverage (including geographic representativeness and completeness);
- 2) quality (including accuracy, sensitivity, specificity and predictive value positive);
- 3) timeliness; and
- 4) transparency (open reporting).

Surveillance systems will vary according to both purpose and implementation, such that the importance of these characteristics vary, for example, by disease or epidemiologic context. Some systems may be best suited to emphasize certain characteristics, and certain characteristics might be emphasized during different phases of an outbreak or pandemic. Our study considers different global surveillance strategies along these lines and how they might be used to improve global influenza surveillance, particularly before a pandemic strikes, when the priority is early detection of cases caused by a novel influenza virus, wherever and whenever they may arise.

## INFLUENZA SURVEILLANCE

### Domestic Surveillance

As noted above, U.S. states have primary responsibility to protect public health through state and local health departments and, as a result, states also take primary responsibility for conducting influenza and other disease surveillance. CDC coordinates domestic influenza surveillance, which includes seven complementary components:

- 1) *WHO collaborating laboratories and National Respiratory and Enteric Virus Surveillance System (NREVSS) Collaborating Laboratories* – About 125 laboratories around the country report, weekly, the number of respiratory specimens tested and number positive for influenza A and B (some also include virus subtyping, e.g., H1N1 or H3N2);
- 2) *U.S. Influenza Sentinel Providers Surveillance Network* – Approximately 2,200 healthcare providers have been designated as sentinel providers by their state health department to report total outpatients seen and total with ILI, by age group, with results weighted by population and compared to baseline thresholds of prevalence by month;
- 3) *122 Cities Mortality Reporting System* – Total and pneumonia/influenza deaths are reported weekly from selected cities and again compared to threshold values;
- 4) *State and Territorial Epidemiologists Reports* – All state and territorial epidemiologists report weekly on the degree of influenza activity in their respective jurisdictions (five categories: no activity, sporadic, local, regional, or widespread)
- 5) *Influenza-Associated Pediatric Mortality* – This includes laboratory-confirmed pediatric influenza deaths. (Note: Added in 2004, this is the only influenza indicator within CDC's NNDSS.)

- 6) *Emerging Infections Program* – Laboratory-confirmed influenza hospitalizations in children under age 18 in 11 metropolitan areas of 10 states.
- 7) *New Vaccine Surveillance Network (NVSN)* – Population-based laboratory-confirmed influenza hospitalizations among children under age 5 in three counties in New York, Ohio, and Tennessee.

Thus, U.S. influenza surveillance is based on a composite picture drawn from several sources of information. Because nearly all information is based on sampling rather than exhaustive reporting, the data represent trends in person, place, and time, and can help detect outbreaks (ILI or pneumonia/influenza deaths) by virtue of exceeding established threshold values. Domestic influenza surveillance is not designed to detect the earliest cases of influenza wherever they may occur. For seasonal influenza, this is appropriate; for early detection of human cases of a novel influenza virus such as H5N1, more-sensitive methods are required.

In addition to the CDC's surveillance of human influenza, the U.S. Department of Agriculture is responsible for monitoring the status of influenza among animals. As in the case of surveillance of human disease, both animal deaths and laboratory-based surveillance are used to monitor influenza among animals. This role seems particularly important as concern grows over the possibility of H5N1 moving from birds to humans.

## **Global Surveillance**

While disease surveillance is the responsibility of individual nations, the WHO is responsible for coordinating global public health surveillance. WHO's main influenza surveillance activity is its Global Influenza Surveillance Network, which was established in 1952 and now comprises 116 National Influenza Centers located in 87 countries (WHO, 2006). Four WHO Collaborating Centers located in the United States (at CDC), Australia, Japan, and the United Kingdom have the ability to perform more specific genetic analysis on all influenza specimens. Four additional laboratories in France, Hong Kong (two laboratories), and the United States have been designated as influenza A/H5 reference laboratories, which means that they can perform all official reference laboratory functions specifically for the H5N1 virus (but not for the full range of influenza viruses). These collaborating centers and reference laboratories also provide test reagents and proficiency testing for WHO's global laboratory network.

WHO is also responsible for administering the International Health Regulations (IHR), which have recently been amended to require countries to notify WHO of any "public health emergency of international concern" (PHEIC) that may constitute a public health risk to other countries and may require a coordinated international response (WHO, 2005). Over the years, all U.S. states have reported to CDC cases of internationally quarantinable diseases as defined in the IHR (which included only plague, yellow fever, and cholera until May 2005 when the IHR were revised to include a longer list of diseases as well as an algorithm to help determine if an event due to an existing or previously unrecognized cause rises to the level of

PHEIC); presumably, U.S. states will continue to report the new broader range of PHEIC, which is the new standard for international notification to WHO. Once the revised IHR take full effect (adoption of measures specifically relevant to influenza was accelerated from 2007 to 2006 because of concerns about influenza H5N1), countries that are WHO Member States will be required to directly notify WHO within 24 hours of any case of the following four diseases: smallpox; poliomyelitis due to naturally occurring (wild-type) virus; human influenza caused by a new subtype; and severe acute respiratory syndrome (SARS).

For animal surveillance at the international level, the World Organization for Animal Health (OIE, Office International des Epizooties) is charged with improving the transparency, efficiency, and speed with which animal health information is disseminated to WHO Member States. In May 2004, OIE member countries approved the creation of a list of diseases notifiable to the OIE. A revised list that includes highly pathogenic avian influenza was approved in May 2005 by the OIE International Committee and came into force in 2006 (OIE, 2006). In addition to WHO, the OIE works closely with other international organizations such as the Food and Agriculture Organization of the United Nations (FAO).

**U.S. role in global surveillance.** The government-wide *National Strategy for Pandemic Influenza* (NSPI) released in November 2005 and the more-detailed NSPI *Implementation Plan* released in May 2006 provide a clear mandate for international engagement related to influenza, and HHS (mostly through CDC) has a lead role for human influenza surveillance.

Through its Member State status in the United Nations, and hence in WHO, the United States is part of the global cooperative surveillance effort for influenza as well as for a broad range of other global health cooperative efforts. The United States is home to a substantial number of WHO Collaborating Centers, which address a wide range of health issues; about two-thirds of those Centers reside within CDC, including one of the four full-service WHO reference laboratories for influenza. In addition, HHS (mostly through CDC) has posted staff members – influenza technical experts – at WHO offices around the world, including at WHO headquarters in Geneva and at some of the WHO regional offices. Thus, HHS provides significant technical support to the global influenza surveillance system coordinated by WHO, as well as to numerous other WHO surveillance and broader global health initiatives.

## BEYOND TRADITIONAL SURVEILLANCE

We were particularly interested in identifying opportunities for HHS to improve its global influenza surveillance activities unconstrained by the traditional approaches, which typically focus on passive reporting of clinical and laboratory information from selected sites. Instead, we sought to approach surveillance in a much broader and more systematic way.

The orientation of our study is consistent with the CDC's new framework for evaluating surveillance aimed at early outbreak detection (CDC, 2004). The CDC is already exploring opportunities for improving U.S. influenza surveillance such as enhanced reporting from clinical sites (including emergency departments, 911 calls, and others); monitoring of proxy data such as pharmaceutical sales, patient encounters, or

laboratory orders; novel data sources (retail sales, veterinary encounters, environmental indicators, absenteeism); and new signal detection methods.

For our study, the RAND team considered potential new sources of information (e.g., the community, the electronic media, nongovernmental organizations), new surveillance signals (e.g., disease events among persons who do not or cannot seek clinical services), and new ways to capture information. We considered such new surveillance strategies alongside more traditional strategies to help identify influenza cases and outbreaks with greater accuracy and timeliness. We also examined ways that HHS could leverage a broader network of actual or potential partners and thus extend its programming reach. The RAND team used new approaches to systematically examine a range of strategies and partnership opportunities that HHS might employ to improve global influenza surveillance. The results are aimed to help HHS target its resources toward promising surveillance activities and strategic partnerships.

### 3. CONCEPTUAL FRAMEWORK

With the current threat of a human influenza pandemic arising from the H5N1 avian influenza virus or another novel strain that may yet emerge, HHS wishes to consider specific strategies to improve its own efforts in global influenza surveillance. The initial step to improving surveillance is taken in this chapter, which addresses our study's first policy question: *What strategies can HHS employ to improve global influenza surveillance, and how can these be implemented?* Here we lay out the architecture for a conceptual framework that describes global influenza surveillance goals and requirements, strategies, and approaches for their implementation.

#### RAND METHODOLOGY

The RAND team approached development of a conceptual framework to guide improvements in global influenza surveillance from several directions. The team first reviewed published literature, particularly published CDC guidance, to glean criteria for evaluating public health surveillance systems and to serve as the basis for a simplified framework representing a core set of surveillance requirements. The team then brainstormed iteratively over several weeks to identify a broad range of reasonable improvement strategies to meet these core requirements. Lastly, the team reviewed the NSPI *Implementation Plan*, with particular attention to the responsibilities of HHS and others related to international surveillance, to identify any surveillance responsibilities not captured through the brainstorming exercise. Based on these reviews and discussions, as well as an iterative process to organize all important elements into a single logical structure, the team developed the conceptual framework described in this chapter.

#### BUILDING THE CONCEPTUAL FRAMEWORK

##### Surveillance Goals

Early detection of influenza cases, especially those resulting from human-to-human transmission, is critical to trigger prompt and effective response to the occurrence of disease caused by a novel influenza virus, including investigation and containment efforts. A delay of just one week can mean two additional generations of disease transmission, i.e., two additional doubling times (based on the commonly used transmission index,  $R_0$ , of approximately 2 and an incubation period of 2-3 days).

The goals of our conceptual framework to guide improvements in global influenza surveillance during the pre-pandemic period are to:

- detect the earliest cases of a novel influenza virus, especially those transmitted from person to person
- limit or delay the spread of disease

## Surveillance Requirements

Surveillance that successfully meets the goals of early detection of cases and use of information to limit or delay disease spread requires optimal achievement. We synthesized surveillance system criteria recommended by CDC into the following four areas, or requirements, around which we could then identify specific surveillance improvement strategies:

- **Comprehensive surveillance coverage:** This encompasses a broad range of sources and signals for surveillance information. Surveillance sources traditionally include selected clinical facilities and providers. Surveillance signals are generally those that arise from such sources as influenza-like illness (ILI), laboratory-confirmed cases, and deaths due to compatible illness or laboratory-confirmed disease.
- **High quality surveillance:** This requires accurate information based on standards, trained personnel, and quality-assured laboratory testing.
- **Timeliness:** This includes rapid data flow, analysis, and dissemination to trigger a timely investigation and response to limit or delay disease spread.
- **Transparency:** This necessitates open reporting and sharing of animal and human virus samples and virus genome information for purposes of global tracking and vaccine development.

## Improvement Strategies

The next step in developing our conceptual framework was elaboration of specific improvement strategies to address each of the four surveillance requirements described above. There is no pre-set minimum or maximum number of strategies to address a given requirement. As described in the methodology section, the RAND team first took an independent systematic approach to considering possible tactical strategies. We then consulted the NSPI *Implementation Plan* to make sure that all surveillance-related responsibilities assigned to federal agencies, especially to HHS, were accounted for in our final proposed list of 16 strategies. These strategies are compiled in Table 3.1, organized under the four surveillance requirements of coverage, quality, timeliness, and transparency. Detailed descriptions of each strategy then follow.

These strategies can and should be combined to offer the most robust improvements in surveillance. Chapter Four describes our process model and associated interactive tool that can be used to quantitatively compare the impact of different strategies and combinations of strategies in terms of improving the probability and timeliness of detection of the earliest cases of disease due to a novel influenza virus.

**Table 3.1**  
**Sixteen Strategies to Meet Global Surveillance Requirements**

<b>COVERAGE: Seek international cooperation and comprehensive surveillance</b>
(1) Work in or with more countries
(2) Increase the number/density of traditional reporting sources
(3) Develop village-based/community-based alert and response systems
(4) Consider new human disease information sources and signals
(5) Increase reporting compliance
<b>QUALITY: Build capacity for accurate, actionable information</b>
(6) Improve human laboratory sample preparation and diagnostic capacity
(7) Implement targeted laboratory testing appropriate to the pandemic phase and location
(8) Monitor viral strains for changes
(9) Improve epidemiologic capacity
<b>TIMELINESS: Ensure rapid case detection and reporting</b>
(10) Support development of early warning networks, including the use of data mining methods
(11) Expand expedited transport of specimens to in-country and international reference laboratories
(12) Streamline notification, analysis, and reporting
(13) Implement active surveillance when appropriate
(14) Develop and deploy rapid laboratory diagnostics with greater sensitivity and reproducibility
(15) Develop and deploy in-country and U.S. rapid response teams to investigate cases/outbreaks
<b>TRANSPARENCY: Ensure open reporting and sharing of virus samples</b>
(16) Facilitate incentives to motivate reporting and sharing of virus strains and genome sequencing information

### Strategies to Improve Coverage

Strategies to improve surveillance coverage seek more comprehensive coverage through traditional as well as innovative approaches.

- 1) **Work in or with more countries.** The first strategy to increase global influenza surveillance coverage is to work directly in, or with, more countries worldwide. While HHS or the U.S. government more broadly cannot necessarily support surveillance improvement efforts in all countries, they can identify (and have done so) priority countries for initial programming investments. Complementary to this planning is examination of all countries worldwide and determination of the next tiers of priority countries and the most efficient or strategic mechanism/s for enhancing surveillance in those countries as well. This is important, since the site where a novel influenza virus may next appear is not entirely predictable.

- 2) **Increase the number/density of traditional reporting sources.** Traditional public health surveillance generally depends on voluntary reporting of specified diseases by selected clinical practitioners and health facilities to government public health authorities. Countries may also have a list of “nationally notifiable diseases,” for which reporting of all cases is, in principle, mandatory from all practitioners and laboratories. In the United States, Canada, and Korea, for example, there are approximately 65 nationally notifiable communicable diseases. While human influenza is a notifiable disease in some countries, e.g., Australia, Canada, and Korea, reporting of all cases is not necessarily required in all countries. For example, in the United States, the only nationally notifiable influenza cases are laboratory-confirmed pediatric influenza deaths – a very small proportion of all influenza cases in the country; and this requirement was added quite recently (in 2004). At the global level and until the revised International Health Regulations take full effect in 2007, the only three notifiable diseases worldwide are cholera, plague, and yellow fever. Most influenza surveillance worldwide is based on voluntary reporting from selected sources (practitioners and facilities). One strategy to improve surveillance coverage is to increase the number of traditional reporting sources, thus increasing the percentage of the population reflected through surveillance.
- 3) **Develop village-based/community-based alert and response systems.** A person who becomes ill with a novel influenza virus may or may not seek medical attention. Hence, even the best traditional public health surveillance system, which depends principally on reporting from selected clinical care sites or laboratories, will not reliably detect the earliest influenza cases wherever they may arise. Therefore, another strategy to increase influenza surveillance coverage is to develop community-based alert and response systems. The NSPI *Implementation Plan* refers to these as “village alert systems”. Such systems would have the advantage of greatly increasing coverage for information related to clinical illness compatible with influenza, including community-level outbreaks that may not otherwise reach government attention.
- 4) **Consider new human disease information sources and signals.** Reporting by health providers or the community of clinical disease may result in gaps in coverage. Therefore, another strategy to improve surveillance coverage is to incorporate reporting from new sources (sites, settings, people) and of new signals, i.e., new types of information that may reflect influenza. Examples of new sources could include workplaces (local businesses, multinational corporations), schools, local media, and web logs; examples of new signals include work or school absenteeism, rumors of compatible cases or outbreaks, or local reports of surge in hospital demand. When taken together with traditional and community-based surveillance, these new sources and signals could contribute to increased coverage and provide a more comprehensive and complete picture of disease occurrence in the area.

- 5) **Increase reporting compliance.** Increasing the number of traditional reporting sources and adding new ones is an important first step to increase surveillance coverage. The second step is to better assure the regular voluntary reporting of cases by these sources (doctors, hospitals, communities, etc.) Both the United States and Korea offer examples in which voluntary or mandatory reporting by clinical providers is irregular and incomplete. Therefore, an explicit strategy to increase reporting compliance is important to further increase surveillance coverage.

### Strategies to Improve Quality

Appropriate public health response requires accurate information about disease occurrence. Nonspecific clinical or community-based information must be complemented by information of sufficient quality, including standardized clinical reporting, accurate laboratory testing, and competent epidemiologic analysis and investigation.

- 6) **Improve human laboratory sample preparation and diagnostic capacity.** Laboratory diagnosis is the cornerstone of specific information on the occurrence of influenza disease and an important element of surveillance quality. Therefore, one strategy to improve influenza surveillance quality is to improve laboratory diagnostic capacity within countries. This involves physical and human infrastructure – laboratory space, equipment and supplies, adequately trained personnel, and laboratory quality assurance. This will allow for detection and confirmation of novel influenza viruses from suspected cases. This strategy involves development (and ideally, widespread deployment) of standard laboratory protocols and training and regular proficiency testing of personnel. Expanded in-country laboratory capacity also contributes to more comprehensive surveillance coverage and timeliness.
- 7) **Implement targeted laboratory testing appropriate to the pandemic phase and location.** Detection of novel influenza viruses during both the pre-pandemic and pandemic periods requires accurate laboratory testing. However, with scarce laboratory resources in some countries and the potential for laboratories to be overwhelmed by excessive demand for testing, an important strategy to improve surveillance quality is targeted laboratory testing that is appropriate to the pandemic phase and location. For example, criteria for appropriate testing during the pre-pandemic period can include clinically compatible cases with specified epidemiologic risk factors. During the pandemic phase, virus strains must still be monitored for possible changes that may carry implications for modification of medical or public health interventions. Because the surveillance goal during a pandemic is monitoring strains for change rather than detecting the earliest cases wherever they may occur, criteria for testing during a pandemic will necessarily evolve. This report does not espouse specific criteria for either period or for specific locations but rather, it points out the importance of

developing criteria for appropriate testing as a specific tactical strategy to improve surveillance quality.

- 8) **Monitor viral strains for changes.** The quality of influenza surveillance, both pre-pandemic and during a pandemic, will depend on monitoring of virus strains to track mutations/changes of potential significance. Major or minor strain changes could have implications for disease transmission or severity, or for the effectiveness of a pandemic vaccine or antiviral drugs. Therefore, an important strategy contributing to surveillance quality is the ongoing monitoring of influenza virus strains. Moreover, an increase in the number of laboratories capable of such monitoring will contribute to global surge capacity during periods when the demand for timely laboratory diagnosis and confirmation may overwhelm the number of laboratories currently performing such tests.
- 9) **Improve epidemiologic capacity.** Public health surveillance involves data collection, analysis, dissemination, and action. Epidemiologists are a cornerstone of the public health workforce and central to disease surveillance. Therefore, another important strategy to improve surveillance quality is to improve in-country epidemiologic capacity through training in surveillance and applied epidemiology, including disease outbreak investigation. Since the early 1980s, the United States, through the CDC, has exported its own domestic Epidemic Intelligence Service training program to other countries through what are now known as Field Epidemiology Training Programs (FETP; these are also known as Field Epidemiology and Laboratory Training Programs, FELTP). Epidemiology training includes both long-term programs such as FELTP, which are generally based on two years of on-the-job apprenticeship training, and shorter courses in applied epidemiology, with appropriate certification. Continuous field practice under qualified mentorship is critical to the development and maintenance of epidemiologic capacity.

### Strategies to Improve Timeliness

Especially during the pre-pandemic period, the timeliness of influenza surveillance is critical. This means the shortest possible time between the occurrence of a disease event and the notification of (or discovery by) relevant authorities.

- 10) **Support development of early warning networks, including the use of data mining methods.** Data mining is a relatively new approach to the collection and analysis of information. It depends on systematic searches of available information in electronic format and powerful computer processing to help discern “signal” from “noise” in terms of desired information. Thus, data mining can include, but is not entirely dependent on, official government reports. Data mining has only recently been applied to public health surveillance: Health Canada developed the Global Public Health Intelligence Network (GPHIN) as a tool for the World Health Organization to identify and then verify suspected outbreaks of infectious disease worldwide. GPHIN employs data mining (so-called

“web-crawling”) techniques to systematically scour the electronic news media in a broad range of languages worldwide for reports of disease occurrences. Central processing by analysts identifies rumors of suspected disease outbreaks, and these are in turn reported to the WHO for verification with relevant government authorities. The United States is in the early stages of implementing a far more expansive effort employing a similar approach known as the National Biosurveillance Integration System (NBIS). Sponsored by the Department of Homeland Security, NBIS systematically examines over one million electronic sources daily to help identify unusual occurrences that constitute “indicators and warnings” and occurrences of infectious disease events worldwide. Influenza is currently among the priorities addressed by NBIS. Thus, one important strategy to improve influenza surveillance timeliness is to capitalize on data mining methods.

- 11) **Expand expedited transport of specimens to in-country and international reference laboratories.** As described above, laboratory diagnosis is an important element of influenza surveillance, including surveillance quality. However, to be most useful for the timely detection of the earliest cases, specimens must reach the laboratory quickly. This means transport of specimens from where the patient is located to the first, most likely local, diagnostic laboratory, then transport onward for more specific testing, and ultimately transport to an international reference laboratory for strain confirmation. The global community has already developed a funding mechanism for the transport of specimens to a WHO-accredited influenza A/H5 reference laboratory. This mechanism must be scaled up to assure that specimens anywhere in the world can reach an international laboratory, and consideration must also be given to rapid transport of laboratory specimens from their point of origin (the patient) to the first and any subsequent in-country diagnostic laboratories.
- 12) **Streamline notification, analysis, and reporting.** Late in the past century, disease surveillance in many parts of the world relied on transmission of physical (paper) reports at specified intervals, usually weekly, monthly, or quarterly. Even today, once reports reach the appropriate government authorities in either paper or electronic form, they must be processed and analyzed and then disseminated or otherwise acted on. An important strategy to improve the timeliness of surveillance is the streamlining of notification, analysis, and reporting using the most efficient modalities for data transmission and effective channels for dissemination of surveillance reports. Reporting electronically or even by telephone should be the desired global norm for surveillance of diseases for which timeliness is a particular priority, including human cases of avian influenza. For example, Voxiva HealthWatch™ has utilized simple telephone or web-based technologies to speed up surveillance reporting in countries around the world, including Peru, India, and Indonesia (see Voxiva HealthWatch). Efficient data processing, prompt epidemiologic analysis, and timely dissemination of surveillance reports are further features of this strategy to streamline influenza surveillance.

- 13) **Implement active surveillance when appropriate.** As described in Chapter Two and above under strategy (2), traditional public health surveillance typically relies on passive reporting of disease occurrences by clinical providers or laboratories to government authorities, at specified intervals that tend to range from weekly to quarterly. Another strategy to improve the timeliness of surveillance is the increased use of active data collection, i.e., active surveillance. This means that government authorities (or others, on their behalf) directly solicit information about disease occurrence from potential sources, such as hospitals and clinical providers. Such efforts are more labor intensive than routine passive reporting, but they can be critical to enhance timeliness of detection of selected events, or to assure adequate information about the extent of disease spread. For example, the United States enhanced its surveillance through the use of active data collection during the October 2001 anthrax attacks and the 2003 global outbreak of Severe Acute Respiratory Syndrome (SARS). In both instances, active surveillance was employed as a timely case detection strategy and also helped assure health officials that all cases had indeed been detected (regarding anthrax, see Williams, 2002; regarding SARS, see Gerberding, 2003 and CDC, 2005). Nonetheless, active surveillance is difficult and resource intensive even in countries such as the United States (Heinrich, 2003).
- 14) **Develop and deploy rapid laboratory diagnostics with greater sensitivity and reproducibility.** Timely laboratory diagnosis of influenza can be critical for both clinical and public health management purposes. Commercially available rapid diagnostic tests can detect influenza A antigen within 15-30 minutes. However, such tests have sensitivity in the 70% range and specificity in the 90% range, and they are not widely deployed in countries at risk worldwide. Therefore, another strategy to improve the timeliness of influenza surveillance is the development and widespread deployment of more accurate rapid diagnostic tests, i.e., tests that singly or in combination can approach 100% sensitivity and 100% specificity and are practical for field use throughout the world. Furthermore, current rapid tests are only able to identify the presence of influenza virus A, that is, they cannot identify by subtype such as H5. The ideal accurate rapid test could identify not only influenza A viruses by type but also by subtype.
- 15) **Develop and deploy in-country and U.S. rapid response teams to investigate cases/outbreaks.** The purpose and proper end point of surveillance is action: timely investigation and appropriate public health intervention. The capacity to respond quickly to worrisome surveillance signals is a critical element in effective disease control. Therefore, another strategy to improve the timeliness of influenza surveillance is the development of in-country and U.S. rapid response teams. Ultimately, in-country capacity across the globe will be the best way to assure timeliness and global surge capacity; in the interim, international rapid response teams, including U.S. teams and experts, can be developed for deployment to other countries within a region or around the world. Such teams must have the capacity to investigate outbreaks in animals and/or humans,

undertake or facilitate timely laboratory diagnosis, and recommend appropriate disease control measures. Team constitution and size remain to be defined within the NSPI *Implementation Plan*, but would be expected to include expertise in veterinary and public health epidemiology, laboratory specimen collection, and local cultural considerations.

### Strategy to Improve Transparency

Even the best surveillance systems and strategies depend in large part on the willingness of people to report cases. Further, the global community has a common interest in being aware of and sharing information on novel influenza strains for purposes of vaccine and other countermeasures that can protect everyone.

- 16) **Facilitate incentives to motivate reporting and sharing of virus strains and genome sequencing information.** Open reporting within and among countries worldwide and the sharing of virus strains and genome sequencing information are critical to timely and effective responses that benefit not only affected countries but also the larger global community. Open reporting can trigger timely investigation and response to limit disease spread. Sharing of viral strains and genome sequencing information can lead to quicker development of new diagnostic tests and an effective pandemic vaccine. However, powerful disincentives can also impede transparency, e.g., when notification of influenza within a country limits tourism or trade and hence impacts the national economy. Therefore, a strategy to improve surveillance transparency is to facilitate incentives to motivate the reporting of influenza cases and to share virus specimens with relevant international partners.

### Approaches to Implementation of Surveillance Improvement Strategies

How can HHS, and the U.S. government more broadly, implement the strategies described above, especially in light of finite resources? Here we describe two main approaches: direct actions that HHS can take itself and leveraging strategic partners.

#### HHS Direct Actions

HHS, particularly through CDC, has been actively and directly involved in international health for many years, including some of the influenza surveillance strategies described above. Below we summarize the mechanisms HHS can use to implement the strategies described above. For the most part, these reflect ways that CDC currently works internationally.

**Long-term overseas technical assistance.** One way that HHS can take direct action to implement the various tactical strategies is through technical assistance to countries, provided by CDC or other HHS staff. HHS has a long history of posting its own staff overseas, generally for a period of two or more years. According to a database excerpt provided to the RAND team, HHS has approximately 250 staff members posted in 41 different countries around the world. While HHS did not provide details regarding the nature of

these positions, overseas staff members address such priority health issues as HIV/AIDS, polio eradication, and influenza, and they oversee capacity building activities such as applied epidemiology training. The advantages of posting staff overseas include the continuity and intensity of technical assistance through permanent on-site staff, which can be important in helping countries achieve their programmatic goals. It costs approximately \$350,000 per year for each overseas assignee; this figure includes regular salary plus additional expenses associated with long-term overseas assignment, e.g., post adjustment, moving and travel expenses, housing and other benefits, and expenses associated with Embassy support services.

**Short-term overseas technical assistance.** Direct technical assistance by HHS staff can also be through short-term consultations. Indeed, most of HHS' international work has traditionally been undertaken through periodic short-term consultation. The advantages of this approach include the larger number and wider range of experts available for short-term international assignment, and the relatively lower cost, i.e., regular salary levels with marginal costs only for international travel. Disadvantages include the lower levels of continuity and intensity of technical assistance afforded by less frequent on-site contact with national counterparts. Nonetheless, short-term consultation by HHS experts will likely remain among the important HHS direct actions to improve global surveillance.

**Contracts/grants with other organizations.** HHS has traditionally undertaken most of its international work through deployment of its own staff, as described above. Only recently has it begun to use a contract/grant mechanism for providing technical assistance to other countries, e.g., in Afghanistan. There may be opportunities to significantly extend the reach of HHS international influenza surveillance programming through contracting with organizations that can provide specific expertise and services. For example, an organization like the Association of Public Health Laboratories (APHL) could be a source of additional laboratory expertise to help build laboratory capacity in other countries and oversee subsequent proficiency testing. Additional epidemiology training expertise could come from the public sector, e.g., through organizations such as the Council of State and Territorial Epidemiologists (CSTE), or from the academic sector, e.g., through the Association of Schools of Public Health (ASPH). A number of private sector firms could provide critical support to build connectivity and streamlined reporting mechanisms. One example is Voxiva HealthWatch, mentioned earlier, which has helped streamline surveillance reporting in other countries through simple telephone technologies and online reporting systems. Identification and procurement of strategic partners through contract or grant mechanisms has the potential to greatly extend the reach of HHS programming to improve influenza surveillance globally.

**Bilateral international agreements.** A final mechanism for HHS direct action to advance international influenza surveillance, which can be combined with one or more of the approaches described above, is direct agreements with foreign countries, e.g., official bilateral agreements between the United States (or HHS on behalf of the United States) and partner countries, or transfer of funds through a grant mechanism. The advantages of such agreements or grants include formalization of the cooperation between the United States government and a foreign government, including a degree of accountability beyond what is

usually possible with more informal arrangements. RAND understands that HHS is beginning to use the grant mechanism in its international influenza programming to transfer funds directly to foreign governments.

### **Leveraging Strategic Partners**

HHS has a daunting set of responsibilities under the new NSPI *Implementation Plan*. While there is no doubt about the technical excellence of HHS to fulfill these responsibilities, there is a significant opportunity for HHS to extend its reach more broadly within countries and across a broader range of countries through proactive engagement in strategic partnerships. RAND's conceptual framework to improve global influenza surveillance places high priority on developing strategic partnerships, both in countries where HHS already has programming and in countries where it does not. Furthermore, partnership networks can contribute in important ways to virtually all sixteen surveillance improvement strategies. Opportunities for different types of partners are highlighted below in general terms. Because of the importance of strategic partnerships, our report explores in detail how HHS can identify strategic partners (Chapter Five) and how it can assess the strengths of such partnerships (Chapter Six).

**Other U.S. government agencies.** Influenza programming, including surveillance programming, can take advantage of a number of U.S. government agencies in-country. For example, it is clear that cooperation and coordination between in-country staff of HHS and the U.S. Department of Agriculture (USDA) is critical to help address the animal–human health nexus. However, other government agencies can also play a critical role for certain strategies to improve influenza surveillance. For example, the State Department has the natural lead role for diplomatic efforts that could be aimed at, for example, encouraging expanded animal surveillance and especially facilitating transparency in surveillance reporting. Because the U.S. Agency for International Development (USAID) has extensive programming in both the agriculture and health sectors and a reach to the grassroots level, it can play a key role in strategies related to village/community-based reporting for both animal and human disease, and capacity building for surveillance of influenza-like illness throughout the health care system. Likewise, the grassroots programming base for the Peace Corps makes Peace Corps Volunteers well suited to work with local communities in the establishment of community-based reporting and local capacity building.

**International organizations.** International organizations comprise the governments of their Member States and include both global organizations, such as the World Health Organization (WHO), and regional organizations such as the WHO regional offices, Group of Eight (G-8) industrialized countries, Asia Pacific Economic Cooperation (APEC), Association of Southeast Asian Nations (ASEAN) and others. The United States is a member of many, though not all, such organizations, e.g. WHO, G-8, APEC, but not ASEAN. HHS has a longstanding and generally positive relationship with the WHO system and has in recent years engaged more with G-8, APEC, and other international organizations. These organizations can provide vital credibility or political neutrality of value to some countries and hence enable U.S./HHS engagement that

might otherwise be more difficult on a bilateral basis. Also, such organizations provide the legitimacy of international law, e.g., the WHO International Health Regulations, and the strength of group (Member State) consensus on cross-border issues. HHS works with and through international organizations, e.g., through the posting of its staff members to the WHO and funding for specific WHO programs such as its Global Outbreak Alert and Response Network (GOARN). HHS could potentially extend the reach of its influenza programming efforts through intensified strategic engagement with these and other relevant international organizations, while also enhancing efficiency and diplomacy. For example, international organizations can help increase surveillance coverage across and within countries, surveillance quality through a number of policies and interventions, surveillance timeliness through data mining and required case reporting, and transparency through international consensus and treaties (e.g., the revised WHO International Health Regulations). As a concrete example, HHS already has posted, and based on the NSPI *Implementation Plan* will post, additional influenza experts to WHO headquarters and regional offices. G-8, APEC, ASEAN, and other international organizations may offer additional strategic partnership opportunities to help improve global influenza surveillance.

**Laboratory Networks.** Laboratory networks such as the U.S. Association of Public Health Laboratory Directors (APHL), the Institut Pasteur, and others have technical competence and, especially for non-U.S. networks, often also well-established relationships with specific countries of strategic interest to the United States and HHS. HHS has already signed an agreement with the Institut Pasteur to enhance its reach specifically related to influenza laboratory issues. Again, systematic assessment of other such networks (e.g., Secretariat of the Pacific Community) could reveal opportunities to extend the reach of HHS programming, specifically to help build and maintain laboratory capacity/proficiency vital to influenza surveillance. Specifically, laboratory networks can contribute to surveillance coverage and quality by helping to expand the number of qualified laboratories in countries, and to surveillance timeliness by contributions to early warning systems and rapid response efforts. The global programming of several laboratory networks is presented in greater detail in Chapter Five.

**Foreign development agencies.** Foreign counterparts to the USAID have considerable programming in countries around the world. For development agencies with health programming, there may be opportunities to interface and synergize efforts relevant to international influenza surveillance. Chapter Five briefly describes and then maps the countries where major development agencies from Australia, Canada, the United Kingdom, Germany, Japan, and Sweden have current programming. These are intended to serve as illustrative rather than comprehensive examples of opportunities to leverage USAID counterpart agencies from other major donor countries, especially those with health-related missions and programming relevant to global influenza. Foreign development agencies could provide particularly valuable support to help increase surveillance coverage, including both facility-based and community-based reporting; surveillance quality, through monitoring virus strains and capacity building in such areas as epidemiology and information technology; surveillance timeliness, through support for early warning surveillance systems, rapid response

team development and/or participation, and potentially active surveillance; and surveillance transparency, by adding to the diplomatic voice and practical support for incentives that facilitate open and timely reporting of influenza cases.

**Academic community.** HHS and USAID have a considerable history of supporting the academic sector for a wide range of research and public health programming, including support for international research and programs. Numerous U.S. and foreign schools of medicine and public health are already working in countries throughout the world and could potentially be harnessed to help extend the reach and quality of influenza surveillance. The academic sector could help enhance surveillance coverage by helping to increase the number of traditional surveillance reporting sites and/or new surveillance sources and signals; surveillance quality, through building laboratory, epidemiology, and information technology capacity, and monitoring influenza virus strains; surveillance timeliness, through potential training of and/or participation in rapid response teams, research to develop rapid diagnostic tests, and possibly contributions to early warning surveillance, expedited specimen transport and/or streamlined surveillance notification; and surveillance transparency, through sharing virus strains and potentially supporting incentives for reporting from clinical or community sites.

**Business/industry sector.** The business sector is attracting increased interest from public sector health authorities as a potentially vital partner in disease prevention and control efforts, as well as a societal component critical to the continuity of operations and maintenance of the economy in the event of a major disaster. International and multinational businesses can complement current public sector efforts to enhance global influenza surveillance in several ways. They can increase surveillance coverage by ensuring that appropriate cases among employees are reported to local health authorities, providing specimen collection supplies, and reporting work absenteeism if warranted; they can increase surveillance quality, particularly through concrete support for targeted laboratory testing; they can increase surveillance timeliness through contributions to early warning systems and active data collection as well as support for development and evaluation of rapid diagnostic tests; and they can increase surveillance transparency through moral and financial support for practical incentives that facilitate open and timely reporting of influenza cases (Moore, 2006).

**Nongovernmental and other organizations.** Nongovernmental organizations (NGOs) can also contribute significantly to HHS and overall U.S. government efforts to improve influenza surveillance. NGOs include, for example, faith-based organizations (i.e., medical and other missionaries), the International Medical Corps, and Aga Khan Health Services. Traditionally, U.S. government programmatic support for such organizations comes from USAID. NGOs can contribute to surveillance coverage by expanding the sources and signals relevant to influenza case reporting and particularly community-based reporting; to surveillance quality through diligent attention to targeted laboratory testing of appropriate cases; to surveillance timeliness, by assuring that local cases reach the attention of health authorities through conventional and/or special reporting modalities, through active participation in early warning systems.

**The Media.** Electronic media (including active electronic communications such as news media and blogs) is an omnipresent actor worldwide and has not been traditionally, actively, or systematically harnessed to help promote public health or disease detection. If appropriately engaged, the media plays a particularly important role in increasing both surveillance coverage and timeliness. Media reports are the basis for such data mining efforts as Canada's Global Public Health Intelligence Network (GPHIN), which feeds information on rumored outbreaks to WHO for verification. HHS and/or other relevant U.S. government agencies can consider ways to more systematically and actively engage with local and international media to help improve global influenza surveillance, beyond the very helpful information already provided through the media.

## FULL CONCEPTUAL FRAMEWORK

Table 3.2 presents our full conceptual framework showing the 16 strategies described above divided among the four surveillance requirements. For each strategy, the table suggests potential approaches to their implementation: HHS direct actions and actions by specific types of partners. These suggestions are intended to be illustrative rather than comprehensive or rigorously analytical, but they highlight the utility of the framework to identify specific programmatic actions that can be implemented to extend the reach of HHS and U.S. government programming for global influenza surveillance.

Our conceptual framework establishes the basis for the ensuing chapters:

- Chapter Four, which presents our process model describing nine paths that can lead to case detection and confirmation of a novel influenza strain, and how the surveillance improvement strategies can be applied to the model. We also introduce an interactive tool, based on this process model, which can be used to compare the impact of different strategies on the probability and timeliness of detecting a novel virus strain, in order to help select promising strategies.
- Chapter Five, which describes a number of agencies and organizations that could be considered for potential partnerships with HHS, presents maps depicting their current global programming, and analyzes opportunities for HHS.
- Chapter Six, which describes a proposed approach to measure the strength of partnerships, a dimension not captured in traditional program monitoring and evaluation.

**Table 3.2**  
**Conceptual Framework to Improve Global Influenza Surveillance**

Strategies (X = potential application mechanism)	<i>HHS Direct Actions</i>				<i>Leveraging Strategic Partners</i>							
	Long-term overseas technical assistance	Short-term overseas technical assistance	Contracts/grants with other organizations	Bilateral international agreements	Other US government agencies	International organizations	Laboratory networks	Foreign development agencies	Academic community	Business/Industry sector	Nongovernmental organizations	Electronic media
<b>SURVEILLANCE COVERAGE</b>												
(1) Work in/with more countries	X	X	X	X	X	X	X	X	X	X	X	
(2) Increase number/density of traditional reporting sources	X	X		X	X		X	X	X		X	
(3) Develop village-/community- based alert & response systems	X	X		X	X			X			X	X
(4) Consider new human disease information sources & signals	X	X		X	X				X	X	X	X
(5) Increase reporting compliance	X	X	X	X	X			X	X	X	X	
<b>SURVEILLANCE QUALITY</b>												
(6) Improve human laboratory sample preparation and diagnostic capacity	X	X	X	X	X	X	X		X			
(7) Implement targeted laboratory testing appropriate to the pandemic phase and location	X	X	X	X	X	X	X		X	X	X	
(8) Monitor viral strains for changes	X		X	X	X	X	X		X			
(9) Improve epidemiologic capacity	X	X	X	X	X	X			X			
<b>SURVEILLANCE TIMELINESS</b>												
(10) Support development of early warning networks, including use of data mining methods	X	X		X	X	X	X					X
(11) Expand expedited transport of specimens to in-country and intl. reference labs	X	X		X		X	X		X			
(12) Streamline notification, analysis, and reporting	X	X	X	X	X	X			X	X		
(13) Implement active surveillance when appropriate	X	X	X	X	X					X	X	
(14) Develop & deploy rapid laboratory diagnostics with greater sensitivity & reproducibility	X	X			X		X		X	X		
(15) Develop and deploy in-country and U.S. rapid response teams	X	X	X	X	X	X	X	X	X		X	
<b>SURVEILLANCE TRANSPARENCY</b>												
(16) Facilitate incentives to motivate reporting & sharing of virus strains and genome sequencing information	X	X				X	X	X	X	X		X



#### 4. A PROCESS MODEL AND INTERACTIVE TOOL FOR COMPARING STRATEGIES TO IMPROVE PROBABILITY AND TIMELINESS OF CASE DETECTION

A key goal of influenza surveillance, especially before the onset of a pandemic but also during the course of a pandemic, is to detect the occurrence of cases caused by a novel strain of the influenza virus, especially those transmitted from person to person. Our conceptual framework developed in Chapter Three synthesizes potential strategies that could be implemented to improve surveillance coverage, quality, timeliness, and transparency. In the interest of efficient resource allocation, it would be helpful to have a quantitative way to compare the potential effectiveness of different strategies, so that investments may be prioritized.

This chapter answers our second policy question: *How can HHS quantitatively compare different strategies in order to select promising ones?* We first describe the process model we developed to examine different ways that influenza cases can be detected, using a hypothetical sick individual to show the various pathways and steps needed for disease detection and confirmation. After reviewing strategies from Chapter Three that can directly influence the outcome of the detection process, we show how the potential effectiveness of different strategies can be compared, in a quantitative way, using an interactive tool based on this model.

##### INFLUENZA CASE OCCURRENCE AND DETECTION: THE PROCESS MODEL

Many factors can prevent the timely detection of a case of influenza caused by a novel strain. The process that goes from occurrence of disease to reference laboratory confirmation of that disease case involves multiple steps. Information is passed from step to step along a path that includes actions by the sick individual, reports, investigations, and tests. For example, a person who is sick might go to a health care provider (labeled “doctor” for purposes of this model), the doctor may order a laboratory test, and the laboratory may pass on the sample for further testing. Only when all the steps along a path have been completed will a sample of a novel strain be confirmed by a reference laboratory.

We identified nine paths that can lead to case detection and used them to build a process model that traces the steps involved in going from a sick individual to confirmation of a novel influenza strain. These steps are complex with many uncertainties, all of which can block or slow the ultimate confirmation of a novel strain of influenza virus. Because the occurrence of each step is uncertain and the time required can vary, we constructed our process model so that each step has its own associated probability and delay. In a later section we show how we incorporated our process model into an interactive tool that allows users to modify these probabilities and delays to compare different strategies to improve influenza surveillance.

The goal of our process model and interactive tool is to help find the most efficient ways, under variable circumstances, to improve the chances that a case of disease caused by a novel influenza strain will be detected and ultimately confirmed by a reference laboratory, and to reduce the time it takes to do so.

## Nine Paths to Detection of a Novel Influenza Strain

Figure 4.1 is our process model. It comprises the following nine paths through which a person who is ill with a novel influenza strain may be detected by health authorities and through which the novel strain may eventually be confirmed by a reference laboratory:

*Sick individual seeks medical care*

- Path 1. Doctor orders laboratory test
- Path 2. Hospital orders laboratory test
- Path 3. Reporting by sentinel doctor
- Path 4. Reporting by sentinel hospital
- Path 5. Active surveillance of doctors
- Path 6. Active surveillance of hospitals

*Illness detected at community level*

- Path 7. Tracking employee sick days
- Path 8. Tracking electronic media
- Path 9. Detection by community-based monitoring system

As shown in Figure 4.1, each path leads to an Investigation Sequence and/or to a Laboratory Sequence.

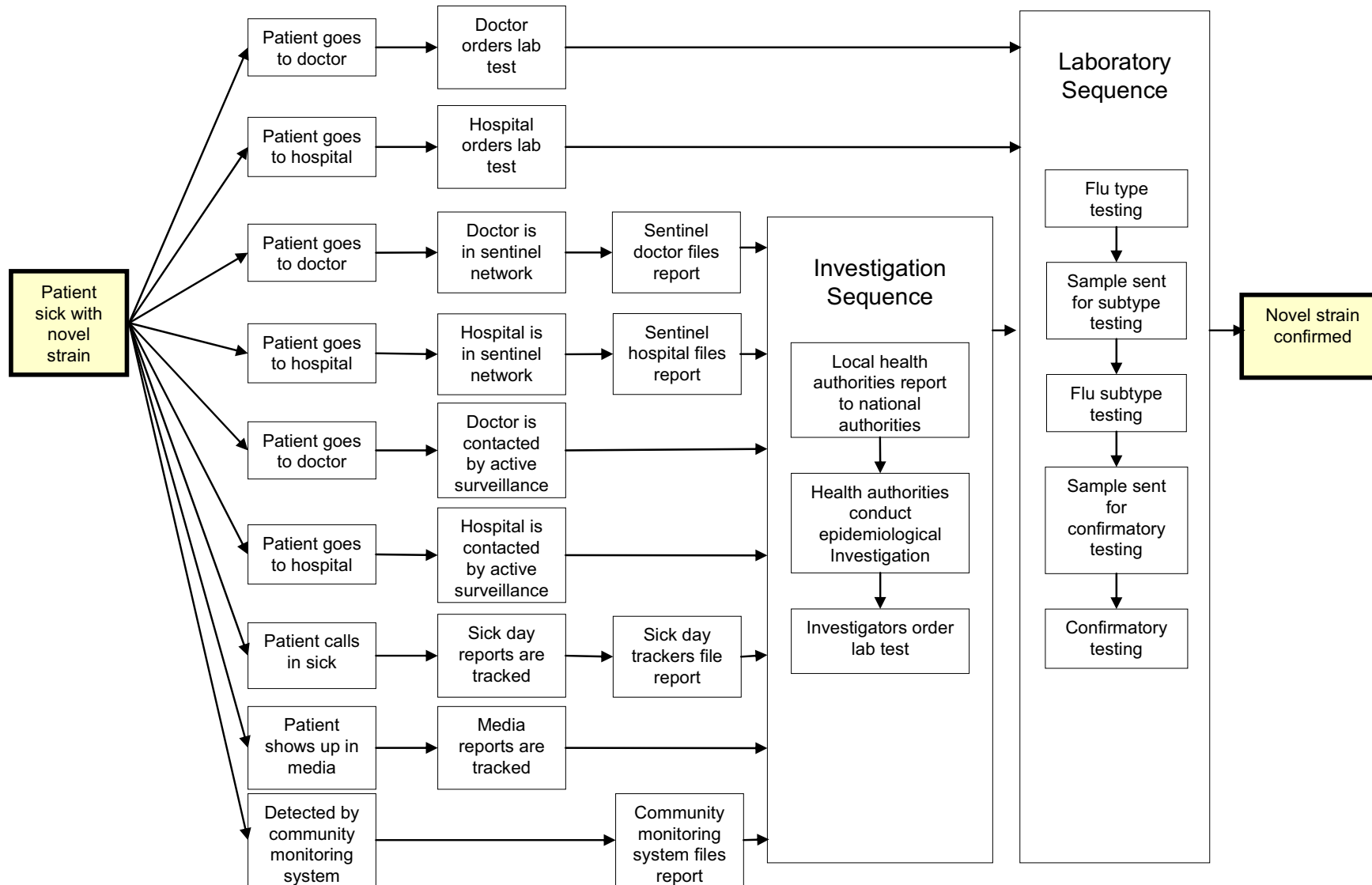
The Investigation Sequence is triggered if local health authorities receive reports of influenza-like illnesses from doctors, hospitals, communities or other sources. They, in turn, notify national health authorities who may begin an epidemiological investigation, depending on the availability of personnel and resources. The investigation would then result in the collection of a sample for testing, whether by the clinical provider or the investigation team. The sample then undergoes the Laboratory Sequence, which is described next.

During the Laboratory Sequence, the sample first undergoes initial testing to identify the presence of an influenza virus and possibly the virus type. Depending on the availability of resources, the sample may be sent for further testing at a more sophisticated laboratory (or tested further at the same laboratory). The steps include sending the specimen for a subtype test, conducting the subtype test, sending the specimen to a reference laboratory, and conducting the final confirmatory testing.

The paths in our process model are not mutually exclusive, i.e., a case can be detected through multiple pathways. The first six paths begin when the sick individual seeks medical care, through either a doctor or a hospital; the last three paths are ways to detect the case at the community level, i.e., they do not depend on the individual seeking medical care. While several of these paths will be familiar to public health professionals, the assembly of them into the process model is a product of the RAND team.

By identifying these paths, our process model can help HHS and other agencies determine where interventions can be made to improve the probability and timeliness of case detection.

Figure 4.1 Process Model for Influenza Detection and Confirmation



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## Step by Step Through the Nine Paths of the Process Model

*Paths 1 through 6:* The first six paths to detection are associated with the traditional ways that health authorities find out about influenza cases, namely through doctors and hospitals. In each of these paths, the sick individual seeks medical care from a doctor and/or hospital.

### Path 1. Doctor orders laboratory test

A patient who is sick with a novel influenza virus may go to a doctor. Once there, the doctor may order a diagnostic laboratory test for influenza. If a lab test is ordered, the sample goes through the Laboratory Sequence.

### Path 2. Hospital orders laboratory test

This path is almost identical to Path 1, except that instead of the patient starting with a visit to a doctor, the patient starts by seeking care at a hospital. The hospital may order a diagnostic laboratory test for influenza. If a lab test is ordered, the sample goes through the Laboratory Sequence. We treat this path as distinct from Path 1 because some of the probabilities associated with the steps may be different.

### Path 3. Reporting by sentinel doctor

A patient who is sick with a novel influenza virus may go to a doctor, and the doctor may be a member of the sentinel surveillance network. This network is a set of doctors who agree to voluntarily submit regular reports to the local health authorities. Compliance is far from certain, however, so there is the possibility that even a sentinel doctor will fail to submit their report regarding the number of patients with influenza-like illnesses they have seen.

If the doctor does submit a report to the local health authorities, this becomes a piece of “nonspecific information.” The health authorities become aware that there is a case or outbreak of influenza-like illness, but they do not have laboratory confirmation that the disease is caused by a novel influenza virus. The report, however, may trigger the Investigation Sequence and ultimately the Laboratory Sequence.

### Path 4. Reporting by sentinel hospital

This path is identical to Path 3, except that the patient starts by seeking care at a hospital, which may be part of a sentinel network, and which may submit a surveillance report.

### Path 5. Active surveillance directed at doctors

A patient who is sick with a novel influenza virus may go to a doctor. The doctor may be contacted by local health authorities if the authorities implement active surveillance, that is, actively contacting doctors to ask if any cases have been seen, rather than waiting for doctors to report cases to them. Because the number of doctors in a country can be quite large and active surveillance is labor intensive, even when it is implemented, the chance that any given doctor is contacted is likely to be very small.

If news of the sick patient is discovered by the active surveillance process, the local health authorities may then trigger the Investigation Sequence, which can lead to the Laboratory Sequence.

### Path 6. Active surveillance of hospitals

This path is identical to Path 5, except that the patient starts by seeking care at a hospital, which may be contacted as part of active surveillance.

***Paths 7 through 9:*** Aside from the traditional ways that local health authorities discover cases of influenza through doctors and hospitals, there are several less traditional means that involve detection at the community level.

Path 7. Tracking employee sick days

A patient who is ill may be absent from his or her workplace, and employee sick day records could be tracked. However, although potentially useful, tracking sick day records is currently not generally done on a systematic or large-scale basis by public health authorities around the world, including the United States. If the information is tracked and, further, then reported to local health authorities, it may then trigger the Investigation Sequence and then the Laboratory Sequence.

Path 8. Tracking electronic media

A patient may represent a unique illness that is newsworthy or may be part of a cluster of ill people who become noticed, and these cases may then be reported in a news article, blog, or some other form of electronic communications or media. These media reports would need to be tracked; while such information is readily available and could potentially be useful, it is currently not systematically followed by most health authorities. If such information is tracked by or reported to health authorities, the authorities may then trigger the Investigation Sequence and the Laboratory Sequence.

Path 9. Detection by community-based monitoring system

In some parts of the world, arrangements called “village alert” or “community-based monitoring” systems are beginning to be established outside the normal health care system of doctors and hospitals. These systems are intended to provide early warning of illnesses and outbreaks that might otherwise escape detection by health authorities. A patient may be detected through such a system, although only a few such systems presently exist. However, of note, the NSPI *Implementation Plan* calls for the United States to help establish such systems in a number of countries. If information on a sick patient is tracked via a community-based monitoring system and, further, then reported to the local health authorities, the authorities may then trigger the Investigation Sequence and the Laboratory Sequence.

## **Review of Surveillance Improvement Strategies Incorporated into the Process Model**

The nine paths to detection described by our process model highlight the complexity and uncertainties that can hamper the ultimate confirmation of a novel strain of influenza virus. Here we review 12 of the 16 strategies to improve surveillance (identified in Chapter Three and included in our process model) that HHS could implement, either singly or in combination, to influence individual steps in those paths and improve the

probability and/or timeliness of case detection.<sup>1</sup> The strategy numbers used here are those used in Chapter Three. In the subsequent section, we introduce an interactive tool, based on our process model, to evaluate the impact of different strategies on the probability and/or timeliness of detection.

(Strategy 2) Increase number/density of traditional reporting sources. This would increase the number of doctors and hospitals in the sentinel network and hence the probability that any given doctor or hospital is in the sentinel network.

(Strategy 3) Develop village-based/community-based alert and response systems. This would increase the percent of the population residing in communities covered by an effective community-based system for tracking and reporting outbreaks, thus increasing the chances that a case or outbreak would be tracked and detected by a community-based alert system.

(Strategy 4) Consider new human disease information sources and signals. One potential new disease signal is tracking of employee sick days. Implementation of such a system would increase the percent of employees whose sick day records would be tracked and reported to the authorities, and thus the probability that a case is detected through employee sick day monitoring.

(Strategy 5) Increase reporting compliance. This would increase the percentage of voluntary surveillance reports submitted by a doctor, hospital, community, or other reporting source, and thus the probability that such reports reach local authorities.

(Strategy 6) Improve human laboratory sample preparation and diagnostic capacity. This would increase the availability of well-qualified in-country laboratory testing, thus contributing to an increased likelihood that a test could be performed by a qualified in-country laboratory.

(Strategy 7) Implement targeted laboratory testing appropriate to the pandemic phase and location. This would increase the chances that a doctor or hospital would send a specimen to the laboratory for testing.

(Strategy 9) Improve epidemiologic capacity. Training staff for disease surveillance, applied epidemiology, outbreak response would increase the percentage of cases/outbreaks that the authorities can investigate, thus increasing the likelihood that a case would be investigated.

(Strategy 10) Support development of early warning networks, including the use of data mining methods. This would increase the likelihood that electronic media reports of illness are tracked by or reported to health authorities, based on automated data mining systems such as Canada's Global Public Health Intelligence Network (GPHIN).

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<sup>1</sup> Although 16 strategies were described in Chapter Three, only 12 of them directly influence the probabilities and/or delays associated with capturing and passing along information in a given country. The other strategies do not fit neatly within the model: Strategy 1 describes working in or with more countries; Strategy 8 describes monitoring viral strains for changes, which is implicitly subsumed within the Laboratory Sequence; Strategy 15 describes developing and deploying rapid response teams, which is the appropriate response following detection (whereas the process model focuses on detection); and Strategy 16 describes facilitating transparency, which is more difficult to attach to specific steps in the process model.

(Strategy 11) Expand expedited transport of specimens to in-country and international reference laboratories. This would reduce the transportation time and thus the delays associated with sending viral samples from the patient's location to the local laboratory and onward to facilities capable of subtype and confirmatory testing.

(Strategy 12) Streamline notification, analysis, and reporting. This would reduce the time it takes for local authorities to communicate information to national authorities.

(Strategy 13) Implement active surveillance when appropriate. This would increase the number (and thus the percentage) of doctors and hospitals that would be actively contacted by local authorities to inquire about possible cases.

(Strategy 14) Develop and deploy rapid laboratory diagnostics with greater sensitivity and reproducibility. This would reduce the amount of time necessary to conduct initial local testing, i.e., to identify influenza virus presence and type.

## **AN INTERACTIVE TOOL FOR QUANTITATIVELY COMPARING SURVEILLANCE IMPROVEMENT STRATEGIES**

In this section, we first describe the variables in the steps within the various paths of our process model in terms of probabilities and delays for each step. Then we demonstrate how these probabilities and delays can be used within an interactive tool to determine the joint probability and total delay for detecting a novel influenza strain via each path in the model. This allows us to evaluate and compare different strategies for improving surveillance.

### **Variables within the Tool: Probabilities and Delays**

#### *Probabilities*

Each of the steps in our process model is a possible point of failure where the flow of information regarding a sick patient may terminate: a report is not filed, an investigation is not conducted, or a viral sample is not sent for further testing. Since each process step may or may not happen, in our model we assign probabilities to each step that estimate how likely it is that the step will occur.

In some cases these probabilities are driven by the relative numbers of things we are interested in, for example, if a country has 1000 doctors in an area, and 30 of them are part of the sentinel reporting network, then the probability that a doctor is in our network is  $30/1000$  or 0.03. In other cases, probabilities are driven by decisions that are made, for example, if health authorities decide to contact 10 percent of the hospitals in a country through active surveillance, then the probability that a hospital is contacted through active surveillance is 0.1. Probabilities may also be estimated from observation of events, for example, if 1 out of 4 people who are sick go to a doctor, then the probability that a sick patient sees a doctor is 0.25. Probabilities may also be a function of compliance, for example, if only half of doctors or hospitals submit surveillance reports, then the probability that reports reach local authorities from these sources is 0.5. As yet another

example, if a report of a sick individual always triggers an investigation by the health authorities, then the probability of an investigation is 1; but if the health sector either lacks sufficient infrastructure and resources, or is overwhelmed and as a result only investigates 1 out of every 8 reports of a sick individual or disease cluster, then the probability of an investigation drops to 1/8 or 0.125.

### *Delays*

In addition to each step having a probability of occurring, each step may also add a delay in the process. Delays are associated with the time until the step occurs or the time needed to perform a task. Delays may be associated with behavior: A person who is sick may wait a few days before seeing a doctor, or a report may only be filed once a week or once a month. Delays may be associated with processes: samples take time to arrive at a lab, and laboratory tests take time to perform. Or delays may be associated with capacity constraints: an epidemiological investigation could be started immediately if the investigators are available, but if they are busy carrying out other responsibilities, there may be a delay before they can start a new investigation.

Each of the 12 strategies described earlier for improving surveillance affects one or more of the steps in our process model. The strategy may increase the probability that a step occurs, such as by increasing the number of items chosen or increasing the compliance with a desired action. They may also decrease the associated delay, such as by speeding up transportation or communication. In some cases, strategies may affect both probability and delay.

### **Structure of the Interactive Tool**

Our process model is the basis for the interactive tool we developed to compare the impact of different strategies to improve influenza surveillance, either singly or in combination, on the probabilities and delays inherent in the paths leading to detection of a novel influenza strain. The interactive tool is an Excel spreadsheet (Appendix A) that consists of input and output tabs. For each of the nine paths in the process model, the input tab asks a series of questions to which users respond by entering their estimates of current probability and delay (baseline) for each step in the path. Users then enter their estimates for probability and delay anticipated after implementing improvement strategies of interest (follow-up).

On the output tab, the tool combines the numbers for each step into two summary numbers—*joint probability* and *total delay*—that provide a snapshot of each path's overall chances, before and after implementation of improvement strategies, of leading to case confirmation by a reference laboratory as well as the overall delay in getting there. The tool calculates joint probability by **multiplying** the probabilities associated with each step in the path. The tool calculates total delay by **summing** the individual delays

associated with each step in the path.<sup>2</sup> The user can compare the joint probability and delay for the different paths, before and after implementation of specific strategies, in order to help select promising strategies.

## Using the Tool: A Demonstration

Here we demonstrate how to use the interactive tool. Clearly, circumstances can vary across different locations; the model is constructed so that the specific characteristics of any given location at any point in time can be considered. For this demonstration, we first inputted what we considered were realistic baseline estimates of probability and delay for each step in the process model for a hypothetical developing country at the present time; then we inputted feasible follow-up estimates of improvements in probability and delay after implementation of each strategy included in the tool. These estimates were based on a review of relevant literature, to the extent possible. When no evidence base could be identified, values were estimated by RAND public health experts. We first describe the input values used for this demonstration, and then show the nine output tables produced by the tool.<sup>3</sup>

The following describes the baseline estimates of probability and delay that we used for our demonstration, and the follow-up estimates we used for the various surveillance improvement strategies. For our demonstration, we chose a 12-month follow-up, which is a fairly typical frequency for program assessment.

### *Demonstration of Tool Inputs*

The first part of Appendix A shows the questions and format for users to input the estimated probabilities and delays for the baseline and follow-up periods. Here we elaborate on each pathway and step in the process model, describing our hypothetical baseline and follow-up estimates and how they were derived.

#### ***Sick individual seeks medical care.***

For the first six paths, the process by which a novel strain of influenza virus can be confirmed in a laboratory begins with a sick individual seeking care from either a doctor or a hospital.

##### Patient goes to doctor

*Baseline estimates:*

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<sup>2</sup> This holds if we make the simplifying assumption that the steps are independent, that is, that the occurrence of one step does not affect the chances that another step will occur.

<sup>3</sup> In some instances for this illustration, no improvement strategy was considered (or none were available) for a particular step. In those cases, we held the probability and delay estimates constant, that is, the same values were used for both baseline and follow-up.

We estimate that 50% of ill persons will seek outpatient medical care based on the planning assumptions in the NSPI *Implementation Plan*. Furthermore, we estimate that ill persons wait 1 day after onset of symptoms before going to the doctor. In our illustration, these values are held constant for follow-up.

#### Patient goes to hospital

##### *Baseline estimates:*

We estimate a 10% chance that a patient will go to the hospital, based on values found in the NSPI *Implementation Plan* (10% lies between the moderate and severe pandemic scenarios). Furthermore, we estimate that the patient will wait an average of 1 day from the time they get sick until seeking hospital care. In our illustration, these values are held constant for follow-up.

#### ***Initial detection steps***

Once an ill person seeks care, the first six of the nine paths to detection of a novel influenza virus come into play.

Path 1. Doctor orders laboratory test. The likelihood of the doctor ordering a diagnostic laboratory test will be affected by the availability of laboratory testing and by sensitization of doctors to the need for targeted laboratory testing (based on dissemination of testing criteria appropriate to the pandemic phase and location). The more available laboratory testing is and the more sensitized doctors are to the criteria for testing, the more likely the doctor will order a test as a matter of routine for cases clinically and epidemiologically compatible with a novel influenza virus.

##### *Baseline estimates:*

Because we found no documented evidence of the percent of patients for whom doctors order influenza laboratory tests, our baseline value is a RAND estimate. We estimate that doctors will order lab tests for 10% of patients with influenza-like illness meeting specified clinical and epidemiological criteria. We estimate that the travel time for transporting the specimen to the initial testing laboratory is 1 day.

##### *Follow-up estimates:*

- *Strategy 7: Implement targeted laboratory testing appropriate to the pandemic phase and location.* The percentage of appropriate lab tests ordered by doctors increases to 50%.
- *Strategy 11: Expand expedited transport of specimens to in-country and international reference laboratories.* Transportation time for specimens from doctors decreases to 0 days (same-day delivery).

Path 2. Hospital orders laboratory test. The likelihood of the hospital ordering a diagnostic laboratory test will be affected by the availability of laboratory testing and the hospital's sensitization to criteria for appropriate (i.e., targeted) laboratory testing. The more available laboratory testing is and the more sensitized a hospital is to criteria for testing, the more likely the hospital will order a test as a matter of routine for cases clinically and epidemiologically compatible with a novel influenza virus.

##### *Baseline estimates:*

As with doctors, we estimate that hospitals will order lab tests for 10% of patients with influenza-like illness. We estimate that the travel time for transporting the specimen to the initial testing laboratory is 1 day.

*Follow-up estimates:*

- *Strategy 7: Implement targeted laboratory testing appropriate to the pandemic phase and location.* The percentage of lab tests ordered by hospitals increases to 80% (this is greater than the increase for doctors; we are assuming it is easier to sensitize a larger proportion of hospitals than physicians regarding targeted laboratory testing).
- *Strategy 11: Expand expedited transport of specimens to local laboratory and to reference laboratory.* Transportation time for specimens from hospitals decreases to 0 days (same-day delivery).

Path 3. Reporting by sentinel doctor

*Baseline estimates:*

We estimate that 1% of all the doctors in an area are designated members of a sentinel influenza reporting network. This is already more optimistic than U.S. estimates from its own influenza surveillance system during the 2005-2006 annual influenza season.

Furthermore, we estimate that sentinel doctors only have a 30% chance of actually filing their reports, based on U.S. influenza-reporting compliance during the 2005-2006 influenza season (CDC, 2006; U.S. Census Bureau, 2004). Assuming doctors report once a week, the average time between a patient being seen and the report being filed is about 3 days.

*Follow-up estimates:*

- *Strategy 2: Increase the number/ density of traditional reporting sources* (includes doctors in the sentinel reporting network). Percentage of doctors in the network increases to 10%.
- *Strategy 5: Increase reporting compliance.* Percentage of doctors filing required sentinel surveillance reports increases to 90%. In our illustration, the delay value is held constant for follow-up.

Path 4. Reporting by sentinel hospital

*Baseline estimates:*

We estimate that 15% of all hospitals in an area are part of a sentinel network. This value is a RAND estimate.

Without information specific to hospital reporting rates, we assigned hospitals the same reporting compliance rate as physicians. We estimate that sentinel hospitals only have a 30% chance of actually filing their reports. Assuming hospitals report once a week, the average time between a patient being seen and the report being filed is about 3 days.

*Follow-up estimates:*

- *Strategy 2: Increase the number/ density of traditional reporting sources* (includes hospitals in the sentinel reporting network). Percentage of hospitals in the network increases to 80% (this is a higher

percentage than estimated for doctors; given the fewer number of hospitals relative to the number of doctors, increasing the percentage of hospitals should be much easier).

- *Strategy 5: Increase reporting compliance.* Percentage of hospitals filing required sentinel surveillance reports increases to 90%. For our illustration, the delay value is held constant for follow-up.

Path 5. Active surveillance of doctors. Doctors may be contacted if the health department implements active surveillance. Because active surveillance is labor intensive, even when it is implemented, the chance that any given doctor is contacted is likely to be very small. Indeed, active surveillance is normally not routine but rather, implemented only in special situations.

*Baseline estimates:*

We assume that at the baseline, active surveillance is conducted extremely rarely, and have therefore assigned a probability of 0.1%. Thus, this path would only come into play in special circumstances. Assuming doctors are contacted once a week, the average time between a patient being seen and the doctor being contacted is about 3 days.

*Follow-up estimates:*

- *Strategy 13: Implement active surveillance when appropriate.* The percentage of doctors contacted via active surveillance increases to 30%. (The average time between a patient being seen and the doctor being contacted remains 3 days.)

Path 6. Active surveillance of hospitals. Hospitals may be contacted if the health department implements active surveillance. The chance that any given hospital is contacted is small, though possibly better than that of doctors, as there are fewer hospitals from which to sample.

*Baseline estimates:*

Again, because active surveillance is not routinely implemented, we have again assigned a probability of 0.1% to reflect rare ad hoc active contact with hospitals. Assuming hospitals are contacted once a week, the average time between a patient being seen and the hospital being contacted is 3 days.

*Follow-up estimates:*

- *Strategy 13: Implement active surveillance when appropriate.* Percentage of hospitals contacted through active surveillance increases to 80%. (The average time between a patient being seen and the hospital being contacted remains 3 days.)

### ***Illness detected at community level***

As described earlier, the final three paths do not rely on a sick patient seeking medical care.

Path 7. Tracking employee sick days. For illustrative purposes, we limit sick day monitoring to employee absenteeism (school absenteeism is a similar signal that could be monitored).

*Baseline estimates:*

We assume that an individual ill with a novel influenza virus will stay home from work and call in sick (100% probability), and thus cause an increase in sick days. We estimate such individuals start taking sick days 1 day after onset of symptoms. These values are held constant for follow-up.

Employee sick days are generally not tracked systematically or comprehensively by public health authorities around the world. Optimistically, we assume that sick day tracking covers only 1% of all employees. We also assume that there is a 5 day delay before any increase in sick days is noticed.

Even if sick days are tracked, the agency tracking this information may not report this information to the local health department. We assume that only 50% of sources that track employee sick days actually submit reports to the local health department, and that if they do so it is once a week, for an average delay of 3 days.

*Follow-up estimates:*

- *Strategy 4: Consider new human disease information sources and signals.* Percentage of employees whose sick day records would be tracked and reported to authorities increases to 20% (again, this may be unrealistically optimistic). Five-day delay is held constant for follow up.
- *Strategy 5: Increase reporting compliance.* Percentage of reports submitted increases to 75%. Three-day delay is held constant for follow-up.

Path 8. Tracking electronic media

*Baseline estimates:*

We assume that an individual with a novel influenza virus has a 75% chance of showing up in some media report, including openly accessible electronic communications of any kind. While the actual percentage of illnesses that enter electronic communications channels is uncertain, this is an estimate made for the purpose of examining the value of this tactical strategy. We also assume that it takes about 2 weeks (14 days) before such a case would show up in a media report. These values are held constant for follow-up.

Media reports are not often tracked by public health officials. While such information is currently available through sources such as WHO's Global Public Health Intelligence Network (GPHIN) or the U.S. government's National Biosurveillance Integration System (NBIS), it is the impression of the RAND team that HHS and other countries currently do not robustly use this information. Therefore, we estimate the percentage of reports that are tracked at 5%. The information is assumed to take 1 day before reaching local health authorities, reflecting daily reporting.

*Follow-up estimates:*

- *Strategy 10: Support development of early warning networks, including the use of data mining methods.* If all media reports were tracked and reached health authorities, percentage increases to 100%, again with a delay of 1 day, reflecting daily reporting. We believe this probability is a not just an optimistic but a realistic estimate.

### Path 9. Detection by community-based monitoring system

#### *Baseline estimates:*

At present, influenza cases and outbreaks are rarely tracked at the community level (outside the reporting of healthcare providers). We estimate that community-based systems cover only 2% of the population. Further we estimate it takes a community system two weeks (14 days) to discover that an outbreak has occurred.

When an outbreak is discovered by a community system, we estimate that only 50% of communities will submit regular reports, and that it takes 3 days before the information is received by local authorities, reflecting weekly reporting.

#### *Follow-up estimates:*

- *Strategy 3: Develop village-based/community-based alert and response systems.* Increasing the number of such systems for reporting outbreaks increases the percentage of covered population from 2% to 25%, which may be unrealistically optimistic for achievement within 12 months. The 14-day delay is held constant for follow-up.
- *Strategy 5: Increase reporting compliance.* Percentage of community surveillance reports submitted to local authorities increases from 50% to 75% for the first 12-month follow-up assessment. Three-day delay is held constant for follow up.

### ***Investigation Sequence steps***

Paths 3 through 9 of our process model result in nonspecific information, i.e., cases of suspected influenza-like illness that are not confirmed by laboratory testing. Not all cases or outbreaks will turn out to be influenza, and not even all influenza cases or outbreaks will be due to a novel virus strain. Therefore, the Investigation Sequence is required to pursue this further. As shown in our process model, this sequence involves the following steps:

#### Local health authorities report to national authorities

##### *Baseline estimates:*

We assume that the local health authorities will always report any nonspecific information they receive to the national authorities; thus they have a 100% probability of doing so. We estimate a delay of 3 days for this to happen, corresponding to the average delay that would occur with weekly reporting.

##### *Follow-up estimates:*

- *Strategy 12: Streamline notification, analysis, and reporting.* Time for local authorities to communicate information with national authorities decreases to 1 day, which corresponds to the average delay that would occur with daily reporting.

Health authorities conduct epidemiological investigation. In response to reports received by local authorities, in-country health authorities (local or national) undertake an investigation. The likelihood that they do so is affected by the investigative resources at their disposal.

*Baseline estimates:*

Because we did not find documentation of the percent of illnesses investigated by in-country authorities, and assuming that trained and available epidemiologists in countries at risk are presently limited, our model values are RAND estimates. We assume that 30% of reports result in investigation by an in-country epidemiologist, and that the duration of the investigation is 3 days.

*Follow-up estimates:*

- *Strategy 9: Improve epidemiologic capacity: train staff for disease surveillance, applied epidemiology, outbreak response.*

Percentage of reports investigated increases to 90% (this is for detecting the earliest cases of a possible evolving pandemic, i.e., not during the pandemic peak). The 3-day delay (to conduct the investigation) is held constant for follow-up.

Investigators order laboratory test*Baseline estimates:*

We assume that all investigations (100%) will result in taking of clinical samples that are then sent for laboratory testing. We estimate that the travel time for transporting the specimen to the initial testing laboratory is 1 day.

*Follow-up estimates:*

- *Strategy 11: Expand expedited transport of specimens to local laboratory and to reference laboratory.* Transportation time for specimens reduces to 0 days (same-day delivery).

***Laboratory Sequence steps***

Because the ultimate goal of our process model is reaching laboratory confirmation of an influenza case caused by a novel strain, all nine detection paths feed into and require the Laboratory Sequence. As shown in our process model, this sequence involves of the following steps:

Influenza type testing*Baseline estimates:*

We assume that once a specimen is sent to a laboratory, it will be tested (i.e., no loss of samples, so 100% are tested). The process for completing the initial laboratory test (for presence of influenza virus and/or virus type) is estimated to take 2 days.

*Follow-up estimates:*

- *Strategy 14: Develop and deploy rapid laboratory diagnostics with greater sensitivity and reproducibility.* Time necessary to conduct initial local testing reduces to 0 days (same day testing).

Sample sent for subtype testing. Following type testing, the sample may or may not be sent for further testing, depending on the availability of resources to transport the sample to a more sophisticated lab. Currently, laboratory capacity in at-risk countries is limited; indeed, building laboratory capacity is a major strategy of WHO and of the U.S. government, as evidenced in the NSPI *Implementation Plan*. For our

illustration, we assumed a “worst case scenario” where at-risk countries are not capable of conducting the subtype characterization themselves.

*Baseline estimates:*

We did not find documentation for the percent of laboratory specimens positive for the presence of influenza virus, or for type A virus in particular, being sent onward for subtype testing. Therefore, our model values are RAND estimates. We estimate that 10% of samples are sent onward for subtype testing. We estimate that the transportation of the specimen for subtype testing takes 3 days.

*Follow-up estimates:*

- *Strategy 6: Improve human laboratory sample preparation and diagnostic capacity.* Percentage of samples subtype tested increases to 80%.
- *Strategy 11: Expand expedited transport of specimens to local laboratory and to reference laboratory.* Transportation time for specimens from local laboratory to subtype testing laboratory decreases to 1 day.

Influenza subtype testing

*Baseline estimates:*

We estimate that all samples that are received (100%) are subtyped and that it takes 3 days to complete subtype testing, using current laboratory tests.

*Follow-up estimates:*

- *Strategy 14: Develop and deploy rapid laboratory diagnostics with greater sensitivity and reproducibility.* Time necessary to conduct subtype testing reduces to 1 day, with widespread implementation of rapid diagnostic tests capable of identifying influenza virus subtype.

Sample sent for confirmatory testing

*Baseline estimates:*

Following subtype testing, the sample may be sent onward to a reference laboratory for final confirmatory testing. We assume that only 30% of samples are sent onward, and the travel time is 4 days.

*Follow-up estimates:*

- *Strategy 6: Improve human laboratory sample preparation and diagnostic capacity.* This would, among other things, increase the likelihood that a country’s laboratory could and would send specimens to a designated international laboratory for confirmation testing. In some countries, percentage of samples sent for confirmatory testing increases to 80%.
- *Strategy 11: Expand expedited transport of specimens to local laboratory and to reference laboratory.* Transportation time from subtype testing laboratory to reference laboratory reduces to 2 days.

Confirmatory testing

*Baseline estimates:*

We estimate 100% of samples that are received at a reference lab will undergo confirmatory testing and that it takes 10 days. These estimates are held constant at follow up.

### *Demonstration of Tool Outputs*

The second part of Appendix A shows what the interactive tool would output for our demonstration, using the baseline and follow-up estimates of probability and delay that we inputted for each step. Comparing the *joint probability* and *total delay* shown at the bottom of each table makes it possible to see how the different strategies increase the probability and decrease the delay for a particular path. For example, the Path 1 table shows that at baseline, the joint probability of the entire path occurring is only 0.15%, and the total delay is 24 days. Twelve months after implementing strategies relevant to this path, the joint probability improves to 16% and the total delay drops to 15 days.

## DISCUSSION

### Identifying Promising Paths and Strategies

The previous sections described our process model and how 12 strategies for improving surveillance were incorporated into our interactive tool. The process model allows for visual qualitative comparisons of various strategies; the tool adds a quantitative dimension to the comparisons which, considered together with the level of effort to implement the different strategies, can better guide programming toward the most efficient and effective strategies. Each strategy may be employed singly or in combination with others, which means that there are far too many possible combinations of strategies for practical purposes. Navigating through all possible combinations would be a difficult task and impractical for public health decision makers. Fortunately, the structure of our process model and the interactive tool derived from it make it possible to approach the strategies in a logical way to identify which strategies would yield the most benefit in terms of probability and timeliness of case detection. When we described the various paths in our process model that lead from a sick patient to a confirmed laboratory result, we noted that many of the paths share a common series of steps, which we termed *sequences*. The two sequences were the *Laboratory Sequence*, which is shared by every path, and the *Investigation Sequence*, which is shared by all but Paths 1 and 2 (in these instances, the doctor or hospital orders a test, thus directly triggering the Laboratory Sequence).

#### *Laboratory Sequence: The Sine Qua Non to Identify Novel Influenza Virus Cases*

All nine paths to detection must go through the Laboratory Sequence to reach the ultimate step of reference laboratory confirmation of a novel influenza virus. If the Laboratory Sequence proceeds slowly or results in the failure of a sample to be tested accurately, all paths to detection are jeopardized. Any strategies that help improve the Laboratory Sequence will help every single detection path. Furthermore, since these strategies will simultaneously help all of the paths, the ability to make use of information arising from multiple sources, i.e., through multiple detection paths, will be increased. Indeed, increasing the number and capacity/quality of in-country laboratories is a major focus among the strategies to improve surveillance in current national planning documents.

The two strategies that influence the Laboratory Sequence the most are:

- Strategy 11 (expand expedited transport of specimens to in-country and international reference laboratories), which reduces the time needed to send samples for initial and subsequent testing; and
- Strategy 6 (improve human laboratory sample preparation and diagnostic capacity), which increases the chances of having a laboratory available to handle orders from doctors and hospitals to conduct a laboratory test, and decreases the time for subtype testing.

### *Investigation Sequence*

The Investigation Sequence also stems from a number of detection paths (3 through 9). As with the Laboratory Sequence, therefore, strategies to improve the Investigation Sequence will increase the probability and timeliness of case detection arising from multiple information sources (detection paths). Aside from the two paths where a doctor or hospital directly orders a laboratory test on seeing a sick patient, all of the other paths require the Investigation Sequence. The strategies that influence the Investigation Sequence the most are

- Strategy 12 (streamline notification, analysis, and reporting), which decreases the time before national authorities are notified, and
- Strategy 9 (improve epidemiologic capacity), which increases the likelihood that an investigation is conducted.

Because both sequences are shared by so many paths, those improvement strategies that favorably affect process steps within either the Laboratory Sequence or the Investigation Sequence will, all other things being equal, provide the most benefit in terms of increasing the probability and reducing the delay in detecting a case due to a novel influenza virus.

### *Additional Promising Strategies*

The commonality of the Laboratory Sequence to all nine paths in our process model, and the Investigation Sequence to seven of the nine paths, argues strongly for interventions that improve in-country epidemiology and laboratory infrastructure. However, additional strategies offer promise for improving surveillance, although we must also take into account practical considerations, e.g., the feasibility and level of effort required to achieve target intervention levels for alternative strategies. Examination of the output tables generated by our interactive tool demonstration suggests several additional strategies that could most easily improve the probability and timeliness of detection of a novel influenza case.

***Tracking electronic media.*** Perhaps the easiest strategy to implement, one that can produce large gains in both probability and timeliness, is Strategy 10 (support development of early warning networks, including the use of data mining methods). This strategy targets tracking of reports in the electronic media. Although a large part of the electronic media consists of online news articles, other forms can be tracked such as blogs. Using data mining methods to track electronic reports is the key to enabling Path 8 to be effective. As one of the three detection paths operating at the community level, this path does not require the sick

individual to seek medical care or be reported by sentinel providers; thus it avoids important “failure points” causing reduced probability of detection. As shown in the output table for Path 8, the strategy to track electronic media greatly improves surveillance coverage and timeliness. It is easy, quick, and inexpensive to implement because at least two data mining systems currently exist (GPHIN and NBIS) that can be drawn upon immediately. Enhancing either system with add-ons, e.g., to expand the range of foreign languages tracked, would be relatively easier to do than establishing new systems.

***Tracking and reporting employee sick days.*** Somewhat more difficult strategies to implement comprehensively, but which are also a promising part of detection at the community level, are Strategy 4 (consider new human disease information sources and signals) and Strategy 5 (increase reporting compliance). These strategies include tracking employee sick days and ensuring that surveillance reports are submitted to local authorities; they are key steps in Path 7. Tracking and reporting employee sick days would probably be more feasible and produce the largest gains in countries with relatively few large employers willing to track and report influenza-like illness to public health authorities. Tracking of employee sick days also permits detection even if a sick individual does not seek medical care, and thus it can greatly enhance surveillance coverage.

***Community-based monitoring and reporting.*** Perhaps the most difficult community-level path, in practical public health terms, is detection of illness by village-based/community-based monitoring systems (Path 9). Implementing Strategy 3 (develop village-based/community-based alert and response systems) and Strategy 5 (increase reporting compliance) can improve the outcomes in this path. While worthwhile and even required by the NSPI *Implementation Plan*, implementation of community-based surveillance and reporting will require mobilization and education of all communities to carry out alert and response activities. Such activities will be labor intensive and take more time (probably measured in years) than some of the other interventions. Once established throughout a country, however, such systems can provide comprehensive surveillance coverage for influenza, as well as for other diseases and conditions, and thus greatly enhance the probability of case detection. Thus, the implementation and benefit of Strategy 3 and the associated Strategy 5 (that would increase reporting compliance from communities) should be considered within a long-term time frame.

***Sensitizing hospitals and doctors to influenza guidelines.*** Paths 1 through 6 in our process model stem from patient visits to doctors or hospitals. Strategy 7 (implement targeted laboratory testing appropriate to the pandemic phase and location) can greatly influence the outcomes of these paths. This strategy involves sensitizing clinical providers to order influenza diagnostic laboratory tests for appropriate clinical cases. Strategy 7 would likely be easier to implement widely and routinely than the alternatives: the addition of substantial numbers of new providers, especially individual doctors, to the sentinel reporting network (Strategy 2) or implementation of active surveillance (Strategy 13). Since there are fewer hospitals than physicians, and sicker patients are more likely to go to a hospital, perhaps the first priority should be to

sensitize all hospitals (and their clinicians) to appropriate guidelines for ordering laboratory testing for suspected cases of novel influenza.

## CONCLUSIONS

In this chapter we presented a process model that systematically assesses the steps and alternative paths that can lead to the detection of a confirmed case caused by a novel influenza virus. While many of the processes and paths reflect traditional public health practice, others do not. Moreover, to our knowledge, the full range of paths and processes has not heretofore been laid out in a systematic way that facilitates policy consideration through quantitative comparison of alternative strategies to improve influenza surveillance.

Based on our process model, we developed an interactive tool to compare strategies to improve global influenza surveillance. The tool enables users to analyze, in a quantitative way, the relative strengths of qualitative improvement strategies. For each step in the model, users input their baseline estimates of current probability and delay as well as their estimates of feasible levels of improvement for each intervention, measured at follow-up. The interactive tool then uses these inputs to calculate the joint probability and total delay for each of the nine possible paths to case detection, that is, the overall chances that each path will lead to a confirmed case of novel influenza strain if the selected strategies had been implemented and the total time required to do so. We demonstrated the tool's application by inputting our own baseline and follow-up estimates of probability and delay for a hypothetical developing country, using a 12-month follow-up time period, to see the potential impact of implementing our various strategies to improve influenza surveillance.

HHS and other agencies can use the interactive tool to compare and help select strategies of interest by using their own baseline estimates of the current probabilities and delays for specific countries, and their own follow-up estimates of what is feasible to achieve with the strategies in the short/medium term. In this way, the tool can be used to identify promising strategies for improving global influenza surveillance.

The utility of the tool is based on having realistic input values and interpreting the implications of the tool's outputs. Obtaining accurate estimates of input values may be difficult. The attractiveness of some strategies may depend heavily on the values chosen, while other strategies may be less sensitive to changes in the input values. Users should vary the input parameters across a range of values and see the effect it has on outcomes.

Although the tool's calculations can suggest promising strategies in quantitative terms, practical public health considerations must also come into play to help balance desired outputs with the realities of cost, labor and time required for the implementation of different strategies. Such considerations can, in turn, inform policy and guide resource allocation and programming. Because the tool is interactive (provided as a software-based tool to HHS), HHS decision makers can use it to examine a wide range of scenarios and input values, based on data from their own programs, to help guide their programming in specific countries or across countries.



## 5. LEVERAGING STRATEGIC PARTNERS: IDENTIFYING PARTNERSHIP OPPORTUNITIES

Our conceptual framework for improving global influenza surveillance, described in Chapter Three, highlights the significant extended reach that HHS and the U.S. government more broadly can achieve by leveraging strategic partners. Moreover, the framework suggests what kinds of partners can address specific surveillance requirements and thus contribute to implementation of specific tactical strategies. This chapter answers our third policy question: *How can HHS identify strategic partners to extend global influenza surveillance?*

After describing the overseas programming of HHS and other U.S. government agencies, we focus on potential partners and the geographic distribution of their current programming. The discussion serves as a basis to identify opportunities for strategic partnerships that HHS and, more broadly, the U.S. government can seek to establish.

### RAND METHODOLOGY

We collected information on the distribution of overseas programming, by country, sponsored by a number of selected U.S. government agencies, multilateral organizations, laboratory networks, foreign development agencies, and nongovernmental and other organizations. We obtained this information through one or a combination of the following sources: public access official websites, annual reports issued by U.S. government agencies and nongovernmental organizations, and U.S. government official databases. The information is presented in a detailed table in Appendix B and through maps generated using geographic information system (GIS) software. Uni-dimensional maps were constructed to describe the global programming presence of individual organizations. Composite maps were constructed to display the presence of multiple organizations of a given type in each country. The maps and table provide the basis for the illustrative analyses presented at the end of this chapter.

### HHS OVERSEAS PROGRAMMING

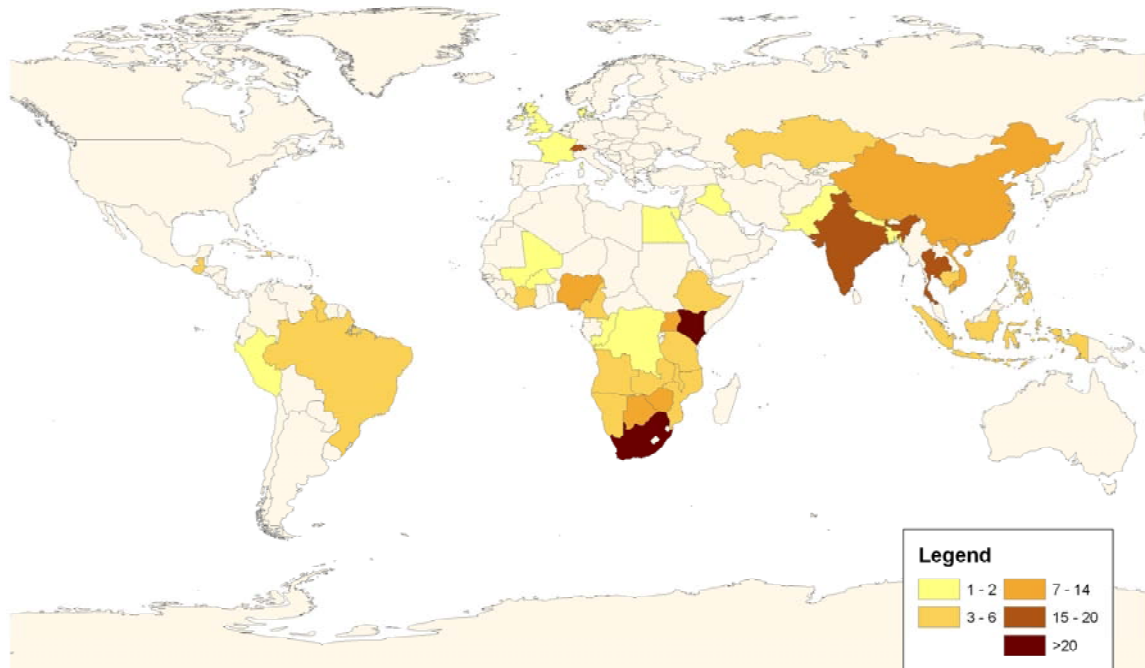
HHS has a long history of international health work, with international surveillance activities carried out primarily through CDC's direct work in other countries and with international organizations such as the World Health Organization (WHO). HHS has been instrumental in helping to build public health infrastructures in foreign countries to meet international standards. Other HHS international work includes the National Institutes of Health's research support for foreign academic institutions and the Food and Drug Administration's regulatory efforts related to imported food, drugs, and other biologic products and devices. While both of these agencies carry out international surveillance work, neither is directly involved in global influenza surveillance.

HHS maintains a database of all staff members posted in foreign countries and provided the RAND team with an extract of this database. As of April 2006, HHS had 249 existing and planned staff positions in

42 different countries (St. Louis, 2006a). The map shown in Figure 5.1 depicts the countries in which HHS has placed long-term staff across all program areas.

Below we highlight an HHS international program that is particularly relevant to global influenza surveillance, that is, beyond current HHS programming that is directly and explicitly related to global influenza.

**Figure 5.1 HHS Presence Overseas: Number of In-Country Staff**



SOURCE: St. Louis (2006a)

### Field Epidemiology Training Programs

The goal of the Field Epidemiology Training Programs (FETP; these are also known as Field Epidemiology and Laboratory Training Programs, FELTP) is to build a strong public health infrastructure in foreign countries by building institutional capacity within their Ministries of Health in epidemiologic investigation, surveillance and response, and to train public health officers to make evidence-based decisions. These programs are modeled after the Epidemic Intelligence Service (EIS), CDC's longstanding applied epidemiology training program. Like EIS, the FETP is a 2-year training and service program designed for health professionals in entry- or mid-level positions and intended to build capacity in applied epidemiology and enhanced public health practice (CDC, 2006c).

FETP trainees have conducted investigations in a wide range of public health areas, including vaccine-preventable disease, diarrheal disease, malaria and other vector-borne disease, human immunodeficiency virus, Ebola virus, occupational and environmental health-related problems, chronic disease, cancer, injuries,

disasters, and nutrition. Furthermore, around 95% of all FETP graduates remain in government service as public health practitioners at local, district, provincial, and national levels of the public health system (CDC, 2006c).

FETPs have been undertaken in Argentina, Brazil, Central America, Central Asia, China, Egypt, Germany, Ghana, India, Italy, Japan, Jordan, Kenya, Mexico, Philippines, Saudi Arabia, Spain, Taiwan, Thailand, Uganda, and Zimbabwe.

## **OTHER U.S. GOVERNMENT AGENCIES**

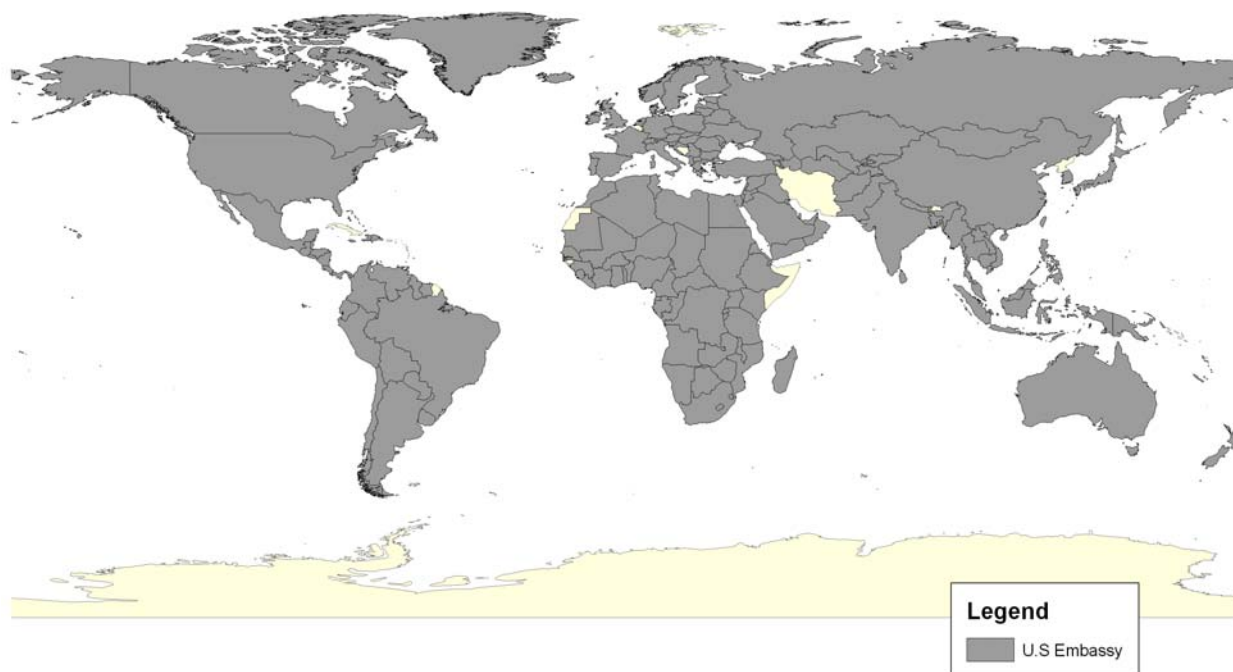
A number of federal agencies also currently play a key role in pandemic influenza preparedness and control and have strong programming presence in other countries. Linking the strengths of each agency to specific strategies to improve global influenza surveillance can help federal partners leverage each other's strengths and extend the reach of U.S. government efforts overall. Below we highlight the role and overseas presence of these key agencies.

### **Department of State**

According to the NSPI *Implementation Plan* (Homeland Security Council, 2006), the Secretary of State is responsible for coordinating the international response to a pandemic. In May 2006 the State Department established an internal Avian Influenza Action Group (Department of State, 2006a) that is charged with leading U.S. Government efforts to advance the international objectives defined by the President's *National Strategy for Pandemic Influenza* (Homeland Security Council, 2005). With the launch of the NSPI *Implementation Plan*, the Action Group is also responsible for the State Department's 83 specific actions to implement the U.S. international engagement strategy based on preparedness and communication, surveillance and detection, and response and containment (Department of State, 2006a).

In September 2005, President Bush announced the International Partnership on Avian and Pandemic Influenza (Department of State, 2005). The Partnership brings together key nations and international organizations to improve global readiness by elevating the issue on national agendas; coordinating efforts among donor and affected nations; mobilizing and leveraging resources; increasing transparency in disease reporting and surveillance; and building capacity to identify, contain, and respond to a pandemic influenza. The State Department has been one of the key federal agencies to spearhead this International Partnership.

**Figure 5.2 Department of State Embassies**



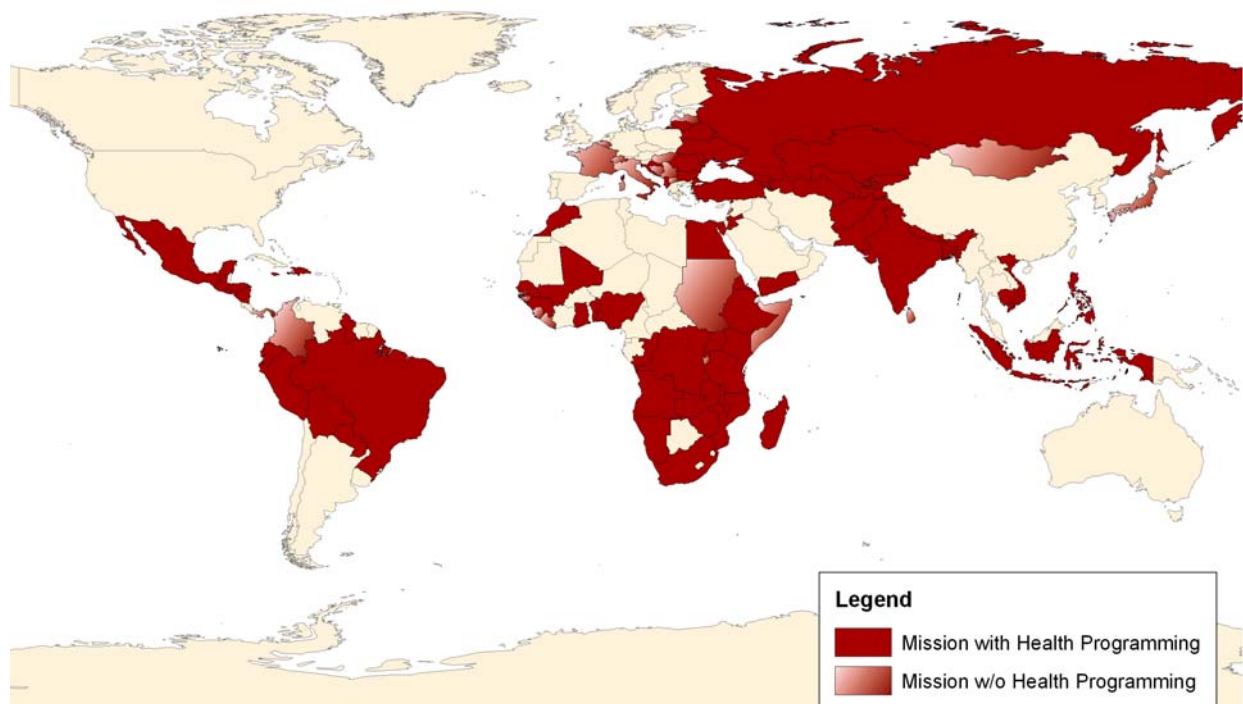
SOURCE: Department of State (2006b)

Currently, the State Department has embassies in almost every country in the world (Figure 5.2). This extensive reach is a potential asset that could be leveraged to improve surveillance around the world, particularly transparency in surveillance reporting and sharing of viral specimens and genome sequencing information.

### **U.S. Agency for International Development**

The United States Agency for International Development (USAID) is the primary organization responsible for most non-military U.S. foreign aid. This aid supports economic growth, agriculture, and trade; global health; and democracy, conflict prevention, and humanitarian assistance. USAID provides assistance to Sub-Saharan Africa, Asia and the Near East, Latin America and the Caribbean, and Europe and Eurasia (USAID, 2006a). USAID has in-country missions in at least 89 developing countries worldwide (Figure 5.3).

**Figure 5.3 United States Agency for International Development (USAID) Missions**



SOURCE: USAID (2006d)

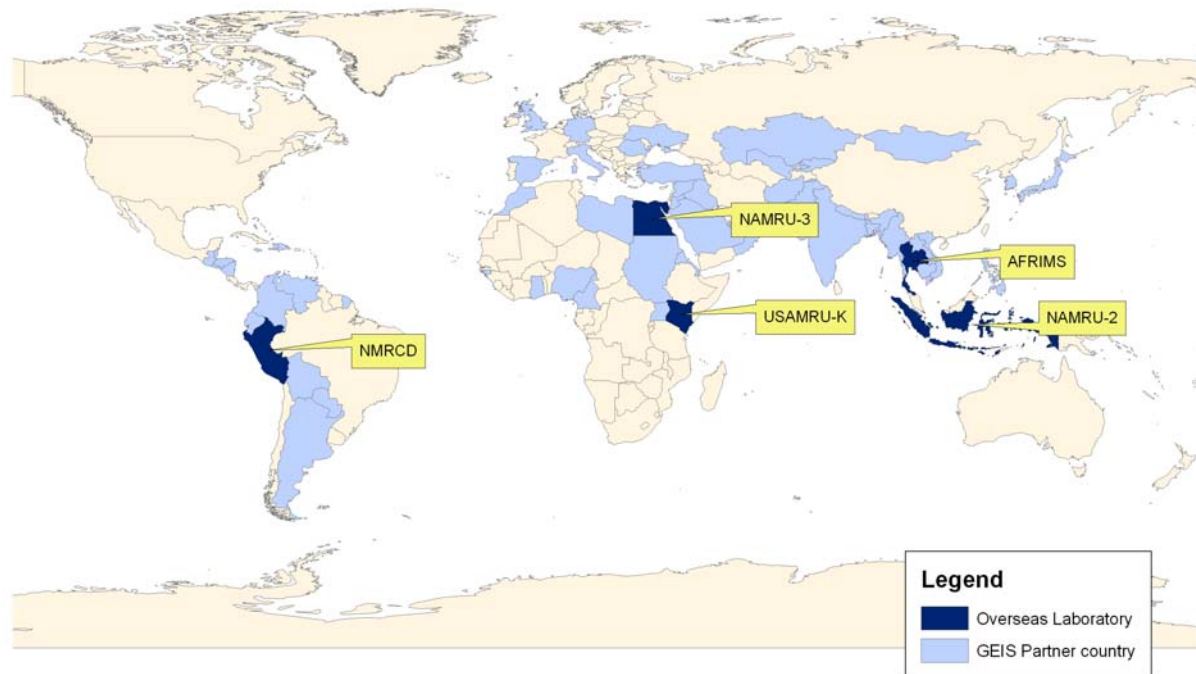
USAID bases its public health surveillance strategy on building local capacity to collect, analyze, and use information. The primary focus areas for USAID support in this area are: incorporating behavioral change strategies into strengthening information use; improving diagnostic capability; developing country-based field epidemiology skills; improving the ability to act on surveillance information and respond effectively; and developing appropriate analytical tools for local use (USAID, 2006c). With regard to influenza, USAID is responsible for 31 actions under the NSPI *Implementation Plan*, all international in scope. These actions include ten related to international surveillance and detection; for six of these ten, USAID has sole or co-lead responsibility. According to the Agency, it is currently implementing \$155 million in foreign assistance for avian influenza response and preparedness (USAID, 2006b).

Like the State Department, USAID's presence in so many countries, in addition to its current health programming and grassroots level orientation, makes it a particularly valuable partner to help improve global influenza surveillance, particularly surveillance coverage, e.g., village based reporting, and quality, e.g., through epidemiology and laboratory training.

## Department of Defense

The mission of the Department of Defense Global Emerging Infections Surveillance and Response System (DoD-GEIS) is to support and coordinate DoD global surveillance, training, public health research, and outbreak response capabilities for microbial threats impacting the health of U.S. forces worldwide and national security. In addition to disease surveillance, GEIS projects support outbreak response preparation, outbreak detection, clinical investigation, microbial agent identification, and communicable disease control and prevention. The priority areas for surveillance and response set out by GEIS include respiratory illness (especially influenza), gastroenteritis, febrile illness (e.g., dengue and malaria), antimicrobial resistance, and sexually transmitted infections. The DoD supports GEIS through five in-country laboratories: the U.S. Army Medical Research Unit-Kenya (USAMRU-K) in Kenya; the Air Force Research Institute for the Medical Sciences (AFRIMS) in Thailand; the Naval Medical Research Unit-3 (NAMRU-3) in Egypt; the Naval Medical Research Unit-2 (NAMRU-2) in Indonesia; and the Naval Medical Research Center Detachment (NMRC) in Lima, Peru (Sanchez, 2006). A sample of activities sponsored by these DoD overseas research laboratories includes civilian and service member specimen collection, regional influenza-like illness surveillance, animal surveillance, research, and regional capacity building for laboratory surveillance and response. The DoD-GEIS international surveillance efforts target regions of increased threat to U.S. military personnel, regions with limited surveillance capability and elevated levels of disease risk or activity.

**Figure 5.4 Department of Defense Global Emerging Infections System**



SOURCES: DoD (2004;2005). Erikson (2006), Sanchez (2006)

**Direct and indirect programming presence of DoD-GEIS.** The five overseas laboratories mentioned above partner with Ministries of Health and in the case of Thailand and Peru, the Royal Thai Army and the Peruvian Navy, respectively, to collect, characterize, and analyze civilian and service member specimens. Each laboratory has a permanent presence characterized by robust collaborative relationships with host countries. Regionally, USAMRU-K, AFRIMS, NAMRU-2, NAMRU-3, and NMRCDC are involved in a variety of projects with a substantial number of countries (Figure 5.4).<sup>4</sup> Partnerships with neighboring countries involve consideration of public health needs and political issues and may be characterized by limited in-country presence particularly for capacity building initiatives.

**Current avian/pandemic influenza initiatives.** A number of projects and initiatives are underway and being sponsored by DoD-GEIS in an effort to collaboratively detect and respond to avian influenza as well as prepare for a human influenza pandemic. Projects focused on capacity and capability development include diagnostic and viral sequencing training; outbreak and case investigation support; migratory bird surveillance; and laboratory infrastructure development. In addition to these projects, DoD-GEIS plans to expand surveillance initiatives to include sentinel surveillance in at least 65 countries with expansion to countries in Latin America, Eastern Europe and the Middle East, Africa and South-Southeast Asia. In FY06 AFRIMS, NAMRU-2, USAMRU-K, and NMRCDC established cooperative projects with partners in Nepal, Myanmar, Thailand, Philippines, Cambodia, Laos, Singapore, Uganda, and Cameroon as part of the DoD-GEIS Avian/Pandemic influenza supplemental plan (Sanchez, 2006).

DoD-GEIS is also responsible for the implementation and oversight of 6 tasks or actions under the NSPI *Implementation Plan* for pandemic influenza preparedness and response, which are also part of the DoD's pandemic influenza implementation plan.

## Department of Agriculture

The U.S. Department of Agriculture (USDA) works together with federal, state, and industry partners to protect the United States against the rapid spread of highly pathogenic H5N1 avian influenza. Safeguards include trade restrictions, wild bird monitoring, federal-state-industry testing of poultry, federal inspection programs at slaughter and processing plants, and rapid response plans (USDA, 2006d).

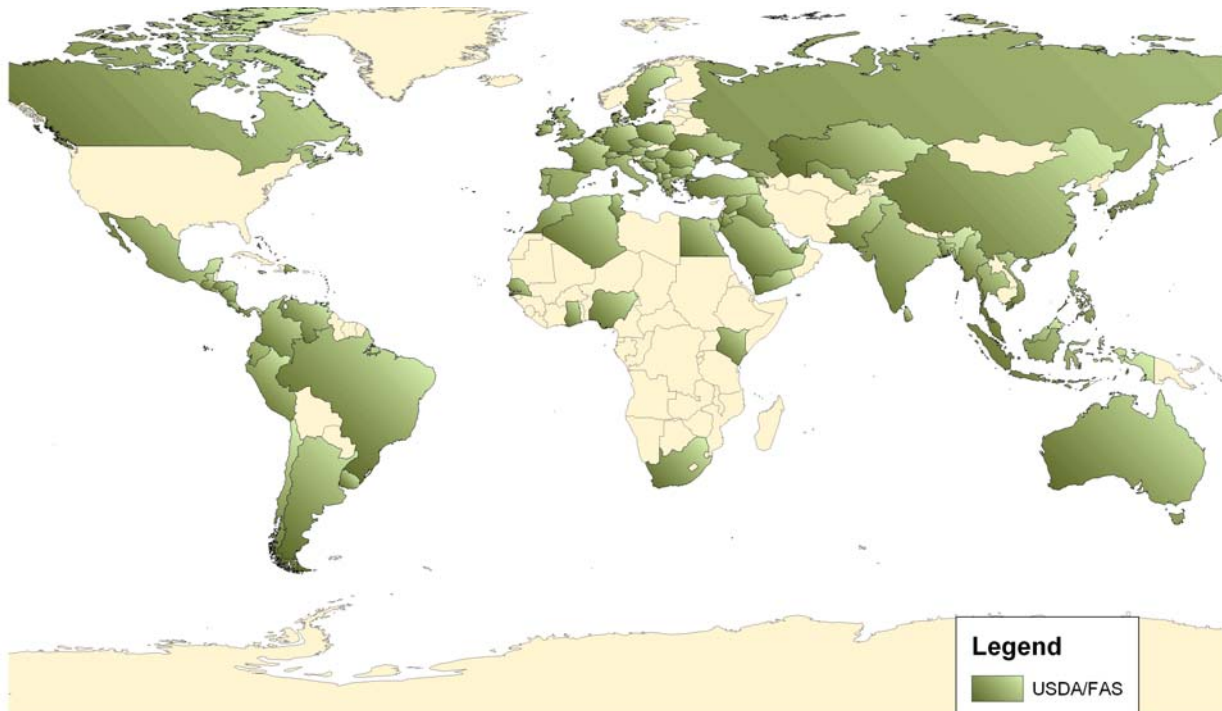
The NSPI *Implementation Plan* directs USDA to play either a leadership or coordinating role in 98 critical actions as the lead agency on avian influenza in poultry (USDA, 2006d). Most importantly, “the

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<sup>4</sup> In FY2005 DoD-GEIS established cooperative projects, capacity building, or training activities related to influenza with the following countries: Azerbaijan, Bolivia, Cameroon, Ecuador, Egypt, El Salvador, Georgia, Germany, Guatemala, Honduras, Indonesia, Iraq, Japan, Kazakhstan, Kenya, Kuwait, Kyrgyzstan, Laos, Mexico, Myanmar, Nepal, Nigeria, Oman, Peru, Qatar, South Korea, Saudi Arabia, Singapore, Syria, Thailand, Ukraine, Uganda, Uzbekistan, and Yemen. In FY06, continued expansion of influenza surveillance efforts was undertaken in a total of at least 53 countries with over 200 sentinel surveillance sites worldwide (Figure 5.4).

National Implementation Plan assigns responsibility to the USDA for leading the Federal Government’s animal health efforts to combat highly pathogenic H5N1 avian influenza worldwide” (USDA, 2006c: p. 2). This responsibility includes initiatives such as continuing to support the coordinated efforts overseas to slow the spread of the disease in poultry; expanding USDA’s domestic testing and early warning systems; and ensuring USDA has a strong plan in place to rapidly and decisively respond to a detection of highly pathogenic H5N1 in U.S. poultry, in coordination with states and industry.

**Figure 5.5 U.S. Department of Agriculture Foreign Agricultural Service**



SOURCE: USDA (2006b)

Currently, USDA is implementing a \$21 million program of international activities including emergency response and technical capacity building (USDA, 2006c). Some examples of current internationally oriented influenza activities include: training veterinary laboratory diagnosticians from around the world to use various diagnostic tests to detect highly pathogenic avian influenza; and providing expertise and funding to assist the United Nations Food and Agriculture Organization with a new Emergency Centre for Transboundary Animal Diseases (ECTAD) to improve response to avian influenza outbreaks worldwide. Since February 2006, USDA has conducted three international H5N1 Influenza Testing Diagnostic Courses at the National Veterinary Service Laboratories (NVSL) in Ames, Iowa, where 99 specialists from 62 countries participated. In addition, USDA is establishing offices and personnel in China, Laos, Cambodia, Thailand (already established), and Indonesia. These offices will be dedicated to avian influenza activities and wherever possible, co-located with offices of the CDC (USDA, 2006c).

**USDA Foreign Agricultural Service.** The Foreign Agricultural Service (FAS) of the USDA has primary responsibility for USDA's international activities including market development, trade agreements and negotiations, and the collection and analysis of market information (USDA, 2006a). FAS agricultural counselors, attaches, trade officers, and locally employed FAS staff are stationed in over 90 countries (Figure 5.5), making the FAS another valuable partner to help improve surveillance around the world, particularly related to animal health.<sup>5</sup>

## Peace Corps

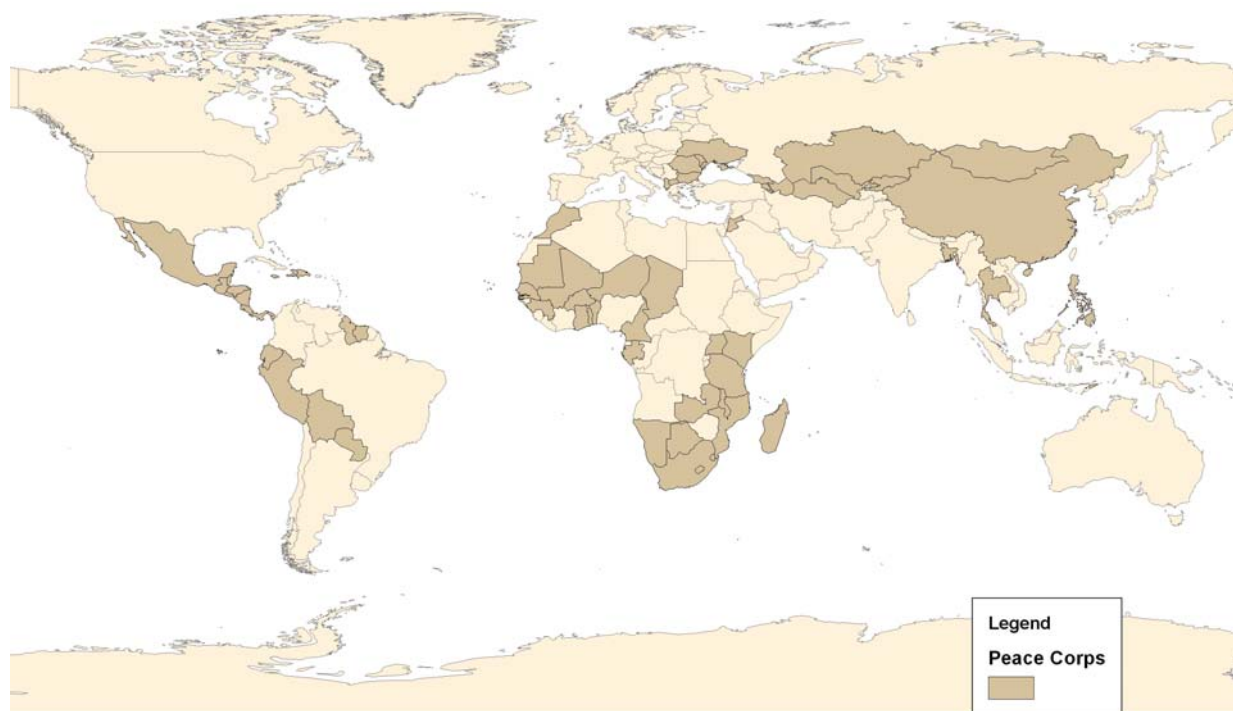
The Peace Corps has trained 182,000 Volunteers to date in 128 countries (Peace Corps, 2006c). One of the six major areas where Volunteers work is in the area of health. Health programming includes health extension, public health education, water and sanitation extension, and HIV/AIDS. Most of these efforts focus on grass roots prevention, capacity building, and education.

Since 2002, the Peace Corps Office of Medical Services has been working on plans to prepare and protect Peace Corps Volunteers around the world against an influenza outbreak (Peace Corps, 2006a). Peace Corps Medical Officers (PCMOs) are the primary health care providers for Peace Corps Volunteers. There are currently more than a hundred PCMOs worldwide, and close to 70% are recruited and contracted in the host countries (Peace Corps, 2006b).

While the Peace Corps does not currently focus on influenza programming as a major area, the number of Volunteers and the breadth of countries in which the Peace Corps operates would make it a helpful partner in U.S. government efforts to increase geographic surveillance coverage around the world (see Figure 5.6), especially through village-based surveillance. Peace Corps Volunteers are usually more embedded in local communities than in-country staff of other U.S. government agencies, and thus they could be a vital resource in helping to detect an influenza outbreak extremely early. By training Volunteers in how to work with communities and detect the symptoms of influenza, and by engaging the 100 PCMOs around the world to report influenza incidents, the Peace Corps could contribute significantly to early detection of community-level outbreaks, thus contributing to both surveillance coverage and timeliness.

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<sup>5</sup> A full examination of ways to improve global influenza surveillance in animals is beyond the scope of this project and beyond the purview of HHS. Nonetheless, descriptions of key organizations relevant to animal influenza surveillance are highlighted in this report. In addition to the USDA activities described here, the work of two international organizations—the World Organization for Animal Health, and the Food and Agriculture Organization—are described in the next section.

**Figure 5.6 Peace Corps**

SOURCE: Peace Corps (2006d)

## INTERNATIONAL ORGANIZATIONS

International organizations comprise member governments, many within the United Nations (UN) system. While several UN agencies address health issues, perhaps the most relevant for purposes of global influenza surveillance are the World Health Organization, the World Organization for Animal Health, and the Food and Agriculture Organization. The first of these organizations focuses on human health, and the last two focus on animal health.<sup>6</sup> All three are described briefly below.

### World Health Organization

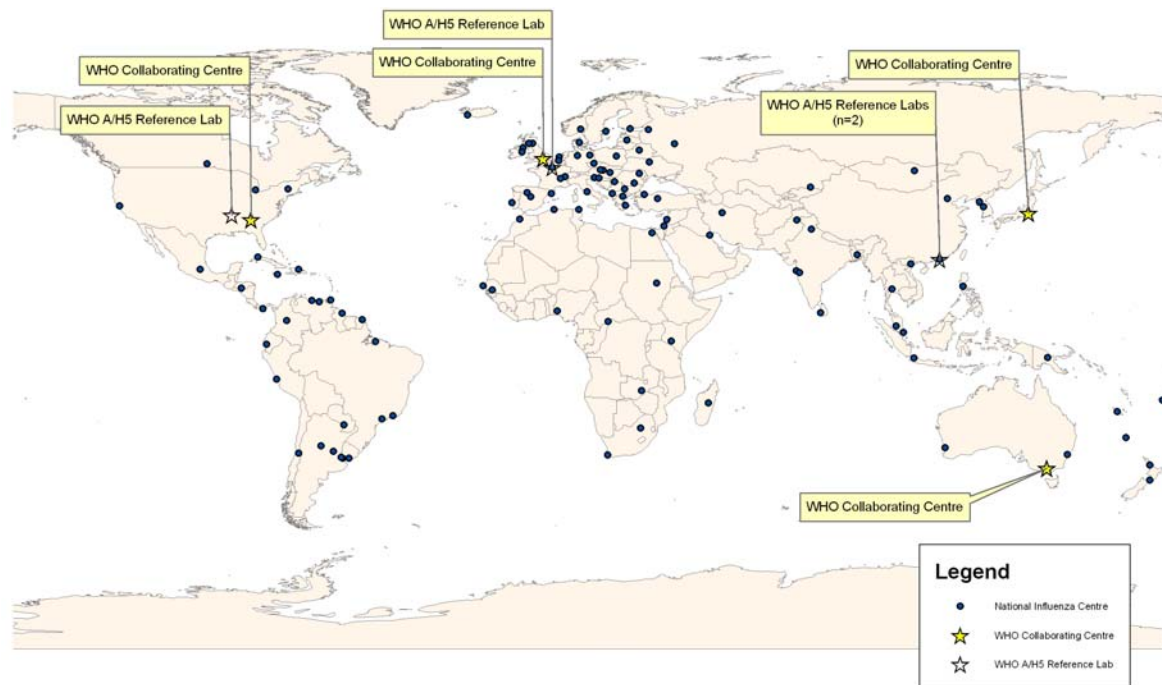
The World Health Organization (WHO) was established in 1948 and currently comprises 192 Member States. Ministers of Health represent their respective governments in the WHO's executive body, the World Health Assembly, which meets annually to review pressing issues, set WHO policy and budget, and direct WHO initiatives. The WHO Global Influenza Surveillance Network is highlighted below.

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<sup>6</sup> Again, while influenza surveillance in animals is beyond the purview of HHS and the scope of this report, these organizational descriptions are included for purposes of completeness.

**WHO Global Influenza Surveillance Network.** The WHO Global Influenza Surveillance Network was established in 1952 and contributes to decisions regarding the composition of the annual influenza vaccine. The network includes four WHO Collaborating Centres (WHO CCs) and 116 institutions in 87 countries that are recognized as WHO National Influenza Centres (WHO NICs). An additional four laboratories have been designated as Influenza A/H5 Reference Laboratories (see Figure 5.7). WHO NICs routinely collect specimens in their country, and perform primary virus isolation and preliminary identification. They send strains to WHO CCs for high-level antigenic and genetic analysis to inform the composition of annual influenza vaccines and as a global alert mechanism to monitor the emergence of new strains with pandemic potential.

**Figure 5.7 World Health Organization (WHO) Global Influenza Surveillance Network**



SOURCE: WHO (2006b; 2006d)

## Food and Agriculture Organization

The Food and Agriculture Organization (FAO) of the United Nations directs international efforts against hunger, serving both developed and developing countries. The FAO has four main roles: 1) it serves as a knowledge network whose staff collect, analyze, and disseminate data that aid development; 2) it shares policy expertise with member countries; 3) it provides a neutral forum for policy-makers and experts from around the world; and 4) it brings knowledge to the field (FAO, 2006b). The FAO's Animal Production and Health Division is entrusted with FAO's program on animal production, animal health, and related information and policy work (FAO, 2006c).

With regard to avian influenza, FAO has chosen to invest donor funds in five major categories: supplies and equipment, human resources, training, studies, and support services (FAO, 2006a). In July 2004, FAO convened an expert meeting on surveillance and diagnosis of avian flu in Bangkok. The product of this meeting was a set of guiding principles for highly pathogenic avian influenza surveillance and diagnostic networks in Asia (FAO, 2004). In West Africa, FAO worked with the African Union's Program for the Control of Epizootics to set up regional networks of laboratories and surveillance teams and organized regional workshops on bird flu control (FAO, 2006d).

## **World Organization for Animal Health**

The World Organization for Animal Health (OIE, Office International des Epizooties) has more than 167 member countries and five missions related to animal health. The OIE's stated objectives are: "to ensure transparency in the global animal disease and zoonosis situation; to collect, analyze, and disseminate scientific veterinary information; to provide expertise and encourage international solidarity in the control of animal diseases; to safeguard world trade by publishing animal health standards for international trade in animals and animal products; to improve the legal framework and resources of national Veterinary Services; to provide a better guarantee of the safety of food of animal origin and to promote animal welfare through a science-based approach" (OIE, 2006a).

Highly pathogenic avian influenza is one of the animal diseases that is reportable to the OIE. The OIE publishes significant epidemiological events immediately, and publishes data weekly, monthly, and annually. The OIE's structure is similar to that of WHO. The OIE has seven Reference Laboratories that deal with highly pathogenic avian influenza. Those laboratories are located in: Canada, Germany, United Kingdom, Australia, United States, Italy, and Japan (OIE, 2006b). In addition, the OIE has 20 Collaborating Centres with expertise in a specific sphere of competence relating to animal health issues (e.g., epidemiology, risk analysis, etc.) (OIE, 2006c).

## **FOREIGN LABORATORY NETWORKS**

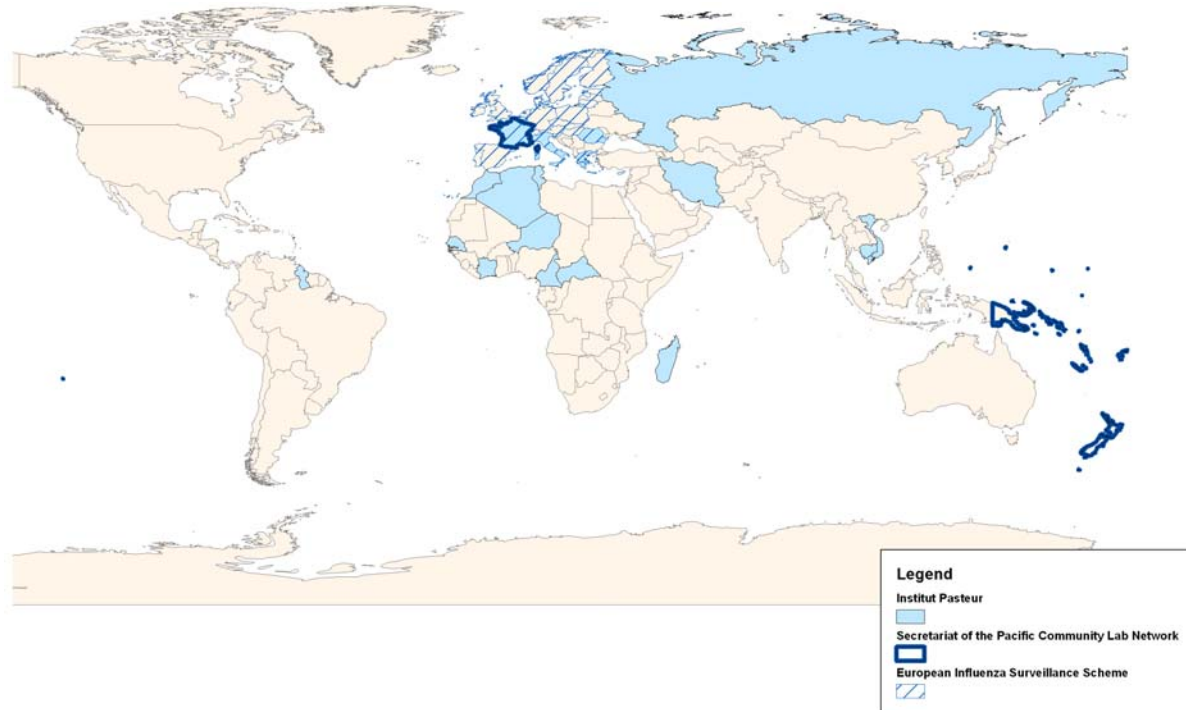
A few foreign governments sponsor laboratory networks across a range of countries around the world. Three illustrative examples of foreign laboratory networks are described below, and Figure 5.8 shows the coverage of each network. Such networks could be important partners for helping to build influenza laboratory capacity, and hence improving surveillance quality.

### **Institut Pasteur**

The Institut Pasteur is a non-profit foundation dedicated to the prevention and treatment of infectious diseases through biological research, education, and public health activities. Institut Pasteur facilities comprise eighteen National Reference Laboratories and one WHO Collaborating Centre; these are observatories

nominated by the French Health Secretary and by WHO to help monitor epidemics and to control outbreaks of infectious diseases (e.g., hepatitis, HIV, influenza, meningitis, listeriosis, salmonella infections, rabies).

**Figure 5.8 Foreign Laboratory Networks**



SOURCES: EISS (2006c), Institut Pasteur (2003), SPC (2006e)

In February 2006, HHS established a Memorandum of Understanding with the Institut Pasteur to carry out joint activities, beginning in Southeast Asia, to strengthen global capacity to detect influenza viruses that could have the potential to trigger a human pandemic. HHS and Institut Pasteur are currently developing collaborative projects including capacity building in the areas of surveillance, epidemiological investigation, testing, diagnosis, and control of infectious disease in countries affected by and at-risk for the spread of the H5N1 influenza strain. They are exchanging technical expertise to foster rapid response to disease threats, and disseminating effective and accurate public information on infectious disease, including in the local language in developing countries (HHS, 2006).

### European Influenza Surveillance Scheme

All 25 European Union Member States, Norway, Romania, and Switzerland participate in the European Influenza Surveillance Scheme (EISS). To further enhance its work, the EISS Coordinating Centre maintains the Community Network of Reference Laboratories (CNRL) for Human Influenza in Europe, which dates back to an effort to perform influenza surveillance through sentinel networks started in 1996 with seven European countries. The CNRL currently includes 38 laboratories in 28 countries (EISS, 2006a). The objective of CNRL is to provide high quality reference services for human influenza surveillance, early

warning, and pandemic preparedness in Europe. Through the Network, accurate virological data is reported to EISS and then to the European Union, to national health professionals, and to the general public (EISS, 2006b). EISS also publishes a weekly surveillance report on influenza activity in 29 countries that is based on data reported by roughly 13,000 sentinel physicians and covers a population of 457 million people (EISS, 2006e). With regard to current influenza activities, the EISS Coordinating Center is implementing the European Commission working paper on Community Influenza Pandemic Preparedness and Response Planning in an effort to prepare a pandemic protocol that will be used to identify gaps in the CNRL network (EISS, 2006d). EISS could prove valuable for cooperation and/or information exchange regarding influenza in the countries encompassed by EISS.

### **Secretariat of the Pacific Community**

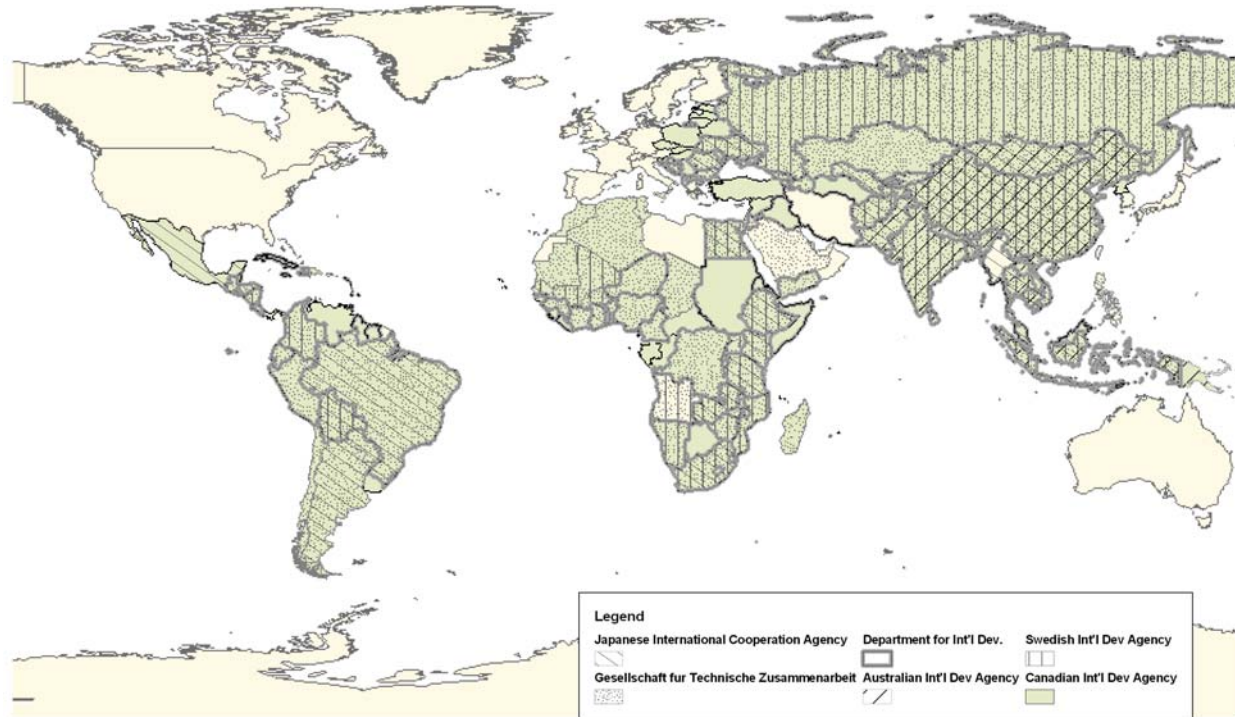
The Secretariat of the Pacific Community (SPC) is an international organization that aims to develop technical assistance; professional, scientific, and research support; and planning and management capabilities to the people of the Pacific Islands (SPC, 2006f). The SPC and WHO created the Pacific Public Health Surveillance Network (PPHSN) in 1996 in an effort to improve surveillance and response in the Pacific Islands. The services provided by PPHSN include PacNet, LabNet, EpiNet, and PICNet. PacNet is a listserv utilized for alert and communication regarding outbreak preparedness (SPC, 2006d). LabNet is a network of existing public health laboratories that provides support to all Pacific Island countries for six initial target diseases (dengue, measles, influenza, leptospirosis, cholera, and typhoid). Public health laboratories in the Fiji Islands, French Polynesia, Guam, and New Caledonia are further supported by reference laboratories on the Pacific-rim countries (SPC, 2006c). EpiNet consists of National EpiNet Teams, nominated by health authorities, that network and coordinate for surveillance and response activities. EpiNet also establishes and maintains disease surveillance and response protocols (SPC, 2006b). Finally, the Pacific regional Infection Control Network (PICNet) is an effort by PPHSN to improve communication, accessibility of expertise, and technical advice. PICNet is still in its infancy, but its main goal is to improve communications among infection control professionals (SPC, 2006a). As with EISS, SPC could be a valuable partner for cooperation and information exchange with HHS and the U.S. government related to influenza surveillance and laboratory capacity in SPC's regional coverage area.

### **FOREIGN DEVELOPMENT AGENCIES**

A number of industrialized countries provide development assistance to lower income countries through agencies that are counterparts to the U.S. Agency for International Development (USAID). Most of these agencies have current health programming and represent potential opportunities for USAID and other U.S. government agencies to consider cooperation related to global influenza surveillance. They may be well suited to contribute to surveillance coverage, e.g., village-based surveillance, and surveillance quality, e.g.,

through training. Example of such foreign development agencies are described below. Figure 5.9 indicates the countries where each of these agencies has current programming.

**Figure 5.9 Foreign Development Agencies**



SOURCES: AusAid (2006b), CIDA (2006c), DFID (2006b), SIDA (2006b), JICA (2006a), GTZ (2005).

### **Australian Agency for International Development**

In November 2005, the Australian Agency for International Development (AusAID) announced that it would commit \$100 million to increase assistance for surveillance, quarantine, and outbreak and infection control of avian influenza in the Asia-Pacific region (AusAID, 2006c). AusAID also supports WHO activities in the Asia-Pacific region in priority areas of communicable and non-communicable disease prevention and treatment, child survival, and strengthening national health systems. In 2006-2007, Australia will provide nearly \$3 billion worth of official development assistance, an increase of \$455 million over the 2005-2006 figure of \$2.5 billion (AusAID, 2006a).

### **Canadian International Development Agency**

The Canadian International Development Agency (CIDA) has identified health as a programming priority (CIDA, 2006a). CIDA's Agenda for Action on Global Health, announced in September 2005, focuses on two issues: poverty-linked diseases such as HIV/AIDS, tuberculosis, and malaria; and support for health systems (CIDA, 2006b). CIDA's work is concentrated in the poorest countries in Africa, Asia, and Latin

America, and the agency supports projects in more than 150 countries, which represent 80% of the world's population.

### **Department for International Development**

The Department for International Development (DFID) is charged with managing the United Kingdom's aid to developing countries. DFID has 64 offices overseas and a staff of over 2500, almost half of which works overseas (DFID, 2006a). DFID has made the United Nations' Millennium Development Goals the main focus of its mission. The health components of the Millennium Development Goals include reducing child mortality; improving maternal health; and combating HIV and AIDS, malaria, and other diseases.

### **Swedish International Development Cooperation Agency**

The Swedish International Development Cooperation Agency (SIDA) has a staff of nearly 760 people, 172 of whom work abroad in field offices in 50 countries (SIDA, 2006a). SIDA's health programming focuses on HIV/AIDS and the intersections of health and development (development of health systems and public health). At its core is cooperation for better health care with the Ministries of Health in the various countries. Half of SIDA's bilateral development cooperation involves countries in Africa (SIDA, 2006c).

### **Japan International Cooperation Agency**

The Japan International Cooperation Agency (JICA) currently maintains offices in about 100 countries worldwide (JICA, 2006a). JICA's health initiatives fall into four broad categories: measures against infectious diseases; maternal and child health, and reproductive health; development and restoration of health systems; and human resource development (JICA, 2006b). The Agency's activities include the dissemination of knowledge about the prevention, detection, and treatment of infectious diseases, and support for human resource development in these areas.

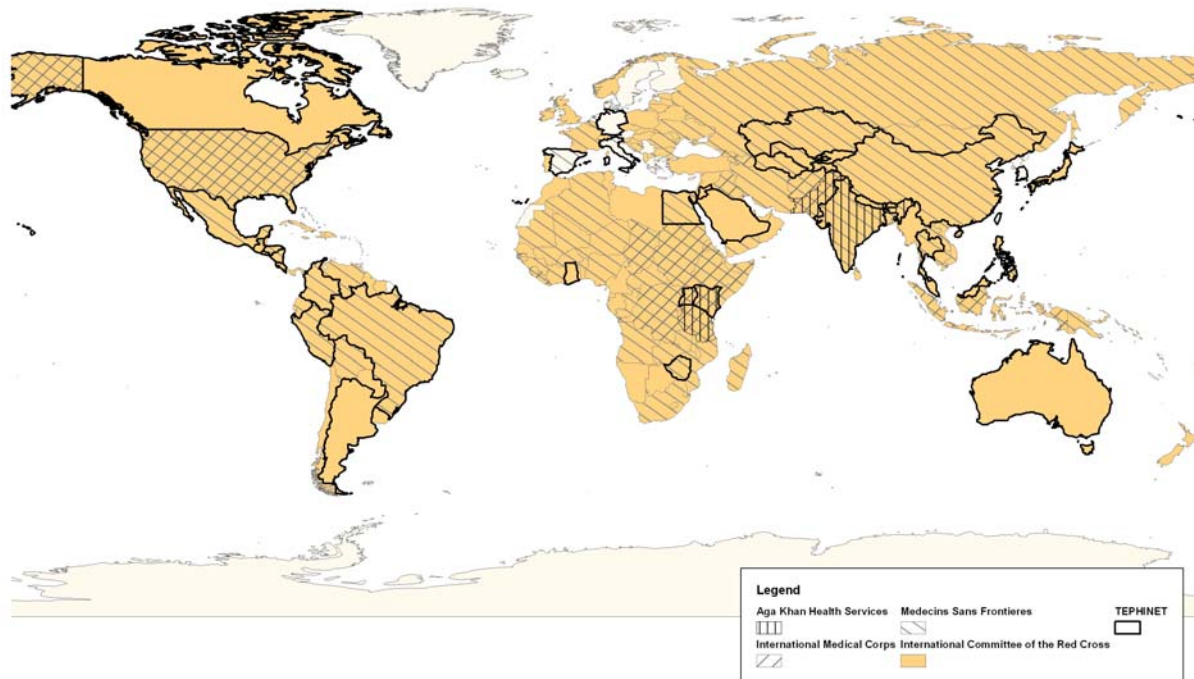
### **Deutsche Gesellschaft für Technische Zusammenarbeit**

The Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ), Germany's development assistance agency, is active in over 130 countries in Africa, Asia, Latin America, the transition countries in Eastern Europe, and the Commonwealth of Independent States; it has its own offices in 67 countries (GTZ, 2006b). One of GTZ's primary themes is social development, including health and population, as well as HIV and AIDS. GTZ contributes to the following health initiatives in more than 80 countries: sexual and reproductive health; reducing sexual exploitation of children; ending female genital mutilation; HIV/AIDS; AIDS in the workplace; special initiatives for HIV/AIDS, TB, and malaria; and development-oriented drug control (GTZ, 2006a).

## NONGOVERNMENTAL AND OTHER ORGANIZATIONS

Nongovernmental organizations (NGOs) often play the important role of helping to implement grassroots programs of national governments and foreign donors. These programs offer opportunities to HHS and other U.S. government agencies to help extend their reach particularly related to influenza surveillance coverage. Some NGOs and other organizations can also contribute to surveillance quality. Examples of such organizations are highlighted below. Figure 5.10 indicates the countries in which each has current programming.

**Figure 5.10 Nongovernmental and Other Organizations**



SOURCES: AKHS (2006c), ICRC (2006a), IMC (2006b), MSF (2006b), TEPHINET (2005)

### Aga Khan Health Services

Aga Khan Health Services (AKHS), a component of the Aga Khan Development Network, is one of the most comprehensive health networks in the developing world with 325 health centers, dispensaries, hospitals, diagnostic centers, and community health outlets (AKHS, 2006a). AKHS primarily works in geographically isolated regions of Kenya, Tanzania, India, Pakistan, and Syria. The organization's current major initiatives include: assisting communities to develop, manage, and sustain needed health care; providing accessible medical care in high quality facilities; working in partnership with other agencies to develop communities and enhance their health; educating physicians, nurses, and allied health professionals; conducting research relevant to AKHS institutions; and contributing to the development of national and

international health policy (AKHS, 2006b). Due to its extensive reach into isolated, vulnerable communities, AKHS could help the U.S. government reach areas where it currently does not have a presence.

### **International Committee of the Red Cross**

The International Committee of the Red Cross (ICRC) is based in about 80 countries with a staff exceeding 12,000. While ICRC is primarily a humanitarian organization, it does strive to ensure health care for people affected by war. As part of this effort, the ICRC has been setting up mobile health units to reach isolated populations (ICRC, 2006b). Despite the fact that the ICRC does not place a separate emphasis on health programming, the organization's expertise in dealing with health issues in armed conflicts and post-conflict regions provide a valuable resource that could be enlisted to support disease surveillance in vulnerable populations that are difficult to reach due to regional conflict or instability.

### **International Medical Corps**

The International Medical Corps (IMC) was established in 1984 by volunteer doctors and nurses and focuses on providing health care and medical assistance to local populations. Of all of the organizations discussed thus far, IMC is the most medically focused. Its goal is to provide medical services and medical training to local populations in war-torn or post-conflict regions. IMC health care services are directed at primary health care; mental health; maternal and child health care; health education and training; emergency relief and disaster response; HIV/AIDS; reproductive health care; water and sanitation; reconstructive and rehabilitative surgery; and nutrition services (IMC, 2006a). Their trained medical staff could contribute to surveillance quality by providing technical expertise to clinical and laboratory aspects of influenza surveillance.

### **Médecins Sans Frontières**

Médecins Sans Frontières (MSF) provides emergency medical assistance to populations impacted by natural or manmade disasters. Unlike IMC, which focuses on solely providing medical care, MSF's mandate is broader in that the organization deliberately sets out to be an advocate for victims of conflict and basic human rights abuses (MSF, 2006a). MSF places pressure on human rights abusers by raising awareness among the international community. While MSF does not have specific influenza surveillance programming, the organization's expertise in unstable regions could provide another means by which influenza surveillance could be extended into vulnerable populations.

### **Training Programs in Epidemiology and Public Health Interventions Network**

The Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) is an alliance of field epidemiology training programs (FETPs, described earlier under HHS Overseas Programming) located in thirty-two countries around the world (TEPHINET, 2006c). TEPHINET's stated goals are to: support and strengthen existing field-based training programs in applied epidemiology and public

health practice; link public health professionals participating in the network to organizations responding to public health situations that require competencies in field epidemiology; support the development of new field-based training programs in applied epidemiology and public health practice; and enhance applied public health research activities of field-based training programs in response to public health problems and threats (TEPHINET, 2006a). Issues related to influenza are a component of TEPHINET's activities; for example, trainees with Thailand's International Field Epidemiology Training Program responded to avian influenza outbreaks in humans in Thailand in 2004 (TEPHINET, 2006b).

## **IDENTIFICATION OF STRATEGIC PARTNERSHIP OPPORTUNITIES**

This section applies the information described above to analyses aimed at identification of opportunities for strategic partnerships to extend the reach of HHS and, more broadly, the U.S. government to implement the tactical strategies described in Chapter Three. We describe these analyses within the context of the four surveillance requirements of coverage, quality, timeliness, and transparency.

The mapping used in this chapter serves as an important tool to analyze the presence of government agencies and nongovernmental organizations around the world. HHS can identify partnership opportunities both in countries where HHS has staff and/or active programming and in countries where HHS has little or no current programming. It can identify countries where other agencies or organizations have programming and seek to strategically extend its surveillance reach, potentially at little or no additional cost, by partnering with such organizations.

### **Improving Surveillance Coverage**

As described in Chapter Three, strategies to improve global influenza surveillance coverage include community-based reporting, increasing the number of traditional (clinical) reporting sites, and adding new reporting sources and signals. All of these are heavily oriented toward the local level. Therefore, organizations focusing on local level programming offer greatest promise as strategic partners for HHS and, more broadly, the U.S. government. The technical strengths of HHS do not necessarily position it as strongly as other organizations to contribute substantially to improving surveillance coverage in other countries, since HHS' work is generally not at the grassroots level. However, within the U.S. government, agencies that do focus on local level programming include USAID and the Peace Corps. The global reach of these two agencies is shown in Figures 5.3 and 5.6, respectively. As indicated on these maps, the Peace Corps has programming in some countries where USAID does not, e.g., China, Thailand, Niger, Chad; and USAID has programming in some countries where the Peace Corps does not, e.g., Indonesia, Vietnam, Turkey, Egypt, Pakistan, Democratic Republic of Congo.

Foreign development agencies (Figure 5.9) and nongovernmental organizations (Figure 5.10) may offer additional opportunities for strategic partnerships to increase surveillance coverage, both in countries where USAID and/or Peace Corps currently have programming and in countries where they do not. Such

agencies and organizations could contribute to the development of community-based/village-based alert and response systems and expansion of traditional surveillance reporting sites. Table 5.1 highlights several examples of countries where USAID and/or Peace Corps do not have current programming, but one or more foreign development agencies or NGOs do. Beyond these countries are those with which the United States does not have official in-country presence, e.g., North Korea, Cuba, and Iran, but where some of these foreign agencies and organizations do have current programming (for North Korea: CIDA, SIDA, MSF, ICRC; for Cuba: CIDA, DFID, SIDA, ICRC; for Iran: DFID, SIDA, MSF, ICRC). Depending on epidemiologic priorities and resources, strategic partnerships could help HHS and the U.S. government extend their reach and enhance influenza surveillance coverage in more countries around the world.

**Table 5.1 Sample Countries without USAID and/or Peace Corps Programming and with Programming of Selected Foreign Development Agencies or Nongovernmental Organizations**

Country	USAID	Peace Corps	Foreign Development Agencies	Nongovernmental Organizations
China	No	Yes	AusAID, CIDA, DFID, GTZ, JICA, SIDA	MSF, ICRC, TEPHINET
Thailand	No	Yes	AusAID, CIDA, DFID, GTZ, JICA, SIDA	MSF, ICRC, TEPHINET
DR Congo	Yes	No	CIDA, DFID, GTZ, SIDA	MSF, IMC, ICRC
Laos	No	No	AusAID, CIDA, SIDA	MSF, ICRC
Myanmar	No	No	DFID, JICA, SIDA	ICRC
Papua New Guinea	No	No	AusAID, CIDA, SIDA	MSF, ICRC
Syria	No	No	CIDA, SIDA	ICRC
Algeria	No	No	CIDA, GTZ, SIDA	MSF, ICRC

### Improving Surveillance Quality

Strategies to improve surveillance quality include building laboratory and epidemiology capacity, targeted laboratory testing, and viral strain monitoring. Indeed, Chapter Four makes a strong case for focusing on building laboratory capacity, since laboratory diagnosis is the final common pathway for laboratory diagnosis and confirmation of any novel influenza case. Enhanced in-country laboratory capacity also contributes to surveillance coverage and timeliness. Technical agencies with laboratory and/or epidemiology capacity are of potential strategic value to help improve international surveillance quality. Within the U.S. government, these technical agencies include HHS, USAID (which provides training at the local level), and DoD (especially its GEIS program). Figures 5.1, 5.3, and 5.4 indicate the countries where HHS, USAID, and DoD-GEIS have current staff or programming. Foreign laboratory networks (Figure 5.8) could help HHS with efforts to build laboratory capacity. TEPHINET could help build epidemiology

capacity, and other NGOs could potentially help sensitize health providers regarding targeted laboratory testing (see Figure 5.10). Such partners could be valuable both in countries where HHS, DoD, and/or USAID have current staff or programming as well as in those where they do not. Table 5.2 highlights several countries where key U.S. government agencies do not have current programming, but relevant foreign partners do. In addition, there may be U.S.-based technical groups (not specifically described in this report) that could be contracted to help build laboratory or epidemiology capacity; examples include the Association of Public Health Laboratories and academic institutions such as schools of medicine or public health.

**Table 5.2**  
**Sample Countries without HHS, DoD, and/or USAID Programming and with Programming of Foreign Laboratory Networks or TEPHINET**

<b>Country</b>	<b>HHS</b>	<b>DoD/GEIS</b>	<b>USAID</b>	<b>Foreign Laboratory Network or TEPHINET</b>
Papua New Guinea	No	No	No	SPC
Madagascar	No	No	No	Institut Pasteur
Iran	No	No	No	Institut Pasteur
Russia	No	Yes	Yes	Institut Pasteur
Malaysia	No	No	No	TEPHINET
Turkmenistan	No	No	Yes	TEPHINET

### **Improving Surveillance Timeliness**

Strategies to improve surveillance timeliness include expedited transport of laboratory specimens within countries and from countries to reference laboratories; streamlined notification and analysis; widespread deployment of rapid diagnostic tests; and development and deployment of rapid response teams. U.S. government agencies well suited to help enhance timeliness include HHS and USAID, as well as DoD (rapid reporting through GEIS program), and Peace Corps (to help sensitize community members and health providers to report suspected cases in a timely fashion).

Perhaps the most important international partner in this area is WHO, which coordinates the Global Influenza Surveillance Network, international specimen transport fund, and often the deployment of international rapid response teams. Strengthening the number and capacity of WHO National Influenza Centres, the core of the WHO global influenza surveillance system, is an important strategy to shorten the time required for laboratory diagnosis; it also contributes to surveillance coverage and quality and global laboratory surge capacity. WHO NICs must be properly equipped and trained and undergo regular proficiency testing. According to the most recent WHO survey (WHO, 2002), the level of testing and actual tests performed by WHO NICs are not standardized, and vary greatly across countries worldwide. Desired improvements should include expanding the range of testing capacity to include influenza subtyping and even strain characterization in more countries. Also, rapid specimen transport has focused mostly on transport

from a WHO NIC to a WHO reference laboratory. Countries and their partners should also pay attention to specimen transport from patient to first and subsequent laboratories within countries, at least in those countries where this remains a source of delay in obtaining laboratory results. As shown in Figure 5.7, there are considerable geographic gaps in WHO NIC coverage and hence in the expected timeliness of laboratory testing for influenza characterization from countries without their own WHO NIC. The greatest gaps appear to be in countries in Sub-Saharan Africa, the Middle East, and Eastern Europe. U.S. government agencies such as HHS and USAID can consider investing both technical and financial resources into establishing and strengthening WHO NICs in selected countries and providing funds to the WHO expedited specimen transport fund. U.S. agencies can also coordinate with foreign development agencies and others that may be targeting similar investments.

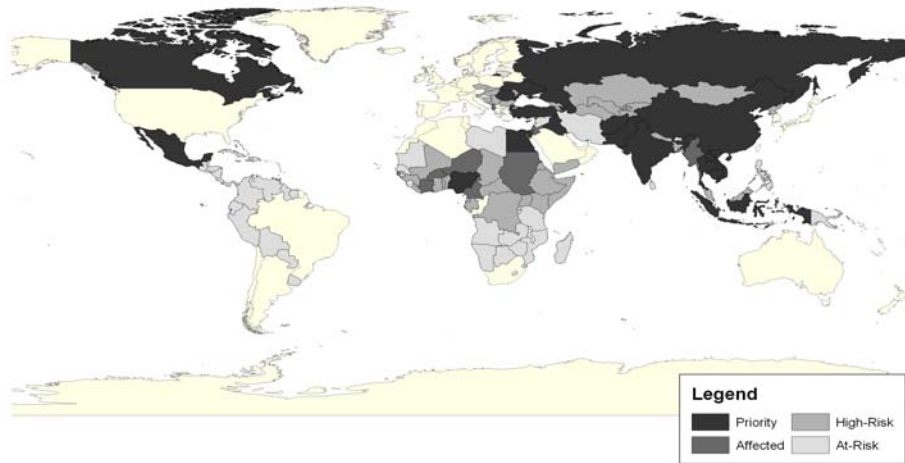
### **Improving Surveillance Transparency**

The main strategy to improve surveillance transparency is provision of incentives or other motivation to openly report suspected cases (in both animals and humans) and to share virus specimens and genome sequencing information. The State Department is probably the best suited U.S. government agency to help address this requirement. The State Department works through diplomatic channels to help exert pressure on national political authorities and multiple ministries/sectors that could be legitimately concerned about economic repercussions associated with public recognition of avian/pandemic influenza in their country, or loss of intellectual property protection through sharing of their virus specimens and information. Also, the State Department can work with other embassies in host countries to further strengthen diplomatic pressure for the transparency required for global influenza surveillance.

### **Partnerships with Priority Countries**

The information presented in this chapter permits examination and planning of strategic partnerships in selected countries, e.g., those designated by the U.S. government as “priority” countries. For purposes of targeting their global activities under the NSPI Implementation Plan, the U.S. government has categorized all countries based on level of priority or risk. These categories are: priority, high risk, affected, low risk, and not applicable (St. Louis, 2006b). Figure 5.11 illustrates which nineteen countries have been designated as priority countries. Table 5.3 shows the U.S. government’s reasons for this designation.

Figure 5.11 U.S. Government Priority Countries



SOURCE: St. Louis (2006b)

**Table 5.3**  
**Priority Countries for U.S. Government Pandemic Influenza Programming**

Country	Reason
Afghanistan	Strategic importance; foreign policy concerns
Azerbaijan	Severity of outbreak
Cambodia	Severity of outbreak; lack of ability to contain disease
Canada	Strategic importance
China	Severity of outbreak; regional role
Egypt	Severity of outbreak
India	Strategic importance; foreign policy concerns
Indonesia	Severity of outbreak
Iraq	Severity of outbreak; foreign policy concerns
Laos	Severity of outbreak in birds; lack of ability to contain disease
Mexico	Strategic importance
Nigeria	Severity of outbreak
Pakistan	Strategic importance; foreign policy concerns
Romania	Severity of outbreak; lack of ability to contain disease
Russia	Severity of outbreak in birds; foreign policy concerns
Thailand	Severity of outbreak; regional role
Turkey	Severity of outbreak
Ukraine	Lack of ability to contain disease
Vietnam	Severity of outbreak

SOURCE: HHS, 2006a.

Assessing potentially valuable partnerships can be approached in a variety of ways, but information on agencies and organizations with current programming in priority countries can help inform such decisions. Based on information extracted from the table in Appendix B, one can assess U.S. government assets in a given country and identify opportunities to establish or enhance surveillance programming through partnerships with selected agencies and organizations. Below we illustrate how the data presented in this

chapter can be used to identify potential strategic partnerships that will strengthen HHS and U.S. government global surveillance efforts. For our example, we selected three priority countries: Azerbaijan, Egypt, and Turkey.

- **Azerbaijan** WHO NIC is not present, but DoD-GEIS does have programming in the country and hence may be a potential partner to help build or provide laboratory capacity, contributing to surveillance quality and timeliness. If this is not possible, then HHS or USAID could consider ways to help strengthen laboratory capacity. Peace Corps and USAID both have programming in Azerbaijan, as do several foreign development agencies, thus providing several opportunities to help increase surveillance coverage. It is unclear if any organizations working in the country are well suited to help build epidemiology capacity or to streamline surveillance notification and analysis; hence this may be a gap for HHS to consider filling itself, given its own technical strengths.
- **Egypt** A number of in-country assets relevant to influenza surveillance exist in Egypt, including a major DoD-GEIS installation, a USAID Mission, in-country HHS staff, TEPHINET, and a WHO NIC. In this case, U.S. government partners can confer and coordinate efforts to improve surveillance without necessarily seeking new partnerships with other foreign agencies or organizations. An important priority may be to examine and help strengthen, if/as warranted, the laboratory capacity of Egypt's WHO NIC.
- **Turkey** The main surveillance-related assets presently in Turkey are the USAID Mission and the WHO NIC. The Canadian and Swedish development agencies (CIDA and SIDA, respectively) are the only other organizations present. Thus, the gaps are great, and the opportunities to leverage in-country partners are few. With Turkey designated as a priority country, USAID will need to play a major role, and more technical and financial resources, e.g., from HHS, will be required to help enhance Turkey's influenza surveillance capacity.

## SUMMARY

The information and analyses presented in this chapter suggest ways to operationalize one of the major approaches to implementing surveillance improvement strategies, as laid out in our conceptual framework: leveraging partners. Once the potential benefits of a broader range of such strategic partnerships in global influenza programming is recognized, HHS and, more broadly, the U.S. government can then use the information and approach presented here for planning, efficiently targeting valuable partners whose mandates, expertise, and mutual interests might make them receptive to partnership with HHS and/or other U.S. government agencies. In Chapter Six, we propose an approach to monitoring the relationships among strategic partners. Quantitative characterization of relationships, or measurement of connectivity, is not captured in traditional program monitoring and evaluation.

## 6. LEVERAGING STRATEGIC PARTNERS: QUANTIFYING RELATIONSHIPS

Chapter Five describes a number of potential partners that could be leveraged to help HHS, and more broadly the U.S. government, improve global influenza surveillance. Developing new partnerships in public health requires organizations to develop sustainable linkages among key partners that combine various missions and organizational structures, under a common goal for shared situational awareness and action (Lurie et al., 2006). Therefore, defining partnerships and building relationships is an important broad strategy to improve global surveillance and response. Networked organizations not only help coalesce efforts to improve influenza surveillance, they also bring together a variety of perspectives, information, and diversity from different cultures and missions as reflected in such organizations as health agencies, Peace Corps, foreign development agencies, foreign laboratory networks, nongovernmental organizations, and the media. The diversity represented by such organizations has been shown to contribute positively to how well a network functions in terms of resource and information sharing (Burt, 1997; Granovetter, 1973, 1982).

As posited by our conceptual framework, working effectively with partners is a key approach to implementing specific surveillance improvement strategies. However, the question remains, how can HHS ensure that existing and potential partners in a surveillance network appropriately connect so that they effectively communicate with one another? This chapter answers our fourth, and last, policy question: *How could HHS monitor its partnerships over time?*

In this chapter we suggest a possible approach to measuring the strength of partner networks that include relevant government agencies and nongovernmental organizations, that is, measuring their interactions in specific areas related to influenza surveillance. Although not a new concept, quantitative characterization of partner networks is typically not captured in traditional public health program monitoring and evaluation. It is, nevertheless, beginning to gain increasing traction in the public health community. In announcing a new leadership initiative grant, the John F. Kennedy School at Harvard said that the “connectivity concept strives to build a seamless web of people, organizations, resources and information that can best catch, contain and control an [influenza outbreak] as well as other emergencies” facing the international community (Harvard, 2004). We believe that for global surveillance to be most effective, it will be ultimately important for HHS not only to actively pursue strategic partnerships but also to periodically measure the strength of the partner network, as reflected by the nature and frequency of their interactions.

### A PROPOSED APPROACH TO QUANTIFYING RELATIONSHIPS

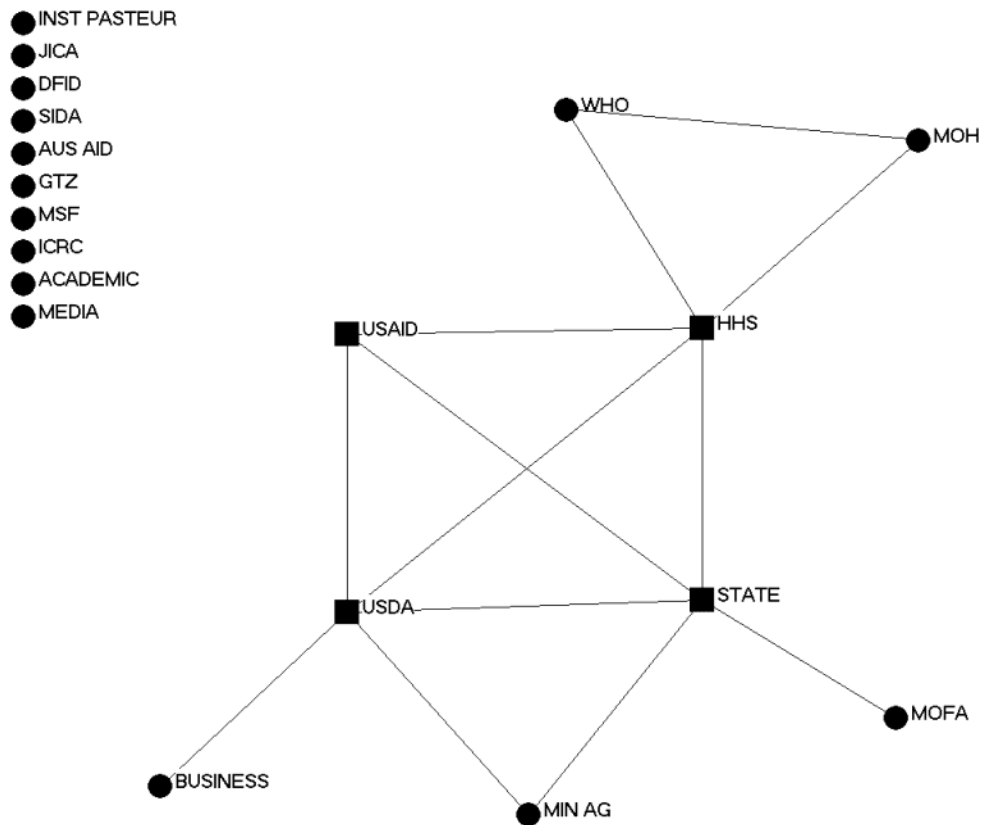
The RAND team believes that using network analysis to understand how well global influenza surveillance partners are connected will be an important component of monitoring and evaluation of global surveillance programming. Network analysis is the study of the structural relationships among interacting entities—in this case, individual organizations—and of how those relationships affect the ability of the

organizations to function collectively in various ways. As applied here, the fundamental property of network analysis is the ability to determine, through mathematical algorithms, whether certain organizations are connected—and to what degree—to one another in terms of interactions related to specific aspects of influenza surveillance. Network analysis provides a mathematical approach to measure the number, length and strength of those connections. In addition, the network can be presented visually as graphs that include network partners as “nodes” and lines to indicate relationships between them. Furthermore, network analytic techniques can quantify the emergence and evolution of networks over time (Monge & Contractor, 2003). A more thorough explanation of network analysis can be found in several recommended texts (Monge & Contractor, 2003; Scott, 1991; Wasserman & Faust, 1994).

Figure 6.1 shows what a global influenza surveillance network in a given country might look like as visualized with network analytic tools (here, visualized in Netdraw (Borgatti et al., 2002)). The RAND team developed this for illustrative purposes based on hypothetical data—it does not represent actual reported data from a specific country. The lines show which organizations are connected - or not - with the others for each specific type of relationship (e.g., for surveillance coverage). The squares represent U.S. government agencies, and the circles represent all other organizations (the acronyms are identified in Chapter 5). The organizations listed at left are potential partners that are not connected to the network (referred to as isolates) at the hypothetical point in time when network data are collected.

Understanding the structural components of a public health organizational network can be an important step toward leveraging partners to help increase the ability to detect and respond to disease outbreaks. Network analysis can be utilized as an evaluation tool once partnerships are established, and it can continue to be applied as the networks evolve and change over time. The next sections provide a brief introduction of network analysis as applied to influenza surveillance partnerships.

Figure 6.1 Hypothetical Global Influenza Surveillance Network for One Country



## Applying Network Analysis

Applying network analysis to global influenza surveillance requires the following two-step data gathering process:

Step 1. An assessment or measure of the *value* of each potential partner's ability to address each of the four surveillance requirements (coverage, quality, timeliness, and transparency).

Step 2. An assessment of *interactions* that U.S. government organizations have with each potential partner in a country. This information establishes which connections exist between the various agencies and frequency of those interactions.

## Data Sources

Data to establish standards. For Step 1, information is gathered to help establish a network standard against which actual interactions will be measured over time. This information is gathered with a brief survey that asks all relevant federal agencies (e.g., HHS, State Department, USAID, DoD, Peace Corps) to assign

“value” to all potential network partners for each of the four surveillance requirements (coverage, quality, timeliness, and transparency). Note that a particular organization can be more valuable for one requirement than another. In our example, value is determined on a scale of 0 to 4, with 4 being most valuable. These scores, along with data regarding the type of organization (e.g., U.S. government, nongovernmental, etc.), are used to weight the importance of having a connection with other network partners and then to determine the network standard for each surveillance requirement. Headquarters-based officials, responding either individually or as a group, can complete this survey, a sample of which is provided in Appendix C. The values for U.S. government agencies can be derived from the number and type of taskings in the NSPI *Implementation Plan*, whereas values for non-U.S. government agencies and organizations will likely be judged more subjectively. In this way, the standard reflects the full U.S. government perspective and can be used government wide.

Data to determine partner interactions. For Step 2, information is needed about the nature of interactions among organizations in individual countries and the frequency with which organizations interact with other partners in a variety of influenza-related and more general (non-influenza related) areas. These data make it possible to create a network structure consisting of multiple relationships. To gather this information, each U.S. agency working in another country is surveyed about its interactions with other in-country organizations as well as its assessment of how the other partners interact with each other.<sup>7</sup> (See Appendix D for a sample of this survey.)

**Outputs.** Data from both surveys are entered into matrices that are then analyzed by a Social Network Analysis program such as UCINET. The outputs from these analyses are:

- 1) Network indices. These are measures describing network characteristics (such as the relative importance of a network member, i.e., based on the values survey described above and how strongly connected a member is to others. These measures make it possible, for example, to identify the key partners in a network by the number of times others indicate a relationship with them.
- 2) Connectivity score. The network indices generated in UCINET are entered into a statistical package (such as Excel, used here) to derive the connectivity score. Several factors go into calculating the connectivity score, such as the different number of organizations present in each country, the types of organizations connected, and the number of connected organizations that are rated valuable. These factors are all weighted individually per network. For each surveillance requirement, the connectivity score reflects the overall connectedness of a country’s network for influenza-related

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<sup>7</sup> Ideally, asking all network partners, not just U.S. agencies, to report their interactions is most desirable. However, it is uncertain whether it is a realistic goal to expect data gathering on a global scale. Asking partners to report on the interactions of others is a practiced network data-collection technique and considered a valid way to collect the information (Marsden, 1987).

interactions, assessed against the country-specific standards developed in Step 1. Periodic measurements of a network's connectivity score permit tracking over time to assess progress in strengthening in-country surveillance partnerships.

- 3) Graphical representations of the network. Using Netdraw, a visualization program embedded within UCINET (Borgatti et al., 2002), a network can be represented graphically. Relationships between network members are indicated by lines drawn between organizations (no line between two organizations means that the relationship does not exist). Attributes of the network members (e.g., organization type) are represented in network graphs visually by either coloring the nodes or assigning specific sizes/shapes to show attribute distinctions. Graphics can be generated to show network connectivity in terms of the individual influenza surveillance requirements (coverage, quality, etc.) as the frequency of partner interactions in each of these areas. This graphical representation can illustrate gaps of untapped opportunities to leverage potential new partners, especially partners considered to be of high value. Each set of partners can have a variety of relationships, and these relationships can be represented in multiple graphs or cumulatively in a single graph.

### **Hypothetical Example**

To illustrate how this method would work to monitor influenza surveillance partnerships, we created hypothetical data sets for a generic developing country. These data were analyzed with UCINET to generate network indices and, subsequently, connectivity scores as well as graphic representations for networks related to each surveillance requirement (coverage, quality, timeliness and transparency) at two different points in time.

Hypothetical consensus levels of value applied to all potential network partners by U.S. agencies, as described in Step 1, are shown in Table 6.1. The first column lists the full range of organizations, both U.S. and foreign, operating in the country. The next four columns represent the hypothetical interagency consensus for their value related to each surveillance requirement. The values “3” and “4” indicate moderate and great value, respectively; the threshold we established for an organization to be considered “valuable” is at or above “moderate” value, i.e.,  $\geq 3$ . These metrics are part of the data used to establish the standards of the ideal network as described earlier. To complete the analyses, hypothetical data were also inputted for each relevant U.S. government agency about their interactions with all the other organizations, as described in Step 2.

**Table 6.1**  
**Hypothetical Consensus Values Assigned to Potential Influenza Surveillance Partners**

Organization	Coverage	Quality	Timeliness	Transparency
Dept. of Health and Human Services (HHS)	3	4	3	3
Dept. of State (State)	2	1	3	4
U.S. Agency for International Devt. (USAID)	4	3	3	3
U.S. Dept of Agriculture (USDA)	3	3	3	3
Peace Corps	4	3	2	3
Ministry of Health (MOH)	4	4	4	3
Ministry of Agriculture (MIN AG)	4	4	4	3
Ministry of Foreign Affairs (MOFA)	2	2	3	3
World Health Organization (WHO)	3	3	4	3
Institut Pasteur (INST PASTEUR)	2	4	3	2
Japan International Cooperation Agency (JICA)	2	3	3	2
Dept. for International Development (DFID)	2	3	3	2
Swedish International Devt. Agency (SIDA)	2	3	3	2
Canadian International Development Agency (CIDA)	2	3	3	2
Australian Agency for International Devt. (AusAID)	3	3	3	3
German development agency (GTZ)	2	3	2	2
Médecins Sans Frontières (MSF)	3	3	2	2
Intl. Committee of the Red Cross (ICRC)	2	2	2	2
Business	3	3	3	3
Academic	2	3	2	2
Media	3	2	3	3

Figure 6.2 shows the actual application of network analysis, based on hypothetical datasets generated to reflect interactions among organizations in the country. For each of the four surveillance requirements, the graphics visualize the state of the network at two time periods, baseline and follow up (e.g., at 6 or 12 months), and display the associated connectivity scores. In these graphics, solid square nodes represent U.S. government agencies, and solid circle nodes represent all other organizations. The connecting lines indicate that partner interactions occur at least monthly (which here is considered a minimum for effective partner connectedness). Network members not connected to others (isolates) lacked ties strong enough at that

particular time to make the cut-off and are therefore seen as single, unconnected nodes along the left side of the graphics. The value of each partner is indicated by node size: those rated as “moderately” or “greatly” valuable for a given requirement are indicated with large nodes (squares or circles), and those of “little” or “no” value are indicated with small nodes. Of note, a given partner can be rated as “valuable” for one requirement but not for another, based on programmatic orientation and areas of special strength. Thus, the ideal networks for each surveillance requirement may vary, but in every instance the standard for each requirement is expressed as 100%, and the connectivity scores are expressed against the 100% standard.

The usefulness of a graphical representation is evident in Figure 6.2. We can see who is connected to whom, and how those connections change from baseline to follow-up measurement. For example, the hypothetical networks for each surveillance requirement became more robust between baseline and follow-up, though to somewhat differing degrees. Also, some partners that were isolated before become connected at the time of follow-up measurement. In these hypothetical networks, the important presence of the State Department, HHS, and USDA is easy to spot. These U.S. organizations are crucial because they connect others that would otherwise be isolated. For example, the State Department connects to the country’s Ministry of Foreign Affairs (MOFA). Without this connection, MOFA would be isolated from the rest of the network.

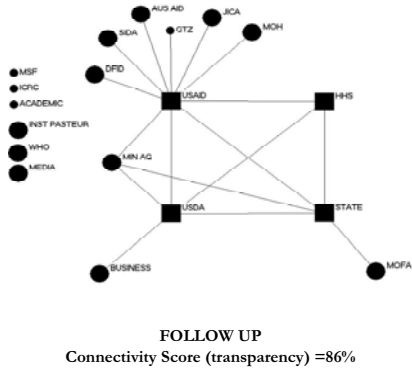
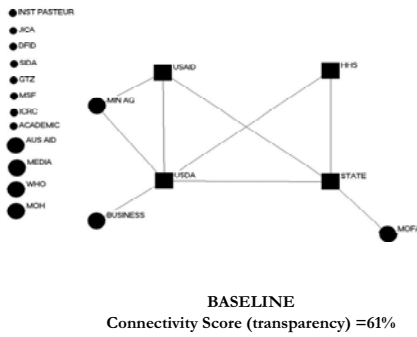
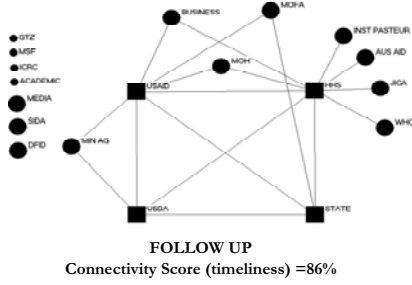
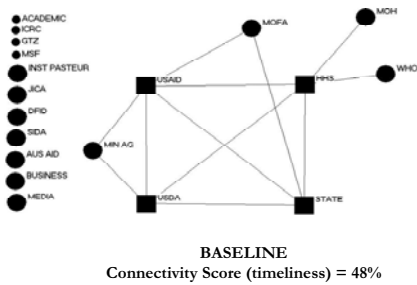
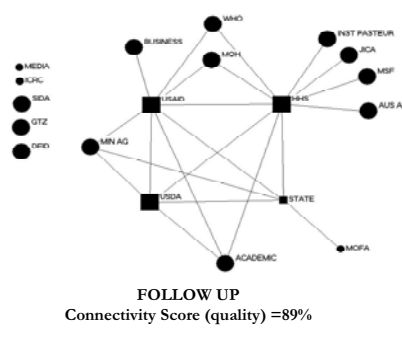
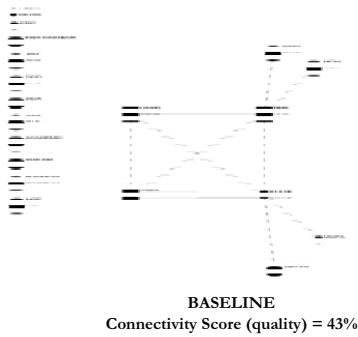
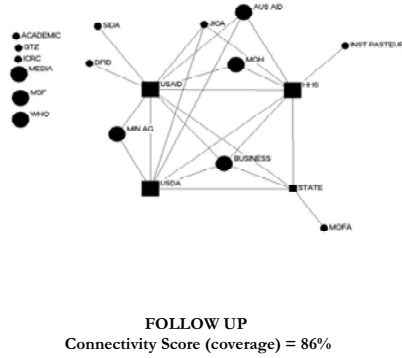
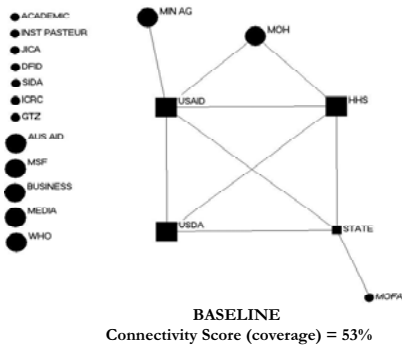
Table 6.2 summarizes the connectivity scores from Figure 6.2 and shows the percent change between baseline and follow-up measurements. The two hypothetical network analyses presented here are simple. Variations in the level and depth of analysis can be undertaken, as deemed necessary and useful for program purposes.

**Table 6.2 Hypothetical Connectivity Scores at Baseline, Follow-Up, and % Change for the Four Surveillance Requirements**

<i>Influenza-related Interactions</i>	<b>Baseline (%)</b>	<b>Follow Up (%)</b>	<b>Change (%)</b>
Coverage	53	86	34
Quality	43	89	46
Timeliness	48	86	38
Transparency	61	86	25

### Figure 6.2 Hypothetical Baseline and Follow-up Connectivity Scores for the Four Surveillance Requirements

Comparisons between countries or over time in a given country do not indicate why observed changes



## CONCLUSIONS

RAND's conceptual framework to improve global influenza surveillance places high priority on strategic partnerships, and the ability to quantitatively characterize these partnerships over time can be an important element to enhance surveillance. One possible approach is network analysis. This is a valuable tool that HHS, and more broadly the U.S. government, can use to measure and monitor strategic partnerships, making it possible to target actions to strengthen them. Our proposed network analysis approach to assessing partner connectivity can be used to help organizations think about where to invest resources to strengthen key partnerships, where holes in networks exist, and how to target efforts to improve partnerships/connectivity.

Using network analysis, U.S. federal agencies can focus on development and strengthening of partnerships/relationships targeting the surveillance requirements for which each partner organization is particularly well suited. Although not specifically illustrated here, comparisons across countries can help U.S. government agencies understand and strengthen targeted partnerships with specific organizations, for example, by flagging those with particularly successful surveillance partnerships and potentially seeking similar partnerships and/or applying lessons to other countries.

Partnerships are critical to a wide range of public health programming. Using network analysis to assess the strength of partnerships for influenza surveillance is only one example of its many potential uses. This same approach can be used in any context where partners should interact, that is, be sufficiently connected to achieve the desired goal. Thus, it would be applicable to any public health preparedness effort, including domestic ones, or to any other public health program requiring interaction among key organizational partners. The network members will change and the frequency and value of interactions will vary, but all of this can quickly be accommodated. Whatever the reason for relationship building, network analysis can be adapted to obtain timely measures and to track progress over time in the strength of strategic partnerships; as such, network analysis can provide an important complement to traditional programmatic monitoring.



## 7. CONCLUSIONS AND RECOMMENDATIONS

Surveillance is the cornerstone of public health and disease control. The goals of influenza surveillance during the pre-pandemic period are the timely detection of the earliest cases of novel influenza infection wherever and whenever they may arise and prompt action to limit disease spread. Since the global community shares the risks of an influenza pandemic, it also has a shared stake in country, regional, and global pandemic preparedness. WHO coordinates global influenza surveillance and draws heavily from the technical expertise of its Member States, including the United States. The United States' own national plan, the *National Strategy for Pandemic Influenza Implementation Plan*, recognizes the importance of global cooperation and assigns major responsibilities to HHS and USAID, in particular, to work with other countries to help build capacity and improve human influenza surveillance.

U.S. investments in global pandemic preparedness will be substantial and carry expectations for results. Expectations related to surveillance may be particularly high, but the stakes are also high: The ability to detect novel influenza cases anywhere they may arise can make a difference in the ability to contain disease spread.

The RAND study provides a timely and systematic examination of different ways HHS can help improve global influenza surveillance. We addressed four key policy questions that follow a logical progression:

- 1) *What strategies can HHS employ to improve global influenza surveillance, and how can these be implemented?*
- 2) *How can HHS quantitatively compare different strategies in order to select promising ones?*
- 3) *How can HHS identify strategic partners to extend global influenza surveillance?*
- 4) *How can HHS monitor its partnerships over time?*

In answering these questions, we:

- 1) created a conceptual framework to logically organize a set of surveillance improvement strategies and approaches to implementing them;
- 2) provided a process model and interactive tool to help guide selection of promising strategies;
- 3) focused on strategic partnerships as an important approach to extending global influenza surveillance and identified opportunities to leverage different kinds of partners;
- 4) proposed a specific approach to assess the strength of such partnerships.

We systematically identified 16 possible strategies to improve global influenza surveillance in terms of coverage, quality, timeliness, and transparency. Our examination revealed some strategies that are consistent with traditional public health practice and others that represent more novel approaches. Our process model and interactive tool permits comparison of different strategies in terms of anticipated improvements in the

probability and timeliness of case detection. Although we used estimated baseline and follow-up input values to demonstrate the use and potential utility of the tool, HHS decision makers can use estimates from their own international programs and planning targets to assess the relative merits of these different strategies and select promising ones. This, in turn, can inform program policy and guide resource allocation.

How can improvement strategies be implemented? Although HHS can do a lot to implement strategies through its own direct actions, we argue that HHS can greatly extend its programmatic reach by leveraging strategic partners. In support of this, we describe a range of promising partners and suggest strategies for which they may be particularly well suited to help improve surveillance coverage, quality, timeliness, and/or transparency. Further, we provide a table indicating the presence (or absence) of each potential partner organization in all countries of the world. This information can help HHS identify and target strategic partners in specific countries. Several potential partnerships, for example, with other US government agencies and foreign development agencies, require no financial investment from HHS but mainly the expenditure of effort to build relationships, establish partnerships, and coordinate surveillance efforts with mutual interests and complementary contributions. Finally, because of the important role that partnerships can play in HHS' overall surveillance efforts, we suggest network analysis as one approach to assess the strength of partner networks so improvements can be made when needed. A decision to pursue network analysis, or a similar approach, would require adapting and testing it to permit establishment of calculated partnership standards against which network strength could be measured.

## RECOMMENDATIONS

HHS is in a position to use the information and analyses presented in this report to guide program decisions and resource allocation as it embarks on markedly stepped-up global influenza programming. Therefore, we offer the following recommendations:

- 1) Assess different surveillance strategies in terms of anticipated improvements in the probability and timeliness of case detection. The interactive tool developed by RAND may be one way to assess the relative merits of different strategies and select promising ones.
- 2) Pursue strategic partnerships that will complement HHS' own technical expertise and extend its reach within and across countries worldwide to improve influenza surveillance. Appendix B, which lists organizations present in 210 countries, can help HHS identify potential partnership members that might improve global influenza surveillance the most in different countries.
- 3) Plan to measure over time the strength of partnerships with an appropriate assessment method. Network analysis is one method to assess the strength of partner networks and identify needed improvements.

## APPENDIX A. INTERACTIVE TOOL FOR COMPARING SURVEILLANCE IMPROVEMENT STRATEGIES

**How to use this tool:** This tool is an Excel spreadsheet that contains functions for calculating joint probability and total delay, at both baseline and follow-up, for the nine paths in our process model for influenza detection and confirmation. By comparing the calculated baseline and follow-up values, users can see the effects of improvement strategies.

The tool is already filled in with RAND's inputs, in blue, from the tool's demonstration in Chapter 4. On the tab labeled "Inputs", users substitute their own estimates of baseline probability and delay for each step in the path. Likewise, users substitute their own estimates for follow-up probability and delay for each step in the path based on the improvement strategy(ies) being considered. Summary results are shown on the tab labeled "Outputs", which initially contains the results for RAND's probability and delay values. Any changes users make to the input values will automatically change the values on the output tab.

### Inputs

#### SICK INDIVIDUAL SEEKS MEDICAL CARE

What *percent* of people sick with influenza will go to a doctor, and what delay would you expect?

	Baseline		Follow-up	
	Probability	Delay	Probability	Delay
Patient goes to doctor	50%	1	50%	1

What *percent* of people sick with influenza will go to a hospital, and what delay would you expect?

	Baseline		Follow-up	
	Probability	Delay	Probability	Delay
Patient goes to hospital	10%	1	10%	1

#### INITIAL DETECTION PROCESS STEPS

##### Path 1. Doctor orders laboratory test

Based on the availability of laboratories with flu diagnostic capability and current level of sensitization of doctors regarding appropriate cases for targeted flu testing, what is the *probability* that a doctor (not in hospital) will order a viral diagnostic lab test for a patient with disease clinically and epidemiologically compatible with a novel influenza virus?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Doctor orders lab test	10%	1	50%	0

**Path 2. Hospital orders laboratory test**

Based on the availability of laboratories with flu diagnostic capability and current level of sensitization of doctors and hospitals regarding appropriate cases for targeted flu testing, what is the *probability* that a hospital (doctor, etc.) will order a viral diagnostic lab test for a patient with disease clinically and epidemiologically compatible with a novel influenza virus?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Hospital orders lab test	10%	1	80%	0

**Path 3. Reporting by sentinel doctor**

What *percent* of doctors are designated to participate in sentinel reporting for influenza?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Doctor is in sentinel network	1%	n/a	10%	n/a

What *percent* of sentinel doctors actually submit reports regularly to the sentinel reporting system, and what is the average delay in information reaching local authorities?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Sentinel doctor files report	30%	3	90%	3

**Path 4. Reporting by sentinel hospital**

What *percent* of hospitals are designated to participate in sentinel reporting for influenza?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Hospital is in sentinel network	15%	n/a	80%	n/a

What *percent* of sentinel hospitals actually submit reports regularly to the sentinel reporting system, and what is the average delay in information reaching local authorities?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Sentinel hospital files report	30%	3	90%	3

**Path 5. Active surveillance of doctors**

If active surveillance were to be implemented, what *percent* of doctors would you expect to be contacted, and what delay would you expect before local authorities receive the information?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Doctor is contacted by active surveillance	0.1%	3	30%	3

**Path 6. Active surveillance of hospitals**

If active surveillance were to be implemented, what *percent* of hospitals would you expect to be contacted, and what delay would you expect before local authorities receive the information?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Hospital is contacted by active surveillance	0.1%	3	80%	3

**Path 7. Tracking employee sick days**

What *percent* of ill people with influenza would call in sick, and what is the delay from when they experience symptoms until they take their first sick day?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Patient calls in sick	100%	1	100%	1

What *percent* of ill people with influenza are tracked via employee sick day reporting, and what is the delay before any increase in sick days is noticed?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Sick days are tracked	1%	5	20%	5

Of the sources that do track sick day information, what *percent* of them would actually submit reports to the local health department, and what is the delay before they do so?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Sick day trackers file report	50%	3	75%	3

**Path 8. Tracking electronic media**

What *percent* of single or clusters of novel influenza cases will end up being reported in electronic media, discussed through weblogs and/or other public access news-type sources?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Patient shows up in media reports	75%	14	75%	14

What *percent* of electronic media, weblog and other public access news-type information is tracked through active data mining or similar methods, and what is the delay in such information reaching local public health authorities?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Media reports are tracked	5%	1	100%	1

### Path 9. Detection by community-based monitoring system

What *percent* of community outbreaks are tracked by public health authorities, e.g., via village alert systems, and what is the expected delay before information about possible cases or clusters of novel influenza disease reaches local authorities?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Detected by community monitoring system	2%	14	25%	14

Of the community-based monitoring systems, what *percent* of them would actually submit reports to the local health department, and what is the delay before they do so?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Community monitoring system files report	50%	3	75%	3

### INVESTIGATION SEQUENCE PROCESS STEPS

What is the *probability* that nonspecific (i.e., non-lab diagnosed) reports of influenza-like illness compatible w/ a novel flu virus, e.g., via village alert reporting, media tracking and/or sick day reporting, will be transmitted from local to national authorities, and what delay would you expect?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Local authorities report to national	100%	3	100%	1

Given current epidemiological capacity in the country, what is the *probability* that a potential case or cluster of novel human influenza will trigger an investigation by in-country public health officials, and how much time (what delay) would you expect an investigation to take?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Health authorities conduct investigation	30%	3	90%	3

What is the *probability* that an epidemiological investigation will result in a sample for lab testing (influenza presence/type), and what is the delay from when the sample were generated until the sample arrived at a laboratory?

	Baseline		Follow-up	
	Percent	Delay	Percent	Delay
Investigators order lab test	100%	1	100%	0

## LABORATORY SEQUENCE PROCESS STEPS

When a sample arrives at a laboratory for testing (influenza presence/type), what is the *probability* that it will be tested, and what is the delay until the testing is completed?

	<b>Baseline</b>		<b>Follow-up</b>	
	Percent	Delay	Percent	Delay
Influenza type testing	100%	2	100%	0

Following initial testing, what is the *probability* of a lab specimen being sent onward from initial testing to subtype testing, and what are the delays from initial testing to the laboratory for subtype testing?

	<b>Baseline</b>		<b>Follow-up</b>	
	Percent	Delay	Percent	Delay
Sample sent for subtype testing	10%	3	80%	1

When a sample arrives at a laboratory for subtype testing, what is the *probability* that it will be tested, and what is the delay until the testing is completed?

	<b>Baseline</b>		<b>Follow-up</b>	
	Percent	Delay	Percent	Delay
Influenza subtype testing	100%	3	100%	1

Following subtype testing, what is the *probability* of a lab specimen being sent onward from subtype testing to reference/confirmatory testing, and what are the delays from the completion of subtype testing to the arrival at the laboratory for reference/confirmatory testing?

	<b>Baseline</b>		<b>Follow-up</b>	
	Percent	Delay	Percent	Delay
Sample sent for confirmatory testing	30%	4	80%	2

When a sample arrives at a laboratory for confirmatory testing, what is the *probability* that it will be tested, and what is the delay until the testing is completed?

	<b>Baseline</b>		<b>Follow-up</b>	
	Percent	Delay	Percent	Delay
Confirmatory testing	100%	10	100%	10

## Outputs

<b>Path 1. Doctor orders laboratory test</b>		<b>Baseline</b>		<b>Follow-up</b>	
		Probability	Delay	Probability	Delay
Initial detection	Patient goes to doctor	50%	1	50%	1
	Doctor orders lab test	10%	1	50%	0
Laboratory sequence	Influenza type testing	100%	2	100%	0
	Sample sent for subtype testing	10%	3	80%	1
	Influenza subtype testing	100%	3	100%	1
	Sample sent for confirmatory testing	30%	4	80%	2
	Confirmatory testing	100%	10	100%	10
<b>Joint Probability and Total Delay</b>		<b>0.15%</b>	<b>24</b>	<b>16%</b>	<b>15</b>

<b>Path 2. Hospital orders laboratory test</b>		<b>Baseline</b>		<b>Follow-up</b>	
		Probability	Delay	Probability	Delay
Initial detection	Patient goes to hospital	10%	1	10%	1
	Hospital orders lab test	10%	1	80%	0
Laboratory sequence	Influenza type testing	100%	2	100%	0
	Sample sent for subtype testing	10%	3	80%	1
	Influenza subtype testing	100%	3	100%	1
	Sample sent for confirmatory testing	30%	4	80%	2
	Confirmatory testing	100%	10	100%	10
<b>Joint Probability and Total Delay</b>		<b>0.03%</b>	<b>24</b>	<b>5%</b>	<b>15</b>

<b>Path 3. Reporting by sentinel doctor</b>		<b>Baseline</b>		<b>Follow-up</b>	
		Probability	Delay	Probability	Delay
Initial detection	Patient goes to doctor	50%	1	50%	1
	Doctor is in sentinel network	1%	n/a	10%	n/a
	Sentinel doctor files report	30%	3	90%	3
Investigation sequence	Local authorities report to national	100%	3	100%	1
	Health authorities conduct investigation	30%	3	90%	3
	Investigators order lab test	100%	1	100%	0
Laboratory sequence	Influenza type testing	100%	2	100%	0
	Sample sent for subtype testing	10%	3	80%	1
	Influenza subtype testing	100%	3	100%	1
	Sample sent for confirmatory testing	30%	4	80%	2
	Confirmatory testing	100%	10	100%	10
<b>Joint Probability and Total Delay</b>		<b>0.001%</b>	<b>33</b>	<b>3%</b>	<b>22</b>

<b>Path 4. Reporting by sentinel hospital</b>		<b>Baseline</b>		<b>Follow-up</b>	
		Probability	Delay	Probability	Delay
Initial detection	Patient goes to hospital	10%	1	10%	1
	Hospital is in sentinel network	15%	n/a	80%	n/a
	Sentinel hospital files report	30%	3	90%	3
Investigation sequence	Local authorities report to national	100%	3	100%	1
	Health authorities conduct investigation	30%	3	90%	3
	Investigators order lab test	100%	1	100%	0
Laboratory sequence	Influenza type testing	100%	2	100%	0
	Sample sent for subtype testing	10%	3	80%	1
	Influenza subtype testing	100%	3	100%	1
	Sample sent for confirmatory testing	30%	4	80%	2
	Confirmatory testing	100%	10	100%	10
<b>Joint Probability and Total Delay</b>		<b>0.004%</b>	<b>33</b>	<b>4%</b>	<b>22</b>

<b>Path 5. Active surveillance of doctors</b>		<b>Baseline</b>		<b>Follow-up</b>	
		Probability	Delay	Probability	Delay
Initial detection	Patient goes to doctor	50%	1	50%	1
	Doctor is contacted by active surveillance	0.1%	3	30%	3
Investigation sequence	Local authorities report to national	100%	3	100%	1
	Health authorities conduct investigation	30%	3	90%	3
	Investigators order lab test	100%	1	100%	0
Laboratory sequence	Influenza type testing	100%	2	100%	0
	Sample sent for subtype testing	10%	3	80%	1
	Influenza subtype testing	100%	3	100%	1
	Sample sent for confirmatory testing	30%	4	80%	2
	Confirmatory testing	100%	10	100%	10
<b>Joint Probability and Total Delay</b>		<b>0.0005%</b>	<b>33</b>	<b>9%</b>	<b>22</b>

<b>Path 6. Active surveillance of hospitals</b>		<b>Baseline</b>		<b>Follow-up</b>	
		Probability	Delay	Probability	Delay
Initial detection	Patient goes to hospital	10%	1	10%	1
	Hospital is contacted by active surveillance	0.1%	3	80%	3
Investigation sequence	Local authorities report to national	100%	3	100%	1
	Health authorities conduct investigation	30%	3	90%	3
	Investigators order lab test	100%	1	100%	0
Laboratory sequence	Influenza type testing	100%	2	100%	0
	Sample sent for subtype testing	10%	3	80%	1
	Influenza subtype testing	100%	3	100%	1
	Sample sent for confirmatory testing	30%	4	80%	2
	Confirmatory testing	100%	10	100%	10
<b>Joint Probability and Total Delay</b>		<b>0.000%</b>	<b>33</b>	<b>5%</b>	<b>22</b>

<b>Path 7. Tracking employee sick days</b>		<b>Baseline</b>		<b>Follow-up</b>	
		Probability	Delay	Probability	Delay
Initial detection	Patient calls in sick	100%	1	100%	1
	Sick day are tracked	1%	5	20%	5
	Sick day trackers file report	50%	3	75%	3
Investigation sequence	Local authorities report to national	100%	3	100%	1
	Health authorities conduct investigation	30%	3	90%	3
	Investigators order lab test	100%	1	100%	0
Laboratory sequence	Influenza type testing	100%	2	100%	0
	Sample sent for subtype testing	10%	3	80%	1
	Influenza subtype testing	100%	3	100%	1
	Sample sent for confirmatory testing	30%	4	80%	2
	Confirmatory testing	100%	10	100%	10
<b>Joint Probability and Total Delay</b>		<b>0.00%</b>	<b>38</b>	<b>9%</b>	<b>27</b>

<b>Path 8. Tracking electronic media</b>		<b>Baseline</b>		<b>Follow-up</b>	
		Probability	Delay	Probability	Delay
Initial detection	Patient shows up in media reports	75%	14	75%	14
	Media reports are tracked	5%	1	100%	1
Investigation sequence	Local authorities report to national	100%	3	100%	1
	Health authorities conduct investigation	30%	3	90%	3
	Investigators order lab test	100%	1	100%	0
Laboratory sequence	Influenza type testing	100%	2	100%	0
	Sample sent for subtype testing	10%	3	80%	1
	Influenza subtype testing	100%	3	100%	1
	Sample sent for confirmatory testing	30%	4	80%	2
	Confirmatory testing	100%	10	100%	10
<b>Joint Probability and Total Delay</b>		<b>0.03%</b>	<b>44</b>	<b>43%</b>	<b>33</b>

<b>Path 9. Detection by community-based monitoring system</b>		<b>Baseline</b>		<b>Follow-up</b>	
		Probability	Delay	Probability	Delay
Initial detection	Detected by community monitoring system	2%	14	25%	14
	Community monitoring system files report	50%	3	75%	3
Investigation sequence	Local authorities report to national	100%	3	100%	1
	Health authorities conduct investigation	30%	3	90%	3
	Investigators order lab test	100%	1	100%	0
Laboratory sequence	Influenza type testing	100%	2	100%	0
	Sample sent for subtype testing	10%	3	80%	1
	Influenza subtype testing	100%	3	100%	1
	Sample sent for confirmatory testing	30%	4	80%	2
	Confirmatory testing	100%	10	100%	10
<b>Joint Probability and Total Delay</b>		<b>0.01%</b>	<b>46</b>	<b>11%</b>	<b>35</b>

## APPENDIX B. ORGANIZATIONS PRESENT IN 210 COUNTRIES

Country	U.S. Government Agencies <sup>1</sup>	Foreign Laboratory Networks <sup>2</sup>	Foreign Development Agencies <sup>3</sup>		NGOs <sup>4</sup> / TEPHINET	WHO Global Influenza Surveillance Network <sup>5</sup>
Afghanistan	US Embassy USAID Mission (w/health) DoD-GEIS	<i>none</i>	DFID CIDA SIDA	GTZ JICA	MSF IMC ICRC	<i>none</i>
Albania	US Embassy USAID Mission (w/health) Peace Corps USDA/FAS	<i>none</i>	DFID CIDA	SIDA GTZ	MSF  ICRC	WHO NIC
Algeria	US Embassy USDA/FAS	Institut Pasteur	CIDA	GTZ	MSF ICRC	WHO NIC
Angola	US Embassy USAID Mission (w/health)  HHS	<i>none</i>	DFID SIDA	GTZ	MSF ICRC	<i>none</i>
Anguilla	USDA/FAS	<i>none</i>	DFID CIDA			<i>none</i>
Antigua & Barbuda	USDA/FAS	<i>none</i>	DFID CIDA			<i>none</i>
Argentina	US Embassy DoD-GEIS (Partner) USDA/FAS	<i>none</i>	CIDA	GTZ JICA	ICRC TEPHINET	WHO NIC

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- 2 SPC=Secretariat of the Pacific Commission Laboratory Network; EISS=European Influenza Surveillance Scheme
- 3 SIDA=Swedish International Development Agency; CIDA=Canadian International Development Agency; GTZ=Gesellschaft für Technische Zusammenarbeit (Germany); DFID=Dept. for International Development (UK); JICA=Japanese International Cooperation Agency; AusAID=Australian Agency for International Development
- 4 ICRC=International Committee of the Red Cross; MSF=Medecins Sans Frontieres; IMC=International Medical Corps; AKHS=Aga Khan Health Services; TEPHINET=Training Programs in Epidemiology and Public Health Interventions Network
- 5 WHO NIC=WHO National Influenza Center; WHO CC=WHO Collaborating Center

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Armenia	US Embassy USAID Mission (w/health) Peace Corps USDA/FAS	<i>none</i>	DFID CIDA     GTZ	MSF ICRC	<i>none</i>
Aruba	USDA/FAS	<i>none</i>			<i>none</i>
Australia	US Embassy USDA/FAS			ICRC TEPHINET	WHOCC, A/H5 Reference laboratory
Austria	US Embassy USDA/FAS	EISS			WHO NIC
Azerbaijan	US Embassy USAID Mission (w/health) Peace Corps	<i>none</i>	DFID CIDA     GTZ	MSF IMC ICRC	<i>none</i>
Bahrain	US Embassy	<i>none</i>		ICRC	<i>none</i>
Bangladesh	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) HHS USDA/FAS	<i>none</i>	DFID     SIDA CIDA     GTZ AusAID   JICA	MSF ICRC	WHO NIC
Barbados	US Embassy DoD-GEIS (Partner) USDA/FAS	<i>none</i>	DFID CIDA		<i>none</i>
Belarus	US Embassy USAID Mission (w/health)	<i>none</i>	CIDA	ICRC	WHO NIC

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Belgium	USAID Mission USDA/FAS	Institut Pasteur EISS		MSF ICRC	WHO NIC
Belize	US Embassy Peace Corps DoD-GEIS (Partner 2004)	<i>none</i>	DFID	MSF ICRC	<i>none</i>
Benin	US Embassy USAID Mission (w/health) Peace Corps	<i>none</i>	DFID CIDA GTZ	MSF ICRC	<i>none</i>
Bermuda	USDA/FAS	<i>none</i>			<i>none</i>
Bhutan	<i>none</i>		CIDA AusAID	ICRC	<i>none</i>
Bolivia	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004)	<i>none</i>	DFID GTZ CIDA JICA SIDA	MSF ICRC	<i>none</i>
Bosnia & Herzegovina	USAID Mission USDA/FAS	<i>none</i>	DFID SIDA CIDA GTZ	MSF ICRC	<i>none</i>
Botswana	US Embassy Peace Corps HHS	<i>none</i>	DFID CIDA	ICRC	<i>none</i>
Brazil	US Embassy USAID Mission (w/health)  HHS USDA/FAS		DFID GTZ CIDA JICA	MSF ICRC TEPHINET	WHO NIC
British Virgin Islands	US Embassy USDA/FAS				<i>none</i>

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Brunei	US Embassy	<i>none</i>			ICRC	<i>none</i>
Bulgaria	US Embassy USAID Mission (w/health) Peace Corps USDA/FAS		DFID CIDA	GTZ JICA	MSF ICRC	WHO NIC
Burkina Faso	US Embassy Peace Corps HHS	<i>none</i>	CIDA SIDA	GTZ	MSF ICRC	<i>none</i>
Burundi	US Embassy USAID Mission	<i>none</i>	DFID CIDA	GTZ	MSF IMC ICRC	<i>none</i>
Cambodia	US Embassy USAID Mission (w/health) DoD-GEIS (Partner 2004) HHS	Institut Pasteur	DFID CIDA AusAID	SIDA GTZ JICA	MSF ICRC	<i>none</i>
Cameroon	US Embassy Peace Corps HHS	Institut Pasteur	DFID CIDA	GTZ	ICRC	<i>none</i>
Canada	US Embassy USDA/FAS	<i>none</i>			ICRC TEPHINET	WHO NIC
Cape Verde	US Embassy Peace Corps	<i>none</i>	CIDA		ICRC	<i>none</i>
Cayman Islands	USDA/FAS	<i>none</i>				<i>none</i>
Central African Republic	US Embassy	Institut Pasteur	CIDA		MSF ICRC	WHO NIC

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Chad	US Embassy Peace Corps	<i>none</i>	CIDA GTZ	MSF IMC ICRC	<i>none</i>
Chile	US Embassy USDA/FAS	<i>none</i>	CIDA GTZ	ICRC	WHO NIC
China	US Embassy Peace Corps HHS USDA/FAS	<i>none</i>	DFID SIDA CIDA GTZ AusAID JICA	MSF ICRC TEPHINET	WHO NIC WHO A/H5 Ref Lab
Colombia	US Embassy USAID Mission USDA/FAS DoD-GEIS	<i>none</i>	DFID SIDA CIDA GTZ	MSF ICRC TEPHINET	WHO NIC
Comoros	<i>none</i>	<i>none</i>	CIDA	ICRC	<i>none</i>
Congo, Republic of	US Embassy USAID Mission (w/health) HHS	<i>none</i>	CIDA	MSF ICRC	<i>none</i>
Congo, Democratic Republic of	US Embassy USAID Mission (w/health)	<i>none</i>	DFID CIDA GTZ	MSF IMC ICRC	<i>none</i>
Cook Islands	<i>none</i>	SPC	CIDA AusAID		<i>none</i>
Costa Rica	US Embassy Peace Corps USDA/FAS	<i>none</i>	DFID CIDA GTZ	MSF ICRC TEPHINET	<i>none</i>

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Cote d'Ivoire	US Embassy	Institut Pasteur	DFID CIDA GTZ	MSF ICRC	<i>none</i>
Croatia	US Embassy USAID Mission (w/health) USDA/FAS	<i>none</i>	DFID SIDA CIDA GTZ	ICRC	WHO NIC
Cuba	<i>none</i>	<i>none</i>	DFID SIDA CIDA	MSF ICRC	WHO NIC
Cyprus	US Embassy	EISS			<i>none</i>
Czech Republic	US Embassy USDA/FAS	EISS	CIDA	ICRC	WHO NIC
Denmark	US Embassy HHS USDA/FAS	EISS			WHO NIC
Djibouti	US Embassy DoD-GEIS (Partner 2004)	<i>none</i>	CIDA	ICRC	<i>none</i>
Dominica	US Embassy DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	CIDA		<i>none</i>
Dominican Republic	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	CIDA GTZ	ICRC	<i>none</i>
East Timor	US Embassy Peace Corps	<i>none</i>	DFID AusAID CIDA	MSF ICRC	<i>none</i>

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Ecuador	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID    GTZ CIDA	MSF ICRC	WHO NIC
Egypt	US Embassy USAID Mission (w/health) DoD-GEIS (Lab) HHS USDA/FAS	<i>none</i>	DFID    GTZ CIDA    JICA SIDA	MSF ICRC TEPHINET	WHO NIC
El Salvador	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID    GTZ CIDA	MSF ICRC TEPHINET	<i>none</i>
Equatorial Guinea	US Embassy	<i>none</i>	CIDA	MSF ICRC	<i>none</i>
Eritrea	US Embassy USAID Mission (w/health) DoD-GEIS	<i>none</i>	DFID CIDA	MSF IMC ICRC	<i>none</i>
Estonia	US Embassy	EISS	CIDA	ICRC	<i>none</i>
Ethiopia	US Embassy USAID Mission (w/health) HHS	<i>none</i>	DFID    GTZ CIDA    JICA SIDA	MSF IMC ICRC	<i>none</i>
Fiji	US Embassy Peace Corps	SPC (Ref. Lab)	CIDA AusAID    JICA	ICRC	WHO NIC
Finland	US Embassy	EISS			WHO NIC

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France	US Embassy USAID Mission HHS USDA/FAS	Institut Pasteur SPC EISS		MSF ICRC	WHO NIC WHO A/H5 Ref Lab
French Guiana	DoD-GEIS	<i>none</i>			WHO NIC
French Polynesia	<i>none</i>	SPC (Ref. Lab)			
Gabon	US Embassy Peace Corps	<i>none</i>	CIDA	ICRC	<i>none</i>
Gaza Strip	<i>none</i>	<i>none</i>	CIDA		<i>none</i>
Georgia	US Embassy USAID Mission (w/health) Peace Corps  USDA/FAS	<i>none</i>	DFID SIDA CIDA GTZ	MSF IMC ICRC	<i>none</i>
Germany	US Embassy DoD-GEIS (Partner 2004) USDA/FAS	EISS		TEPHINET	WHO NIC
Ghana	US Embassy USAID Mission (Health 2004) Peace Corps DoD-GEIS (Partner) USDA/FAS	<i>none</i>	DFID GTZ CIDA JICA	ICRC TEPHINET	<i>none</i>
Greece	US Embassy USDA/FAS	Institut Pasteur EISS			WHO NIC
Greenland	US Embassy	<i>none</i>			<i>none</i>

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Grenada	US Embassy DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID CIDA	ICRC	<i>none</i>
Guadeloupe	USDA/FAS	Institut Pasteur			<i>none</i>
Guam	US Embassy	SPC (Ref. Lab)			<i>none</i>
Guatemala	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) HHS USDA/FAS	<i>none</i>	DFID    SIDA CIDA    GTZ	MSF ICRC TEPHINET	<i>none</i>
Guinea	US Embassy USAID Mission (w/health) Peace Corps	<i>none</i>	DFID    SIDA CIDA    GTZ	MSF ICRC	<i>none</i>
Guinea-Bissau	USAID Mission DoD-GEIS	<i>none</i>	CIDA	MSF ICRC	<i>none</i>
Guyana	US Embassy USAID Mission (w/health) Peace Corps HHS	Institut Pasteur	DFID CIDA	ICRC	WHO NIC
Haiti	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) HHS	<i>none</i>	DFID    SIDA CIDA    GTZ	MSF ICRC	<i>none</i>

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Honduras	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID SIDA CIDA GTZ	MSF ICRC TEPHINET	WHO NIC
Hungary	US Embassy USAID Mission USDA/FAS	EISS	CIDA	ICRC	WHO NIC
Iceland	US Embassy	<i>none</i>			WHO NIC
India	US Embassy USAID Mission (w/health) HHS USDA/FAS DoD-GEIS	<i>none</i>	DFID SIDA CIDA GTZ AusAID	MSF AKHS ICRC TEPHINET	WHO NIC
Indonesia	US Embassy USAID Mission (w/health) DoD-GEIS (Lab) HHS USDA/FAS	<i>none</i>	DFID SIDA CIDA GTZ AusAID JICA	MSF IMC ICRC	WHO NIC
Iran	<i>none</i>	Institut Pasteur	DFID	MSF ICRC	WHO NIC
Iraq	US Embassy DoD-GEIS (Partner) HHS USDA/FAS	<i>none</i>	DFID CIDA	MSF IMC ICRC	<i>none</i>

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Ireland	US Embassy USDA/FAS	EISS		ICRC	WHO NIC
Israel	US Embassy USDA/FAS	<i>none</i>	SIDA	ICRC	WHO NIC
Italy	US Embassy USAID Mission USDA/FAS DoD-GEIS	Institut Pasteur EISS		MSF TEPHINET	WHO NIC
Jamaica	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID CIDA	ICRC	WHO NIC
Japan	US Embassy USAID Mission DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>		ICRC TEPHINET	WHOCC, A/H5 Reference laboratory
Jordan	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID CIDA GTZ	ICRC TEPHINET	<i>none</i>

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Kazakhstan	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) HHS USDA/FAS	<i>none</i>	DFID CIDA      GTZ	MSF ICRC TEPHINET	WHO NIC
Kenya	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Lab) HHS USDA/FAS	<i>none</i>	DFID      GTZ CIDA      JICA SIDA	MSF IMC AKHS ICRC TEPHINET	WHO NIC
Kiribati	Peace Corps	SPC	CIDA AusAID	ICRC	<i>none</i>
Korea, Democratic Peoples Republic of	<i>none</i>	<i>none</i>	CIDA	MSF	WHO NIC
Korea, Republic of	US Embassy	<i>none</i>			WHO NIC
	DoD-GEIS (Partner 2004)			TEPHINET	
	USDA/FAS				
Kuwait	US Embassy	<i>none</i>		ICRC	WHO NIC
Kyrgyzstan	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2005)	<i>none</i>	DFID      GTZ CIDA	ICRC TEPHINET	<i>none</i>
Laos	US Embassy DoD-GEIS (Partner 2004)	<i>none</i>	CIDA      SIDA AusAID	MSF ICRC	<i>none</i>

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Latvia	US Embassy USAID Mission	EISS	CIDA	ICRC	WHO NIC
Lebanon	US Embassy USAID Mission	<i>none</i>	CIDA	MSF ICRC	WHO NIC
Lesotho	US Embassy Peace Corps	<i>none</i>	DFID CIDA	ICRC	<i>none</i>
Liberia	US Embassy USAID Mission	<i>none</i>	DFID CIDA	MSF IMC ICRC	<i>none</i>
Libya	US Embassy	<i>none</i>		ICRC	<i>none</i>
	DoD-GEIS				
Lithuania	US Embassy USAID Mission (w/health)	EISS	CIDA	ICRC	<i>none</i>
Luxembourg	US Embassy	EISS		MSF	<i>none</i>
Macedonia	US Embassy USAID Mission Peace Corps USDA/FAS	<i>none</i>	DFID    SIDA CIDA    GTZ	MSF ICRC	<i>none</i>
Madagascar	US Embassy USAID Mission (w/health) Peace Corps	Institut Pasteur	CIDA    GTZ	MSF ICRC	WHO NIC
Malawi	US Embassy USAID Mission (w/health) Peace Corps HHS	<i>none</i>	DFID    GTZ CIDA    JICA	MSF ICRC	<i>none</i>

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Malaysia	US Embassy USDA/FAS	<i>none</i>	DFID CIDA JICA	ICRC TEPHINET	WHO NIC
Maldives	<i>none</i>	<i>none</i>	CIDA AusAID	ICRC	<i>none</i>
Mali	US Embassy USAID Mission (w/health) Peace Corps HHS	<i>none</i>	CIDA GTZ SIDA	MSF ICRC	<i>none</i>
Malta	US Embassy	EISS			<i>none</i>
Marshall Islands	<i>none</i>	SPC	CIDA	ICRC	<i>none</i>
Mauritania	US Embassy Peace Corps	<i>none</i>	CIDA GTZ	MSF ICRC	<i>none</i>
Mauritius	US Embassy	<i>none</i>	CIDA	ICRC	<i>none</i>
Mexico	US Embassy USAID Mission (w/health) Peace Corps  USDA/FAS	<i>none</i>	CIDA JICA	MSF ICRC TEPHINET	WHO NIC
Micronesia	US Embassy Peace Corps	SPC	CIDA AusAID	ICRC	<i>none</i>
Moldova	US Embassy USAID Mission (w/health) Peace Corps	<i>none</i>	DFID SIDA CIDA JICA	ICRC	<i>none</i>
Mongolia	US Embassy USAID Mission Peace Corps DoD-GEIS	<i>none</i>	DFID CIDA GTZ AusAID JICA	MSF ICRC	WHO NIC

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Montserrat	USDA/FAS	<i>none</i>	DFID CIDA		<i>none</i>
Morocco	US Embassy USAID Mission (w/health) Peace Corps USDA/FAS DoD-GEIS	Institut Pasteur	CIDA    GTZ	ICRC	WHO NIC
Mozambique	US Embassy USAID Mission (w/health) Peace Corps HHS	<i>none</i>	DFID    SIDA CIDA    GTZ	MSF ICRC	<i>none</i>
Myanmar	US Embassy DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID    JICA	ICRC	<i>none</i>
Namibia	US Embassy USAID Mission (w/health) Peace Corps HHS	<i>none</i>	DFID    SIDA CIDA    GTZ	ICRC	<i>none</i>
Nauru	<i>none</i>	SPC	CIDA AusAID		<i>none</i>
Nepal	US Embassy USAID Mission (w/health) DoD-GEIS (Partner 2004) HHS	<i>none</i>	DFID    GTZ CIDA    JICA AusAID	MSF ICRC	<i>none</i>
Netherlands	US Embassy USDA/FAS	EISS			WHO NIC

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Netherlands Antilles	USDA/FAS	<i>none</i>			<i>none</i>
New Caledonia		Institut Pasteur SPC (Ref. Lab)			WHO NIC
New Zealand	US Embassy USDA/FAS	SPC		ICRC	WHO NIC
Nicaragua	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID    SIDA CIDA    GTZ	MSF ICRC TEPHINET	<i>none</i>
Niger	US Embassy Peace Corps	Institut Pasteur	DFID    SIDA CIDA    GTZ	MSF ICRC	<i>none</i>
Nigeria	US Embassy USAID Mission (w/health) DoD-GEIS (Partner 2005) HHS USDA/FAS	<i>none</i>	DFID    SIDA CIDA    GTZ	MSF ICRC	WHO NIC
Niue	<i>none</i>	SPC	CIDA AusAID		<i>none</i>
Northern Mariana Islands	US Embassy	<i>none</i>			<i>none</i>
Norway	US Embassy	EISS		ICRC	WHO NIC
Oman	US Embassy DoD-GEIS (Partner 2005)	<i>none</i>		ICRC	

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Pakistan	US Embassy USAID Mission (w/health) DoD-GEIS (Partner 2004) HHS USDA/FAS	<i>none</i>	DFID CIDA    GTZ AusAID    JICA	MSF IMC AKHS ICRC	WHO NIC
Palau	US Embassy Peace Corps	SPC	CIDA	ICRC	<i>none</i>
Panama	US Embassy USAID Mission Peace Corps USDA/FAS	<i>none</i>	CIDA	ICRC	<i>none</i>
Papua New Guinea	US Embassy	SPC	CIDA AusAID	MSF ICRC	WHO NIC
Paraguay	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS	<i>none</i>	CIDA    GTZ JICA	ICRC	WHO NIC
Peru	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Lab) HHS USDA/FAS	<i>none</i>	DFID CIDA    GTZ	MSF ICRC TEPHINET	WHO NIC

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Philippines	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) HHS USDA/FAS	<i>none</i>	AusAID GTZ JICA	MSF ICRC TEPHINET	WHO NIC
Pitcairn Islands	<i>none</i>	SPC	DFID		<i>none</i>
Poland	US Embassy USDA/FAS	EISS	CIDA	ICRC	WHO NIC
Portugal	US Embassy USDA/FAS	EISS		ICRC	WHO NIC
Qatar	US Embassy DoD-GEIS (Partner 2004)	<i>none</i>		ICRC	<i>none</i>
Romania	US Embassy USAID Mission (w/health) Peace Corps USDA/FAS DoD-GEIS	Institut Pasteur EISS	DFID GTZ CIDA JICA	MSF ICRC	WHO NIC
Russia	US Embassy USAID Mission (w/health) USDA/FAS	Institut Pasteur	DFID SIDA CIDA GTZ	MSF ICRC	WHO NIC
Rwanda	US Embassy USAID Mission (w/health)	<i>none</i>	DFID SIDA CIDA GTZ	MSF ICRC	<i>none</i>
Samoa	US Embassy Peace Corps	SPC	CIDA AusAID	ICRC	<i>none</i>
Sao Tome & Principe	<i>none</i>	<i>none</i>	CIDA	ICRC	<i>none</i>

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Saudi Arabia	US Embassy DoD-GEIS (Partner 2005) USDA/FAS	<i>none</i>	GTZ	ICRC TEPHINET	<i>none</i>
Senegal	US Embassy USAID Mission (w/health) Peace Corps USDA/FAS	Institut Pasteur	CIDA GTZ SIDA JICA	ICRC	WHO NIC
Serbia	US Embassy USAID Mission USDA/FAS	<i>none</i>	CIDA		WHO NIC
Seychelles	US Embassy	<i>none</i>	CIDA	ICRC	<i>none</i>
Sierra Leone	US Embassy USAID Mission	<i>none</i>	DFID CIDA	MSF IMC ICRC	<i>none</i>
Singapore	US Embassy DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>		ICRC	WHO NIC
Slovakia	US Embassy	EISS	CIDA	ICRC	WHO NIC
Slovenia	US Embassy	EISS	CIDA	ICRC	WHO NIC
Solomon Islands	<i>none</i>	SPC	CIDA AusAID	ICRC	<i>none</i>

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Somalia	USAID Mission	<i>none</i>	DFID CIDA	MSF IMC ICRC	<i>none</i>
South Africa	US Embassy USAID Mission (w/health) Peace Corps HHS USDA/FAS	<i>none</i>	DFID    GTZ CIDA    JICA SIDA	MSF ICRC	WHO NIC
Spain	US Embassy USDA/FAS DoD-GEIS	EISS		MSF  TEPHINET	WHO NIC
Sri Lanka	US Embassy USAID Mission  USDA/FAS	<i>none</i>	DFID    SIDA CIDA    GTZ AusAID   JICA	MSF IMC ICRC	WHO NIC
St. Kitts & Nevis	USDA/FAS	<i>none</i>	DFID CIDA		<i>none</i>
St. Lucia	USDA/FAS	<i>none</i>	DFID CIDA		<i>none</i>
St. Vincent & the Grenadines	USDA/FAS	<i>none</i>	DFID CIDA		
Sudan	US Embassy USAID Mission DoD-GEIS (Partner 2004)	<i>none</i>	DFID CIDA	MSF IMC ICRC	WHO NIC
Suriname	US Embassy Peace Corps	<i>none</i>	DFID CIDA	ICRC	<i>none</i>

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Swaziland	US Embassy Peace Corps	<i>none</i>	DFID CIDA	ICRC	
Sweden	US Embassy USDA/FAS	EISS			WHO NIC
Switzerland	US Embassy USAID Mission HHS USDA/FAS	EISS		ICRC	WHO NIC
Syria	US Embassy DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	CIDA	ICRC	<i>none</i>
Tajikistan	US Embassy USAID Mission (w/health)	<i>none</i>	DFID SIDA CIDA GTZ	MSF ICRC TEPHINET	<i>none</i>
Tanzania	US Embassy USAID Mission (w/health) Peace Corps HHS	<i>none</i>	DFID GTZ CIDA JICA SIDA	MSF IMC AKHS ICRC	<i>none</i>
Thailand	US Embassy Peace Corps DoD-GEIS (Lab) HHS USDA/FAS	<i>none</i>	DFID SIDA CIDA GTZ AusAID JICA	MSF ICRC TEPHINET	WHO NIC
The Bahamas	US Embassy  USDA/FAS	<i>none</i>			<i>none</i>

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The Gambia	US Embassy Peace Corps	<i>none</i>	DFID CIDA	ICRC	<i>none</i>
Togo	US Embassy Peace Corps	<i>none</i>	CIDA GTZ	ICRC	<i>none</i>
Tokelau	US Embassy	SPC	AusAID		<i>none</i>
Tonga	Peace Corps	SPC	CIDA AusAID	ICRC	<i>none</i>
Trinidad & Tobago	US Embassy DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID CIDA		WHO NIC
Tunisia	US Embassy USDA/FAS	Institut Pasteur	CIDA GTZ	ICRC	WHO NIC
Turkey	US Embassy USAID Mission (w/health) USDA/FAS DoD-GEIS	<i>none</i>	CIDA	ICRC	WHO NIC
Turkmenistan	US Embassy USAID Mission (w/health) Peace Corps	<i>none</i>	DFID CIDA	MSF ICRC TEPHINET	<i>none</i>
Turks & Caicos Islands	USDA/FAS	<i>none</i>	DFID CIDA		<i>none</i>
Tuvalu	<i>none</i>	SPC	CIDA AusAID	ICRC	<i>none</i>

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Uganda	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) HHS	<i>none</i>	DFID    SIDA CIDA    GTZ	MSF IMC AKHS ICRC TEPHINET	<i>none</i>
Ukraine	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID    GTZ CIDA    JICA SIDA	MSF ICRC	WHO NIC
United Arab Emirates	US Embassy USDA/FAS	<i>none</i>	GTZ	ICRC	<i>none</i>
United Kingdom	US Embassy DoD-GEIS (Partner 2004) HHS USDA/FAS	EISS		ICRC	WHOCC, A/H5 Reference laboratory
United States	US Embassy HHS	<i>none</i>		MSF IMC ICRC TEPHINET	WHOCC, A/H5 Reference laboratory
Uruguay	US Embassy USDA/FAS	<i>none</i>	CIDA	ICRC	WHO NIC

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Uzbekistan	US Embassy USAID Mission (w/health) Peace Corps DoD-GEIS (Partner 2004) USDA/FAS	<i>none</i>	DFID    GTZ CIDA    JICA	MSF ICRC TEPHINET	<i>none</i>
Vanuatu	Peace Corps	SPC	CIDA AusAID	ICRC	<i>none</i>
Vatican City	US Mission	<i>none</i>			<i>none</i>
Venezuela	US Embassy USDA/FAS DoD-GEIS	<i>none</i>	CIDA	MSF ICRC	WHO NIC
Vietnam	US Embassy USAID Mission (w/health) DoD-GEIS (Partner 2004) HHS USDA/FAS	Institut Pasteur	DFID    SIDA CIDA    GTZ AusAID    JICA	MSF ICRC	WHO NIC
Wallis & Futuna	<i>none</i>	SPC			<i>none</i>
West Bank	USAID Mission (w/health)	<i>none</i>			<i>none</i>
Yemen	US Embassy USAID Mission (w/health) USDA/FAS	<i>none</i>	DFID    GTZ CIDA	MSF ICRC	<i>none</i>
Zambia	US Embassy USAID Mission (w/health) Peace Corps HHS	<i>none</i>	DFID    GTZ CIDA    JICA SIDA	MSF ICRC	WHO NIC

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Zimbabwe	US Embassy USAID Mission (w/health) HHS	<i>none</i>	DFID    SIDA CIDA    GTZ	MSF ICRC TEPHINET	<i>none</i>

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## APPENDIX C APPLICATION OF SOCIAL NETWORK ANALYSIS TO GLOBAL INFLUENZA SURVEILLANCE: SAMPLE VALUE SURVEY

Directions: Please answer the following questions from the perspective of your particular agency. Please enter the value from the scale provided in the corresponding row under each organization for items 1-4 below.																								Date completed:				
Your organization (please circle or check):	1 ( )	HHS	2 ( )	State	3 ( )	USAID	4 ( )	DoD	5 ( )	USDA	6 ( )	Peace Corps	7 ( )	Dept Commerce	Your contact information	Name:	Tel:	Email:										
USG				HOST govt				All Other																				
								IO				Foreign Lab Networks				Foreign National Development Agencies				NGOs				Other				
HHS	State Dept	USAID	DoD	USDA	Peace Corps	DOC	MOH	Min Ag	MOFA	Other	WHO	Inst Pasteur	EISS	TEPHI NET	SPC	JICA	DFID	SIDA	AusAID	GTZ	MSF	ICRC	IHC	CARITAS	Academic	Business	Media	Other
1	Please rate the <b>VALUE</b> that your organization attaches to each organization listed, specifically with regard to their potential contributions <b>related to influenza surveillance COVERAGE</b> . This includes such activities as raising awareness among veterinary or human health providers or at the community level, increasing number of clinical reporting sites or type of information reported, developing a village-/community-based reporting. 0=not applicable, 1=no value, 2=minimal value, 3=moderate value, 4=great value																											
																								1	2	3	4	
2	Please rate the <b>VALUE</b> that your organization attaches to each organization listed, specifically with regard to their potential contributions to <b>influenza surveillance QUALITY</b> . This includes such activities as improving animal or human diagnostic laboratory capacity (e.g., through training, provision of equipment and supplies, support to establish new laboratories), support to monitor influenza viral strains for changes, building epidemiology capacity. 0=not applicable, 1=no value, 2=minimal value, 3=moderate value, 4=great value																											
																								1	2	3	4	
3	Please rate the <b>VALUE</b> that your organization attaches to each organization listed, specifically with regard to their potential contributions to <b>influenza surveillance TIMELINESS</b> . This includes such activities as in-country early warning networks and rapid/transparent outbreak reporting, expedited shipment of laboratory specimens, streamlined surveillance reporting and dissemination, active (versus passive) data collection, in-country/regional/international rapid response teams, and development/evaluation/deployment of accurate rapid diagnostic tests. 0=not applicable, 1=no value, 2=minimal value, 3=moderate value, 4=great value																											
																								1	2	3	4	
4	Please rate the <b>VALUE</b> that your organization attaches to each organization listed, specifically with regard to their potential contributions to <b>influenza surveillance TRANSPARENCY</b> . This includes such activities as enhancing motivation and/or incentives to openly and rapidly report suspected cases or outbreaks in animals and humans. 0=not applicable, 1=no value, 2=minimal value, 3=moderate value, 4=great value																											
																								1	2	3	4	







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