DoD-GEIS

Annual Report

Fiscal Year 2007

Partnering in the Fight Against Emerging Infectious Diseases

DoD-GEIS

DoD Global Emerging Infections Surveillance and Response System

Annual Report

Fiscal Year 2007

Partnering in the Fight Against Emerging Infections

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DoD-GEIS is grateful to all its partners throughout the military health system, at the DoD overseas laboratories, and in the nonmilitary organizations for their ongoing efforts to combat emerging infections around the world:

18th Medical Command

Air Force Institute for Operational Health

Armed Forces Institute of Pathology

Armed Forces Research Institute of Medical Sciences *(Bangkok, Thailand)*

Brooke Army Medical Center

Center for Disaster and Humanitarian Assistance Medicine

Johns Hopkins University Applied Physics Laboratory

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Welcome Letter

Hello from DoD-GEIS Headquarters in Silver Spring, Maryland, just eight miles from the White House and the Capitol! It has been another remarkable year for our global team of preventive medicine, infectious disease, and laboratory professionals. In this year we have made great strides in building our laboratory-based emerging disease surveillance network to better support the Force Health Protection needs of our Combatant Commands around the world, while collaborating ever more closely with our US government interagency partners. I am sure that you will enjoy this annual report that compiles many of the significant contributions of our Army, Navy, and Air Force team members in FY07.

Go Team!

Ralph Loren Erickson

Ralph Loren Erickson, COL, MC
Director, DoD Global Emerging Infections Surveillance and Response System

DoD-GEIS Headquarters Staff 2008

Left to right: Mr. Mario DaRocha, COL Robert DeFraites, Ms. Robin Miliner, LtCol Victor MacIntosh, Dr. Jose Sanchez, Dr. Tracy Du Vernoy, Mr. J. Jeremy Sueker, Dr. Jean Otto , Dr. Luther Lindler, COL Ralph Erickson, Dr. Joel Gaydos, CAPT Clara Witt, Ms. Jennifer Bondarenko, Ms. Jennifer Rubenstein, Mr. Steve Gubenia, LCDR Jean-Paul Chrétien, Mr. Jay Mansfield, LTC Kelly Vest.

Executive Summary

The expansion of the Department of Defense Global Emerging Infections Surveillance and Response System (DoD-GEIS) continued in FY07. Increased infectious disease surveillance sites, augmented containment laboratory facilities, and coordination of laboratory methods across the military health system characterize the DoD-GEIS activities that support force health protection, the combatant commands, and the global medical community. DoD-GEIS continues to identify and address critical gaps in emerging infectious disease preparedness and to develop, with partners, solutions to address those vulnerabilities.

After a decade of DoD-GEIS programs and support, the five DoD overseas laboratories are more secure in their funding and direction than in prior years. Each has broad public health missions under coordinated DoD-GEIS programs in addition to research missions. The CDC, USAID, Defense Threat Reduction Agency, and NIH have sought relationships with the DoD overseas laboratories to leverage the infectious disease work of each agency. These relationships demonstrate that the DoD overseas laboratories are recognized as important US government assets within and outside the military for the detection and identification of emerging infectious diseases.

With the emergence of one such disease, avian influenza, in Hong Kong in 1997 that was followed by the rapid spread and increase in human disease in 2004–2005, the world and this nation recognized the need for coordinated pandemic influenza plans and programs. What followed in 2005 in the United States included the recognition that DoD-GEIS was the best positioned government agency to develop and manage enhancements to the DoD influenza surveillance system, mainly through the existing DoD-GEIS partnerships.

With an annual core budget of approximately $11.5 million, leveraged through its extensive partnerships within the five DoD overseas laboratories, military health system, and other US and foreign agencies, DoD-GEIS supports broad emerging infectious disease programs. In January 2006, DoD-GEIS was directed to administer $39 million in congressional supplemental funding for avian and pandemic influenza surveillance. Shortly thereafter in May 2006, the United States developed its implementation plan that furthered its National Strategy for Pandemic Influenza (2005). The implementation plan specified tasks for DoD and built on a framework developed by WHO. Then in early FY07 DoD-GEIS received follow-on funding of $40 million to continue its work in avian and pandemic influenza.

With the FY06 supplemental funding and continued support in FY07, DoD-GEIS has implemented long-term initiatives to centralize coordination and expand influenza and respiratory disease surveillance, laboratory support, and communication. Early results of this effort are presented in this report.

The DoD developed a plan that followed the US strategy closely; both are now published and widely available. DoD-GEIS and its partners enhanced influenza laboratory capacity, increased sentinel sites and the number and coverage of countries in which surveillance is conducted (emphasizing Africa and areas of the world where WHO and national surveillance is weak or nonexistent), expanded laboratory diagnostic capability and BSL-3 laboratory capacity, and established centralized communications through Headquarters.

Also in 2006 Headquarters requested that the Institute of Medicine of the National Academy of Sciences undertake an external evaluation of the DoD-GEIS influenza programs. At this time significant expansion of laboratory-based capabilities and programs was underway at AFIOH, NHRC, and the overseas laboratories. USAMRIID had added influenza to its mission, and CHPPM had developed methods to provide timely, rapid serosurveillance from serum repository resources as needed. To manage the expanded mission of DoD-GEIS, Headquarters grew to meet the need for the enhanced influenza program.

At the close of FY07 the Institute of Medicine published its evaluation: *Review of the DoD-GEIS Influenza Programs: Strengthening Global Surveillance and Response.* The report found that the DoD overseas laboratories "constitute an impressive network that has laudably utilized the supplemental funding to strengthen influenza surveillance, in addition to continuing their historically primary research activities." The report also stated that "At DoD-GEIS headquarters as well as at the domestic and overseas laboratories, DoD-GEIS personnel absorbed the large increase in funding into programs aimed to successfully build DoD and host-country laboratory and human resource capacity, to globally expand information about avian influenza and acute respiratory diseases, to benefit the health of U.S. military personnel, and to strengthen U.S. relations within the global community."

The value of these investments goes beyond enhanced influenza surveillance. The list of publications, presentations, and GenBank submissions found in this report is an outstanding record of accomplishment in many areas of emerging infectious disease work and of the extensive contribution by DoD-GEIS to the literature, to professional meetings, and to conferences related to the military. Publication in the peer-reviewed literature, as evidenced by the extensive listing, demonstrates the importance and quality of the work accomplished throughout the DoD-GEIS network.

DoD laboratory-based respiratory disease and influenza surveillance programs led directly to better understanding of naturally occurring biological threats (e.g., avian and pandemic influenza and adenovirus 14) and to improved vaccination efforts. Malaria diagnostic resources have been standardized and improved, and international efforts to address antimalarial resistance have been supported. Special surveillance programs in Korea provided valuable information for understanding and combating the troubling reemergence of malaria on the Korean peninsula. The mortality surveillance program established at AFIP for careful monitoring of all possible infectious disease deaths in US military forces ensures that sentinel infectious disease deaths will not be missed. EWORS underwent careful evaluation to determine how to improve surveillance systems in resource-constrained or developing countries.

This year also featured the inclusion of DoD-GEIS in two Government Accountability Office (GAO) investigations, one on worldwide pandemic influenza preparedness and one on US government efforts to build infectious disease surveillance capacity overseas. Although the largest US government budgets for international capacity building are with USAID and CDC/DHHS programs, DoD-GEIS was included in the second GAO investigation because of the work accomplished by the DoD overseas laboratories. In contrast to the first GAO investigation and Institute of Medicine report, both of which covered influenza work only, the second GAO investigation evaluated the entire DoD-GEIS program as it involved capacity building. The second GAO review led to an invitation to the director of DoD-GEIS to testify before the Senate Committee on Homeland Security and Government Affairs. This testimony occurred in early FY08, and the response was enthusiastic and favorable.

Systems supported by DoD-GEIS were invaluable in many outbreaks throughout FY07, notably the timely prediction of the Rift Valley fever outbreak in Kenya by the NASA remote sensing model. NASA and USAMRU-K, with DoD-GEIS support, have collaborated in a Rift Valley fever prediction model based on satellite data since the inception of DoD-GEIS. In the fall of 2006 NASA investigators accurately predicted the outbreak months before human and animal cases began to appear and correctly directed an entomology team to locations where Rift Valley fever virus was subsequently found and confirmed by laboratory analysis at USAMRU-K.

DoD-GEIS partners made substantial headway throughout FY07 in malaria surveillance, one of the DoD-GEIS priority surveillance conditions. The international malaria diagnostics center of excellence, established in Kisumu, Kenya, by the WRAIR Division of Experimental Therapeutics with USAMRU-K and the Kenya Medical Research Institute, is actively improving microscopy accuracy in surveillance, research, and clinical programs. More than 47 microscopists from 10 countries were trained in FY07, and improvements in performance were significant. The DoD overseas laboratories continue to monitor antimalarial drug resistance, supplementing ministry of health and WHO efforts with sophisticated laboratory methods. Critical overseas laboratory surveillance in Southeast Asia, where antimalarial drug resistance has emerged, has reported early indications of artemisinin resistance. Mosquito collections by 18th MEDCOM (Korea) linked with molecular analysis and modeling at the Walter Reed Biosystematics Unit have precisely identified the species involved in malaria transmission and the reemergence of malaria near the demilitarized zone. Work led by WRAIR Division of Experimental Therapeutics and the Biosystematics Unit are bringing together DoD malaria surveillance activities and the efforts of international partners and foundations. These are promising developments toward developing a global malaria surveillance system.

DoD-GEIS enters its second decade with a robust, well-developed system ready to conduct health surveillance by monitoring infectious disease outbreaks using a combination of syndromic and diagnostic/laboratory-based methodologies. The program continues to fulfill its mission that was set forth in Presidential Decision Directive NSTC-7, which established DoD-GEIS in June 1996. Through its broad capabilities, DoD-GEIS contributes to force health protection and is a vital partner in the global effort to identify and control emerging infectious diseases.

Introduction

In FY07 DoD-GEIS continued to expand its support to the DoD and the United States by identifying vulnerabilities to emerging infectious diseases and addressing these threats through effective programs. Under the Executive Agency of the Army, Office of the Surgeon General, DoD-GEIS supports and coordinates these activities through a global network of military and nonmilitary partners. During FY07 DoD-GEIS, a triservice organization, operated on all seven continents to fulfill its mission described in Presidential Decision Directive NSTC-7 and subsequent US government and DoD policies and plans.

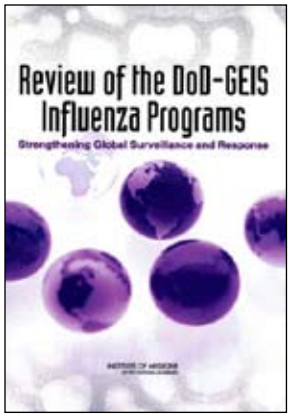
The DoD-GEIS strategic plan is based on the following four goals:

- Surveillance and detection
- Response and readiness
- Integration and innovation
- Cooperation and capacity building

These four goals form the pillars of DoD-GEIS and give it the ability to recognize and identify emerging diseases, either in training or deployed forces, that pose a threat to readiness. Although DoD-GEIS monitors all infectious diseases in military forces, the following remain the priority surveillance conditions:

- Respiratory diseases, especially influenza
- Gastroenteritis syndromes
- Febrile illness syndromes, especially dengue and malaria
- Antimicrobial resistance
- Sexually transmitted diseases and illnesses

To address the current threat of pandemic and avian influenza, DoD-GEIS has enhanced DoD and global capacity to capture and characterize viral strains for vaccine development, risk assessment, and response. In two years, DoD-GEIS has more than doubled its global influenza surveillance network from 30 countries in FY05 to more than 75 countries in FY07. This network encompasses more than 275 sites at which specimens are collected from DoD beneficiaries or foreign host country patients. DoD-GEIS supported establishment of BSL-3 facilities for respiratory virus characterization at the Landstuhl Regional Medical Center (Germany), AFRIMS (Thailand), NHRC (San Diego), NMRCD (Peru), and 18th MEDCOM (Korea); initiated a diagnostic evaluation and development program with USAMRIID; and enhanced capabilities at other DoD laboratories for influenza. These efforts have been coordinated with the CDC, WHO, and agencies of many nations. Much of this work was identified as tasks in the president's National Strategy for Pandemic Influenza (2005) and the subsequent Implementation Plan (2006). The DoD-GEIS strategic plan and its implementation in pandemic influenza surveillance and preparedness were lauded by the Institute of Medicine in its review of DoD-GEIS published in September 2007 (Figure 1).



Effectively expand global influenza surveillance program in FY06–FY07.

Continue funding in FY08 and outyears to ensure continuity of efforts.

Obtain DoD triservice executive agency status for DoD-GEIS to manage and coordinate activities.

Expand mission statement of OCONUS laboratories to include public health surveillance and response to complement research mission.

Figure 1. *Left*, cover of September 2007 review by the Institute of Medicine of the work accomplished by DoD-GEIS with the congressional supplemental funding for pandemic and avian influenza. *Right*, report's key directives for DoD-GEIS.

Additional FY07 accomplishments by DoD-GEIS in pandemic and avian influenza surveillance include the following:

- Establishment of enhanced influenza surveillance throughout EUCOM, through a partnership among Landstuhl Regional Medical Center, USACHPPM-Europe, and AFIOH;
- Expansion of influenza surveillance in Africa, where little information on circulating strains is available, through a partnership with USAMRU-K (Kenya) and the US Military HIV Research Program;
- Identification of changing influenza strains that spread globally by the Nepal satellite laboratory of AFRIMS (Thailand);
- H5N1 avian influenza outbreak investigations by NAMRU-3 (Egypt) and NAMRU-2 (Indonesia).

The ongoing work of DoD-GEIS to combat emerging infectious diseases other than influenza continued in FY07. In September 2006, DoD-GEIS and NASA, through a longstanding partnership through which satellite data are used to forecast epidemics, predicted a Rift Valley fever outbreak in East Africa approximately 2 months before cases were seen. This forecast allowed USAMRU-K to deploy an entomology team to collect mosquitoes that tested positive for Rift Valley fever virus in the exact areas that later were affected by the epidemic. Early warning of the outbreak was given to Kenya, DoD, and international public health professionals. This warning occurred at the same time that indigenous military forces were required in nearby Somalia where Rift Valley fever infection was also likely and where little disease surveillance information was available. As the outbreak progressed, the likely areas of spread were accurately assessed by ongoing use of the NASA model. This DoD-GEIS outbreak prediction and response underscore the value of the long-term investment in the sustained collaboration among DoD-GEIS, NASA, and USAMRU-K.

To improve rapid detection and response for malaria epidemics, DoD-GEIS supported the Walter Reed Army Institute of Research Division of Experimental Therapeutics and USAMRU-K in establishing an international malaria diagnostics center of excellence in Kisumu, Kenya, in 2005. Since its inception, the center has trained more than 250 personnel from 10 African countries. The WRAIR Division of Experimental Therapeutics also achieved significant progress synchronizing surveillance for antimalarial drug resistance across the DoD-GEIS overseas laboratory network. This progress will make malaria surveillance data more useful, particularly for deploying US forces, international travelers, and global health programs.

In addition to detailing these accomplishments, this report covers the progress in surveillance, response, and capacity building made by DoD-GEIS and its partners. These actions collectively illustrate how DoD-GEIS is improving emerging infectious disease preparedness, consistent with the vision and mission of Presidential Decision Directive NSTC-7, through a broad DoD program supporting public health at home and abroad.

Financial Management and Accountability

Since its establishment in 1996 by Presidential Decision Directive NSTC-7, the budget of DoD-GEIS has grown from $2.3 million in FY97 to $52 million in FY07. The $52 million budget for FY07 comprised DoD-GEIS core (Defense Health Program) funding of $11.5 million and a DoD continuation of the FY06 congressional supplemental funding for pandemic and avian influenza surveillance and response of $40 million. The allocation of DoD-GEIS core and pandemic and avian influenza funding is shown in Figures 2 and 3, respectively.

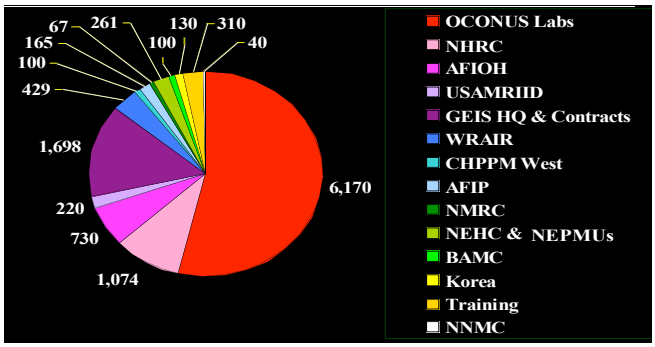


Figure 2. DoD-GEIS FY07 core budget distribution, expressed in thousands of dollars. Total $11,494,000.

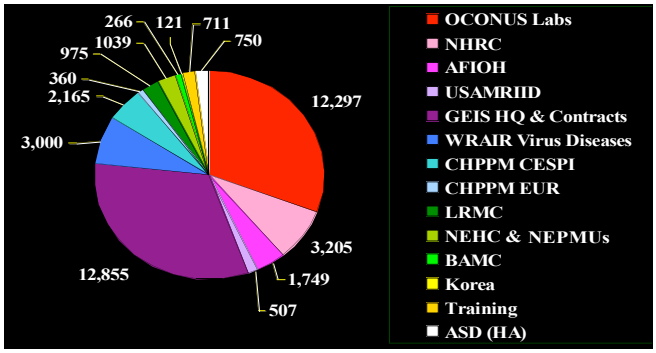


Figure 3. DoD-GEIS FY07 pandemic and avian influenza surveillance budget distribution, expressed in thousands of dollars. Total $40,000,000.

The DoD-GEIS FY07 Defense Health Program (P8) budget through the Tricare Management Activity totaled $11.5 million. Of these funds, DoD-GEIS allocated $5,370,000 to the Army, $5,394,000 to the Navy, and $730,000 to the Air Force to support DoD-GEIS projects worldwide. DoD-GEIS funds for the two Army overseas laboratories (AFRIMS and USAMRU-K) and the three Navy overseas laboratories (NAMRU-2, NAMRU-3, and NMRCD) are included in the Army and Navy amounts, respectively. All funds were budgeted programmatically by Headquarters through an internal and external protocol peer review process. Air Force and Navy funds were directly distributed the Tricare Management Activity and did not pass through US Army Medical Research and Materiel Command and DoD-GEIS.

Following its previous practice, Headquarters communicated its FY07 funding guidance to the Executive Agency Directorate at the Office of the Army Surgeon General, the Force Health Protection Council, and the Assistant Secretary of Defense for Health Affairs to receive concurrence before commencing distribution.

The program initiated in FY06 by congressional supplemental funding for pandemic and avian influenza surveillance and response was continued in FY07. The additional pandemic and avian influenza funding of $40 million in FY07 enabled the enhancement of global disease surveillance by leveraging existing DoD-GEIS partners' infrastructure platforms and enabling the expansion of functionality to address this new global challenge. Through this initiative, $5,730,000 was directed to the Army overseas laboratories in Thailand and Kenya, and $6,567,000 was directed to the Navy overseas laboratories in Egypt, Peru, and Indonesia.

The Air Force received $1,749,000 for AFIOH. The Navy received $3,205,000 for the Naval Health Research Center and $1,039,000 for the Navy Environmental Health Center. The Army distributed $3,000,000 to the Department of Virus Diseases at the Walter Reed Army Institute of Research, $2,165,000 to the Center for Serosurveillance and Epidemiology for Pandemic Influenza at USACHPPM, $507,000 to USAMRIID, $975,000 to Landstuhl Regional Medical Center, and $266,000 to Brooke Army Medical Center.

The remaining influenza funds supported various proposal-driven initiatives related to pandemic and avian influenza preparedness. A $14,983,000 government contract was issued to conduct training for the combatant commands, develop a 24/7 communications center, and provide the nucleus of the required infrastructure to oversee and manage this program.

The GAO visited Headquarters for two separate actions, the reports of which were released in 2007. The first report (June 2007) described US and international efforts to forestall pandemic influenza, and officials from GEIS were interviewed primarily in connection with the influenza work conducted by the OCONUS laboratories. The second report, "U.S. Agencies Support Programs to

Build Overseas Capacity for Infectious Disease Surveillance" (September 2007), involved GEIS more directly. The investigation reported on overseas infectious disease capacity building throughout the US government. Four key agencies were covered, and DoD-GEIS was included because of its work through the OCONUS laboratories. The September report resulted in a follow-up invitation to the director of DoD-GEIS to testify before the Senate Committee on Homeland Security and Governmental Affairs on 4 October 2007 (Figure 4). Entitled "Forestalling the Coming Pandemic: Infectious Disease Surveillance Overseas," the hearing was called by the committee to highlight the importance of the report and call attention to its release. Eight leaders in infectious disease surveillance, including the DoD-GEIS director, were invited to testify as witnesses. The response from the Senate hearing regarding DoD-GEIS was favorable.

Figure 4. DoD-GEIS director testifying before the Senate on 4 October 2007.

Headquarters

During FY07 Headquarters responsibilities expanded substantially as did the number of staffmembers needed to coordinate activities throughout the DoD-GEIS network. Duties included establishing the communication center and extending surveillance to many new countries while continuing the efforts in infectious diseases other than influenza and providing consultation on emerging infectious disease surveillance within the military.

Influenza

The DoD-GEIS network of laboratories continues to be vital in global surveillance for influenza by characterizing isolates and monitoring for important mutations, both for seasonal and potentially pandemic strains, and by providing surveillance data and specimens to support national and international influenza surveillance systems. With the expansion of influenza surveillance capabilities as a result of the congressional supplemental funding and the new national pandemic influenza plan, DoD needed additional coordination and communication capabilities within DoD-GEIS that were based at Headquarters.

Typically the DoD overseas laboratories provide critical infrastructure, expertise, and response capabilities that are unavailable elsewhere. AFIOH and NHRC have established extensive sentinel and population-based surveillance systems coupled with state-of-the-art influenza and respiratory laboratory capabilities that are closely coordinated with the CDC. Combined, these overseas and domestic laboratories also serve as the DoD influenza reference laboratories. The number and diversity of the influenza isolates obtained through this global surveillance network help to identify disease trends and guide changes in vaccine strain composition worldwide. Headquarters unifies these efforts for influenza.

The DoD reference laboratories and other organizations in the GEIS network enable broad-based public health programs, based largely on laboratory capability, to detect emerging pathogens. This is especially true as the pathogens may relate to novel, potentially pandemic, strains of influenza virus or other agents with zoonotic potential. Headquarters works to assure that DoD influenza programs augment and support broad-based public health programs for emerging infectious disease surveillance and response.

A central core capability with dedicated personnel in avian and pandemic influenza matters was developed by Headquarters to manage the administration of the $40 million program (funded as a congressional supplement). To support this capability, an avian and pandemic influenza emergency preparedness plan management office and communications center were established at the Headquarters site in Silver Spring, Maryland. This office and communications center would support effective communication and coordinate surveillance strategies among DoD partners and civilian agencies involved in the prevention and control of influenza (including avian and pandemic influenza) among military personnel and other DoD health care beneficiaries.

Communications Center

The physical facilities of the DoD-GEIS communications center were completed in FY07 (Figure 5). Capability includes conference call capacity for up to 37 simultaneous participants (up to 156 participants if all Headquarters staff are included), a video teleconferencing system, certified by MEDCOM and DoD-Health Affairs, with two complete suites, and a 301-319-GEIS telephone number that is answered 24/7 and published system-wide. Activities included continuing improvement and updating of the GEIS public and secure websites with more than 240 postings of military public health relevance. In November 2006, the email address <GEISCommCenter@amedd.army.mil> became operational and has been subsequently used as the primary means of communication among stakeholders.

Created through the supplemental funding for pandemic and avian influenza, the communications center offers benefits that are not limited to influenza surveillance and response. Information is gathered through open sources and regular communication channels and then widely disseminated. Although many recipients of this material are DoD personnel, other government agencies are included, such as the Departments of State, Homeland Security, and Health and Human Services, Office of the Vice President, and the Pan American Health Organization. Currently, 245 individuals representing offices from at least 20 government agencies, international health organizations, universities, and many DoD health commands receive information from GEIS on a daily basis regarding infectious diseases (primarily influenza), surveillance updates, conferences and articles of interest, and new disease outbreaks. An outbreak of respiratory infectious disease was the focus of an exercise conducted at Headquarters this year (Figure 6), which culminated in the activation of the communications center.

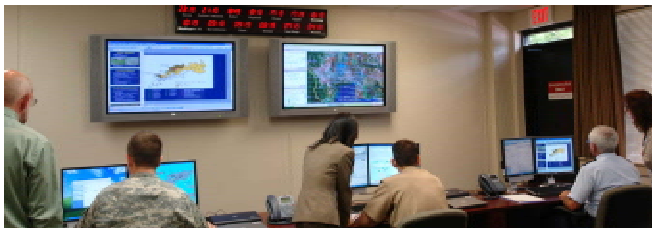


Figure 5. DoD-GEIS communications center in operation.

Figure 6. Members of Headquarters staff during first exercise in DoD-GEIS communications center. Exercise involved a novel respiratory disease that first appears with index cases presenting at an Army recruit training center and then spreads rapidly to civilians, other bases, and other military services.

Reporting Influenza Surveillance Efforts

Worldwide surveillance efforts supported under the avian and pandemic influenza program were brought together by Headquarters through centralized maintenance of influenza surveillance site listings with reports that were updated quarterly. Briefing documents and partners' status reports for more than 275 influenza surveillance sites were included (Figure 7). This effort required close coordination and sharing with CDC as part of the DoD-CDC influenza working group meetings held during FY07.

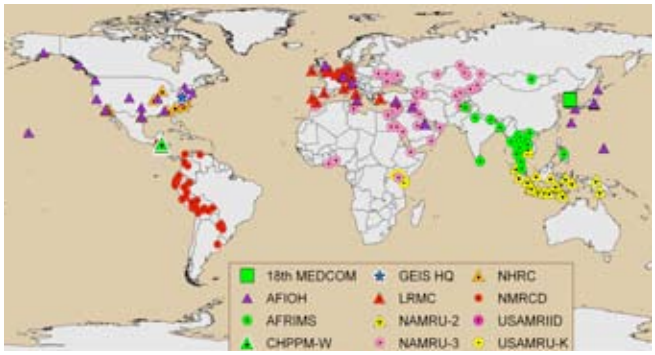


Figure 7. DoD global influenza surveillance sites as of 1 October 2007.

Assessing Influenza Diagnostic Capability

Influenza testing capability varies widely in the DoD; specialized laboratories have exceptional capability, whereas hospitals and medical centers primarily rely on rapid tests combined with virology laboratory services in-house or via reference laboratories. In deployed or austere settings, little testing capability is available. The Laboratory Response Network provides an organized, systematic approach for select agents and some capability for influenza testing but mainly provides an alternative for CONUS or US-based and some overseas military personnel to obtain diagnostic testing for infectious diseases. Headquarters staff and DoD-Health Affairs have established a new working group of clinical and public health experts to assess diagnostic capability on a regular basis and seek solutions where gaps are present.

Emerging Infectious Diseases Other Than Influenza

In FY07, Headquarters worked with partners to integrate efforts in malaria drug resistance surveillance, syndromic surveillance, and risk assessment for vector-borne diseases. Highlights of Headquarters coordination of activities in these areas follow.

Malaria Drug Resistance Surveillance

Malaria drug resistance data are essential for guiding prophylaxis and treatment policy and for developing new drugs. During FY07, Headquarters and partners addressed a challenge in global antimalarial drug resistance monitoring efforts: the wide variety of methods used, which produces results that cannot directly be compared. Led by the WRAIR Division of Experimental Therapeutics, GEIS partners standardized approaches in several overseas areas. GEIS partners also have assumed key roles in a larger international program to coordinate antimalarial drug resistance surveillance, the World Antimalarial Resistance Network that was launched in FY07.

Syndromic Surveillance

Syndromic surveillance systems, which monitor prediagnostic information to detect outbreaks and provide situational awareness, are common in the United States. They also may prove useful in developing countries by reducing demands on a limited public health workforce through automation and by detecting emerging diseases before diagnostic criteria are established. In FY07, Headquarters coordinated the partnership initiated in

FY06 with the Johns Hopkins University Applied Physics Laboratory (JHU/APL) and DoD overseas laboratories to evaluate and pilot syndromic surveillance systems. Staff from JHU/APL, Headquarters, NMRCD, and NAMRU-2 evaluated the NMRCD EWORS system in Peru (The same team evaluated the NAMRU-2 EWORS system in Laos in FY06.) and conducted a system feasibility assessment in the Philippines with AFRIMS. Based on this experience, JHU/APL led a GEIS-supported workshop on syndromic surveillance, hosted by AFRIMS in Bangkok, with participation by WHO and representatives of 14 countries.

Risk Assessment for Vector-borne Diseases

Assessing risk of vector-borne diseases, such as malaria, to military forces may be difficult without epidemiological data from the area. Headquarters is coordinating a partnership with the Walter Reed Biosystematics Unit (WRBU), 18th MEDCOM (Korea), and NASA to develop, validate, and operationalize models to predict risk of vector-borne diseases using satellite observations. As part of WRBU's GEIS-funded program to develop an online, global malaria vector map and modeling tool, WRBU is developing fine-scale malaria prediction models for Korea. In FY07, WRBU staff joined 18th MEDCOM in malaria vector collection missions to assess preliminary model predictions. The team used satellite imagery provided by NASA to target their collections. As WRBU, 18th MEDCOM, and NASA refine the malaria prediction model for Korea, they will adapt their integrated field-based and modeling approaches to other disease threats and other regions.

Consultation on Emerging Infectious Disease Surveillance in Military

Consultation and personnel assistance were provided by Headquarters to the MHS and other partners for vaccine development and implementation plans, testing of vaccines, and programs for surveillance and control of emerging infectious agents. Headquarters was also responsible for 1) screening programs for infectious agents in uniformed members and other populations, such as blood donors and deployed troops, 2) public health laboratory functions in the MHS, and 3) development of infectious disease models and remote sensing systems to predict outbreaks and assess the impact of outbreak interventions.

Headquarters was involved in the development and presentation of sessions related to emerging infectious diseases for the following meetings: Annual Syndromic Surveillance Conference (2006 and 2007), the South Carolina Department of Health and Environmental Control 2007 Annual Epi Conference, the American Society of Tropical Medicine and Hygiene 2007 Annual Meeting, and the 10th Annual Force Health Protection Conference.

For the force health protection conference, Headquarters developed and cosponsored a large pandemic influenza preparedness workshop aimed at training military public health professionals to respond to and manage an unfolding influenza pandemic. This workshop featured a collaboration of the nation's leading disease researchers, emergency planners, and public health experts; 300 participants from all military services attended. A tabletop exercise was included that focused on the following:

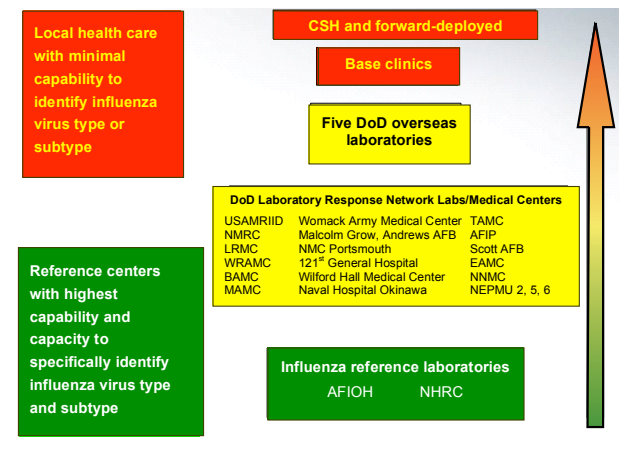
Improved Influenza A Diagnostics Throughout Military Health System

Preparing for and preventing pandemic influenza require the ability to detect the earliest human infection with a newly emerged strain with greater than typical virulence. Much attention in the medical community has been focused on the highly pathogenic avian influenza strain H5N1 currently circulating in Asia. Experience suggests that human pandemic influenza strains may not belong to the same subtype as the circulating zoonotic strains of the influenza A virus. For example, the 1957 Asian pandemic was caused by an H2N2 strain, the 1968 Hong Kong pandemic by H3N2, and the 1977 Russian epidemic by an H1N1 subtype. The genetic traits associated with the most devastating pandemic influenza, the 1918 Spanish influenza (H1N1), are still largely unknown even after obtaining the complete DNA sequence.

Continued

Improved Influenza A Diagnostics, *Continued*

Given these facts, DoD-GEIS recognized that the ability to identify the influenza A subtype causing human infection is critical to recognition and prevention of the spread of a new strain of the virus before it becomes a pandemic. To better understand the US and DoD assets related to influenza A diagnostics, DoD-GEIS conducted an end-to-end survey of capabilities at various levels within the military health system from May to November 2006.



Current DoD influenza A diagnostic capabilities. *Green*, laboratories that can test clinical samples to determine influenza A subtype. *Yellow*, laboratories for which the sole subtyping capability is incomplete for all known influenza A subtypes that infect humans (or are not operated under CLIP compliance). In this group, the testing capability is generally only for influenza A H5. *Red*, laboratories that rely on rapid antigen tests of any type for influenza A testing. *Arrow at right*, increasing risk of undetected influenza A in serviced patient population.

This survey revealed that the DoD assets with the complete ability to identify and characterize clinical samples for influenza A virus were the reference laboratories at AFIOH and NHRC, both of which are CONUS facilities. The second highest ability resides in the military medical centers and DoD laboratories associated with the CDC Laboratory Response Network. The CDC influenza A H5-specific PCR has been distributed throughout many of these Laboratory Response Network sites in the DoD. A special situation exists at the overseas laboratories in that most have high diagnostic capability but have not sought CLIP compliance because their inherent research and surveillance-related missions do not require this. The least capable MTFs for influenza diagnostics are the more forward-deployed units such as combat support hospitals, expeditionary medical support, and medical department activities, all of which use rapid antigen tests for testing. Rapid antigen tests do not recognize the highly pathogenic avian influenza A H5 strain in clinical samples, and some cannot distinguish influenza A from influenza B virus.

The configuration in the DoD resembles that in the civilian sector in which local and state Laboratory Response Network sites may have the influenza A H5 PCR assay, but further subtyping is referred to the CDC reference laboratory. For both the military and civilian sectors, the question is, what if the next pandemic is not caused by subtype H5? GEIS has recognized this uneven ability to diagnose influenza as a potential weakness in DoD pandemic influenza preparedness and has undertaken an initiative to obtain clinically relevant influenza subtype-specific testing for forward-deployed units. GEIS is partnering with the DoD Joint Biological Agent Identification and Diagnostic System (JBAIDS) and CDC to obtain clearance for clinical tests to identify influenza subtypes. The JBAIDS platform is to be deployed at more than 300 sites within DoD, including level III MTFs such as combat support hospitals.

The completion of this project will place DoD at lower risk of a pandemic spread of influenza through early recognition of new strains causing human infections. GEIS has stepped into the diagnostics arena to improve force health protection by reducing the risk of pandemic influenza within the force.

- Establishing situational awareness of potential scenarios that the US military, particularly Public Health Emergency Officers, may face in managing a pandemic;
- Clarifying the functions of Public Health Emergency Officers and other medical/public health personnel in an installation-level response;
- Identifying strengths and gaps in the military public health response to pandemic influenza.

Notably, Headquarters-sponsored sessions at the force health protection conference addressed influenza, malaria, respiratory diseases in military recruits, the emergence of adenovirus 14, *Neisseria meningitis* and *Bordetella pertussis* in the military, methicillin-resistant *Staphylococcus aureus,* Japanese encephalitis virus threat and vaccines, testing for emerging sexually transmitted diseases, Epidemic Information Exchange (Epi-X) training for military public health personnel, and the surveillance value of overseas capacity building investment. Headquarters staff also participated in US interagency antimicrobial resistance task force activities in consultation with GEIS-supported partners who were studying antimicrobial resistance in the MHS.

Prevention of Respiratory Illnesses in Military Populations

Headquarters staff participated on and assisted with committees and other groups involved with vaccine development and testing and reviewed related reports. Vaccine-related data and information were presented and discussed at the Epidemiology Chiefs' biweekly teleconferences and incorporated into programs for formal conferences and workshops, such as the 10th Annual Force Health Protection Conference.

Sexually Transmitted Infections

The Headquarters worked with the Army Medical Surveillance Activity, the Defense Medical Surveillance System, and CHPPM to identify and assess the incidence of sexually transmitted infections and diseases and related sequelae in the military. Through this project, improved methods to diagnose, monitor, and prevent sexually transmitted infections and diseases were identified. Consultation also occurred with regard to the inclusion of issues related to sexually transmitted infections and diseases in the Army Balanced Scorecard management initiative. This work was coordinated with GEIS-supported efforts at NEHC. Headquarters also assisted 18th MEDCOM (Korea) in their effort to establish a *Chlamydia* screening program for Army personnel reporting to Korea.

Antimicrobial Resistance

DoD-GEIS has encouraged the development of a DoD-wide surveillance mechanism for identifying antimicrobial resistance occurrences and trends within the force. Through a cooperative agreement with Focus Bio-Inova, now Eurofins Medinet (Herndon, VA), four military medical centers participate in the nation's largest electronic surveillance system for antimicrobial resistance, The Surveillance Network (TSN):

- Wilford Hall Medical Center, Lackland AFB, Texas
- Keesler Medical Center, Keesler AFB, Mississippi
- Tripler Army Medical Center, Honolulu, Hawaii
- Landstuhl Regional Medical Center, Germany

Standardized and quality-checked data from more than 13,000 positive clinical bacteriology specimens from patients in the DoD with antibiotic sensitivities were added to the TSN database in FY07. As of the end of FY07, DoD results in TSN totaled more than 100,000 since the project began in the late 1990s. With the addition of Landstuhl Regional Medical Center (Germany) during a period of intense concern about antibiotic-resistant wound infections in Iraq and Afghanistan, tracking *Acinetobacter* antibiotic resistance in the MHS has been possible in ways that previously were unavailable.

The interagency task force on antimicrobial resistance developed a public health action plan to combat antimicrobial resistance. An overarching goal of the plan, which was published in 1999, was coordinated national surveillance, including reliable drug susceptibility data from clinical sources and the ability to monitor antibiotic drug use. The task force, co-chaired by the CDC, FDA, and NIH, includes the DoD, Department of Veterans Affairs, USDA, and the Environmental Protection Agency. Headquarters has provided DoD representation to the task force since its formation and continues to regularly review DoD contributions and update the inventory of projects and activities, which is published annually. The action plan is expected to be updated in FY08.

Headquarters has also established a multicenter multidrug-resistant *Acinetobacter* project involving three of the primary MTFs receiving wounded servicemembers from Operation Iraqi Freedom. Multidrug-resistant *Acinetobacter* has been a problem from the onset of operations in Iraq, yet a coordinated effort to address the epidemiology of these infections has been largely lacking. Headquarters has funded a coordinated molecular epidemiology study at WRAMC, BAMC, and NNMC along with historical data from WRAIR to analyze strains causing infections in these MTFs. The goal of this study is to understand

if these strains have unique properties and, if so, where these strains are acquired by the wounded returning from Operation Iraqi Freedom. In conjunction with this effort, GEIS is helping coordinate a genomic sequencing effort to compare multidrug-resistant strains with susceptible strains to identify unique genes that might be associated with organisms causing wound infections and to then develop possible diagnostic testing for those unique genetic properties. BAMC has established a multidrug-resistant bacteria center of excellence with Headquarters funding that will study *Acinetobacter* infections and other infections associated with multidrug-resistant organisms.

Epi-X

The Epidemic Information Exchange (Epi-X) is a web-based system developed by CDC for the exchange of preliminary information among public health officials about emerging and ongoing public health threats. It is a secure communications network for public health professionals at local, state, and federal levels in the United States and other nations (e.g., Canada and Mexico). Headquarters has cosponsored Epi-X training for the services and DoD users, serves on the Epi-X editorial board, and consults with CDC and DoD staff to coordinate the use of Epi-X by the DoD. The more than 100 DoD individuals who use Epi-X represent organizations at installation, major command, service, agency, COCOM, and DoD-wide levels. CDC officials cite regular reports from the DoD global influenza program (AFIOH) and the febrile respiratory illness surveillance among recruits (NHRC), both of which are supported by GEIS, as major contributions by DoD, along with outbreak information such as the emergence this year at Lackland AFB of adenovirus 14. Overall, DoD contributed more than 50 reports to Epi-X in FY07.

Epi-Chiefs

Headquarters regularly conducted DoD-wide teleconferences, designated as the epidemiology chiefs' biweekly teleconference (epi-chiefs). The objective of the epi-chiefs was to exchange information among military public health officials about infectious disease threats to the force. Teleconferences lasted 1 hour and included participants from AFMIC, AFIP, AFIOH, CDC, NORTHCOM, SOUTHCOM, DoD-Health Affairs, NEHC, NHRC, POPM, CHPPM, and WRAIR. More than 20 epi-chiefs teleconferences were held in FY07. Regular agenda items covered outbreaks, recent mortalities, infectious respiratory disease (e.g., emergence of adenovirus 14 at Lackland AFB) and influenza, other febrile illness incidence (e.g., Rift Valley fever and chikungunya), and a roundtable of open discussion. Major benefits of these teleconferences are the provision of current information, stimulation of productive interactions (e.g., to improve surveillance and understanding of emerging infectious disease threats), and provision of assistance when needed (e.g., the identification of laboratories that could provide special testing). The proceedings of the epi-chiefs are transcribed; transcriptions and summaries, sent to participants, were reviewed and are available for review by others with a need. A short summary of highlights of the meeting is sent promptly to participants and the leadership.

Coordination with CDC/Department of Health and Human Services

With an increasing number of new initiatives and programs, DoD and Department of Health and Human Services (HHS) leaders called for a structured, periodic telephone or video conference of key DoD and CDC/HHS personnel to ensure cooperation and collaboration in government efforts to respond to the threat of avian and pandemic influenza and to avoid duplication in all areas of emerging infectious disease interest, particularly at OCONUS sites. This effort began in 2006 as the DoD-CDC/HHS working group, and Headquarters assumed administrative responsibility for the conferences. In FY07, four teleconferences were held. Typically 12–14 individuals from HHS, CDC, DoD-Health Affairs, GEIS, AFIOH, NHRC, and the DoD overseas laboratories participated. These interactions improved understanding of each organization's plans, priorities, and funding for OCONUS surveillance.

Education and Training

One Headquarters staffmember served as primary mentor for an MPH candidate at USUHS during the student's year-long practicum at Headquarters. For the practicum assignment, the student conducted a systematic review of published scientific literature to identify and characterize assessments of epidemic surveillance systems in developing settings. The review focused on systems using automated procedures for processing data or electronic systems for communicating data. Only a few published assessments of such systems were identified, even though many such systems are known to exist, and this shortfall calls attention to the need to evaluate investments in information and communication technology for epidemic surveillance in developing countries. Through this project, the student successfully completed the MPH practicum requirements for USUHS and delivered valuable data for DoD-GEIS.

Staffmembers collectively mentored an undergraduate student at Tufts University (Medford, MA) who, after graduation, joined Headquarters staff in late FY06. The student completed an evaluation of the DoD-GEIS work

DoD-GEIS Develops International Military-to-Military Collaborations

Emerging infectious diseases are a threat to all nations, and it is the mounting of a common defense against this shared adversary that allows significant collaboration between scientists and medical professionals around the globe. Military-to-military cooperation in the early detection of and response to these diseases, especially in the context of complex humanitarian emergencies, is widely accepted. Furthermore, the medical departments of the militaries of developed nations often bring to the fight advanced (and sometimes unique) laboratory and surveillance infrastructure and capacity. DoD-GEIS collaboration with NATO countries, in particular, has been viewed as crucial in extending emerging infectious disease laboratory-based surveillance to countries and regions that are underserved and unprepared.

Cameroon Prime Minister Ephraim Inoni (*right*) meeting with DoD-GEIS director to discuss the establishment of laboratory-based influenza surveillance in Cameroon, June 2007.

Throughout FY07 Headquarters staff enjoyed several opportunities to develop such collaborations through participation in international military meetings and military-to-military exchanges throughout the world. In addition, delegations from militaries of the following countries visited Headquarters and WRAIR to discuss emerging infectious disease surveillance efforts in their respective regions:

Military preventive medicine expert panel at meeting of the Committee of the Chiefs of Military Medical Services in NATO, at which DoD-GEIS director was an invited speaker, Warsaw, September 2007.

Brazil	Japan	Poland	Thailand
France	Morocco	Singapore	Turkmenistan
Germany	Nepal	Taiwan	

In the company of the SOUTHCOM surgeon, Headquarters staffmembers consulted with the surgeon general and senior medical leaders of the Brazilian Ministry of Defense in Brasilia in October 2006 to discuss influenza and malaria surveillance in Latin America. This was followed by Headquarters participation at an NIH-sponsored influenza summit in Buenos Aires, Argentina, in February 2007, a meeting at which 10 South American countries were represented.

Fostering a growing relationship with the Defense Threat Reduction Agency, the DoD-GEIS director traveled to Georgia and Azerbaijan later in February to review progress in the creation of web-based infectious disease reporting in both countries and the renovation of state laboratories for infectious disease surveillance. Since that time DoD-GEIS has been a major US government stakeholder in discussions concerning the creation of a US-Georgian central reference laboratory in Tbilisi funded by the Cooperative Threat Reduction program.

Azerbaijan Deputy Minister of Health (*fourth from right*) with personnel from WRAIR, Defense Threat Reduction Agency, and DoD-GEIS, March 2007.

Continued

Military-to-Military Collaborations, *Continued*

Personnel from the French Military Tropical Medicine Institute and DoD-GEIS, Marseilles, May 2007.

On 16–20 April, several DoD-GEIS partners from PACOM joined Headquarters staffmembers in presenting at the 17th Annual Asia Pacific Military Medical Conference in Manila, a meeting attended by military medical officers from 32 countries. In June, a Headquarters staff visit to Cameroon to establish laboratory-based influenza surveillance led to meetings with military and civilian public health leaders and culminated in an audience of the DoD-GEIS director with the country's prime minister on national television.

During a May 2007 trip to Europe, Headquarters staff actively engaged professional colleagues of the French Military Tropical Medicine Institute (Institut de Médecine Tropicale du Service de Santé des Armées) in Marseilles. During these meetings plans were discussed to share emerging infectious disease surveillance information among the respective networks, especially for chikungunya, which severely affected Reunion Island and East Africa in 2007. On the same trip, the GEIS director toured the German Army Microbiology Institute (Institut für Mikrobiologie der Bundeswehr) and consulted with leaders of the German Army Department of Public Health (Sanitätsamt der Bundeswehr), both in Munich. These discussions centered on the potential for collaboration in tick-borne disease surveillance in central Europe.

Leadership of the German Army Department of Public Health (*left*) and Microbiology Institute (*right*) with DoD-GEIS director, Munich, May 2007.

Also in continental Europe, DoD-GEIS has become a regular presenter at the annual American-Hungarian Military Medical Conferences held each September and recently began participating in meetings of the Military Preventive Medicine Expert Panel that are sponsored by the NATO Committee of the Chiefs of Military Medical Services.

As these military-to-military relationships mature in the coming years, DoD-GEIS will continue to expand its surveillance network and enhance its emerging infectious disease early detection and response mission within the Combatant Commands.

Officers from the Turkmenistan Army and Headquarters staff members at the WRAIR, laying the groundwork for future collaboration in influenza surveillance and pandemic preparedness in central Asia, June 2007.

Director of the Polish Military Institute of Hygiene and Epidemiology (*center*) with DoD-GEIS and USAMRMC personnel, May 2007. Through NATO channels, the Polish military asked to be part of the DoD-GEIS network.

at the OCONUS laboratories. This systematic, longitudinal assessment, which complemented the FY07 GAO and Institute of Medicine evaluations of DoD-GEIS, was based on year-end reports from each laboratory (e.g., changes in extent of collaboration among overseas laboratories on projects) and on semistructured, in-depth interviews with current and former overseas laboratory personnel. Preliminary findings were presented at the force health protection conference in August 2007, and the final report includes prioritized recommendations for improving the DoD-GEIS overseas laboratory program.

Headquarters staff presented and participated in many educational sessions at the Uniformed Services University and other universities to address infectious diseases topics and to acquaint students and faculty with DoD-GEIS.

United States Medicine Institute Roundtables

The United States Medicine Institute for Health Studies (USMI) conducts invitation-only events that bring together prominent federal, military, business, and academic leaders to share information and identify critical matters in medicine and health care. One approach used by USMI and its partners is the roundtable, in which 30 or fewer participants gather for a half-day forum that begins with a few short presentations that are followed by an issue-oriented discussion led by a senior moderator. DoD-GEIS partnered with USMI to conduct two roundtables in 2007: "Addressing Antimicrobial Resistance" (9 February 2007) and "Assessing Syndromic Surveillance: Costs, Benefits, Future" (19 October 2007).

Although an interagency task force has developed a federal action plan to confront antimicrobial resistance and professional organizations have developed programs, little progress has been made. The primary objective of the February roundtable was to assess how these efforts might be better coordinated and available resources used more effectively. Participants heard calls for making control of antimicrobial resistance a national priority, with antibiotic resistance being treated as a patient safety issue. Other recommendations included postmarketing surveillance of new antimicrobials, regular updates on the proper use of antibiotics in drug product labeling, improved communication of resistance data, concerted efforts to isolate and control new resistant organisms (thus preventing their becoming entrenched), and studies to better define resistance and identify the optimum conditions for use of specific drugs.

The participants noted that progress is possible. For example, the Pittsburgh Veterans Affairs Medical Center cut methicillin-resistant *Staphylococcus aureus* infection rates 70% by screening all patients by using nasal swabs and isolating those who tested positive, requiring gowns and gloves for health care providers, and enforcing stringent policies for disinfecting equipment and hand washing. Notably, the success at Pittsburgh was linked to support from the highest levels in the Department of Veterans Affairs. Participants concluded that the essential ingredient for success in confronting rising rates of resistant organisms is leadership.

Chikungunya Spreads Beyond Tropical Regions

Once found only in tropical areas of Asia and Africa, chikungunya virus is transmitted to humans by *Aedes* mosquitoes. Although the fever caused by the virus is not usually fatal, the disease typically incapacitates the individual for weeks to months. Symptoms include high fever, headache, and debilitating joint pain. According to the WHO, the word *chikungunya* derives from a Swahili term meaning "stooped walk," a reference to the hunched posture caused by the arthralgia that accompanies the condition.

Beginning in August 2004, chikungunya virus was identified as the cause of an epidemic in Lamu, a coastal island city in Kenya. Chikungunya fever had not been reported before in the area, and because it clinically resembles endemic acute febrile diseases such as malaria and dengue, control efforts were delayed.

A. aegypti was the most likely vector in Kenya, but *A. albopictus* (Asian tiger mosquito) is thought to be the vector for a massive outbreak that began 7 months later on Reunion Island (500 miles east of Madagascar in the Indian Ocean). More than 100,000 individuals there are estimated to have been infected with chikungunya from March 2005 to February 2006. Since the 2004 appearance in Kenya, chikungunya has swiftly spread far to many islands of the Indian Ocean, India, and beyond. More than 1 million cases are suspected to date.

Continued

Chikungunya, *Continued*

Asian tiger mosquito (*A. albopictus*), vector capable of transmitting viruses that cause infectious diseases such as chikungunya, dengue, and yellow fever. Once exclusive to Southeast Asia, *A. albopictus* has increased its range nearly worldwide, thanks largely to transportation of dormant eggs in scrap and new tires.

The different vector on Reunion Island, *A. albopictus*, is significant because not all mosquitoes transmit all viruses to humans. *A. albopictus* is a vector for several virulent infectious disease pathogens and once was known only in its native Asia. However, in recent years it has become established widely in the Americas, Europe, the Pacific, and parts of Africa. Consequently the appearance of the vector *A. albopictus* indicates that infectious diseases formerly seldom seen in many areas of the world, if at all, may emerge.

The areas that have been affected by chikungunya can be visited by travelers who may be bitten by infected mosquitoes before returning home. Should they be bitten by one or more competent vectors in their home area (or in transit) while viremic, then sustained transmission can follow. When such a sequence occurs, this disease once specific to tropical areas can spread globally, even to temperate zones.

Such a sequence happened in FY07 when chikungunya fever appeared in Italy, south of Venice near Ravenna (205 cases from July to September 2007), and chikungunya virus was confirmed in local *A. albopictus* mosquitoes. A traveler from India was the index case for this outbreak, which represents the first appearance of chikungunya fever in a nontropical region and the first instance in which *A. albopictus* has been involved in an outbreak of human illness in Europe. Cases in travelers without local transmission have already been found in other countries, including the United States.

Many groups including GEIS have closely followed this far-reaching proliferation of chikungunya. GEIS was particularly vigilant after the cases in Italy were reported because US military personnel in Italy are stationed nearby. In effect, these outbreaks comprise a case study in an infectious disease quickly emerging in many areas of the world. The following factors favor spread of chikungunya fever in humans:

- Rapid international transport;
- Previous introduction of exotic mosquito species (*A. albopictus* appeared in Italy in the 1990s);
- Inadequate mosquito control;
- Susceptible population (no prior immunity);
- Favorable climatic conditions.

Other vector-borne diseases that could similarly spread include malaria, dengue, Rift Valley fever, and yellow fever. To prevent or mitigate the threat of these diseases becoming established in regions presently uninfected, nations, through their public health agencies, need effective vector control capability and surveillance, the ability to rapidly investigate and characterize outbreaks, and an understanding of global threats and risk. Military forces are not immune to these concerns. Like the Italian traveler from India this year, a servicemember could return home from a distant location with a virus and, with the right conditions, become the index case.

A newly adopted framework for addressing the threat posed by the spread of infectious disease is embodied in the revised WHO International Health Regulations that went into effect in June 2007 and are legally binding on all WHO member states. The regulations require nations to respond effectively to public health emergencies that could cross national borders.

In 1997, shortly after the startup of DoD-GEIS, DoD-GEIS and WRAIR launched an electronic syndromic surveillance system for DoD. This system quickly captured outpatient ICD codes that were entered into an existing system and grouped these into syndrome categories, which were frequently evaluated for deviations from established baselines. The product was the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE). After subsequent years of concern about bioterrorism and pandemic influenza, interest in syndromic surveillance systems as early warning systems grew, and different versions appeared in the public and private sectors. Nevertheless, the value of syndromic surveillance systems as early earning systems has always been controversial. Recently, some have deemphasized the concept of early warning systems and suggested instead that syndromic surveillance systems should be considered tools for developing *situational awareness*, an aviation term meaning an awareness of factors in the environment in a manner that facilitates predicting and planning for future events. Others have bluntly asked if syndromic surveillance systems have any value.

The October roundtable (Figure 8) addressed the challenges of syndromic surveillance systems, and participants agreed that solid research, not anecdotal reports, was needed to determine the value of the systems. In addition, the definition of syndromic surveillance must be clear and include meaningful criteria for its implementation and for judging its usefulness. Participants agreed that the goal of syndromic surveillance should be to complement public health efforts and surveillance; the tools of surveillance should not be ends in themselves. Additionally, participants deemed that a national strategy for syndromic surveillance is necessary to allow better placement of available funding and the identification of scenarios that should be monitored. The need for local discretion was acknowledged. Participants called for serious consideration about how and where these systems would be used and how they would be evaluated; less emphasis was placed on the hardware and software tools. After the roundtable, plans were made to have small groups within DoD address basic but neglected issues of syndromic surveillance that were identified.

Figure 8. USMI roundtable "Assessing Syndromic Surveillance: Costs, Benefits, Future," 19 October 2007, Washington DC.

Military Health System

Air Force Institute for Operational Health

DoD-GEIS relies on the participation of the Air Force Institute for Operational Health (AFIOH) for its work in influenza surveillance. AFIOH has annually expanded its geographic presence and increased DoD-wide participation in the sentinel site influenza surveillance program in conjunction with the Joint Influenza Surveillance Working Group. AFIOH continues to improve the ability to rapidly identify and respond to increased respiratory disease activity by enhancing the critical sentinel-based surveillance system and clinical laboratory infrastructure of the DoD and the nation. The principal objective is to enable the rapid discovery of novel strain mutations that could trigger a pandemic and to monitor these strains for their ability to transmit and to cause disease.

The aims and objectives of the AFIOH pandemic plan correspond directly with the DoD Implementation Plan for Pandemic Influenza (August 2006) and the federal implementation plan for the National Strategy for Pandemic Influenza (November 2005). In FY07 AFIOH accomplished the following:

- Upgraded laboratory and epidemiological capabilities to enhance year-round influenza surveillance worldwide at MTFs and host nation medical facilities;
- Initiated surveillance for influenza-like illness where needed;
- Enhanced pathogen detection and molecular characterization to include all respiratory specimens submitted;
- Supplied all participating sites with year-round diagnostic and specimen shipping supplies to maintain a minimum of monthly shipments during peak activity;
- Performed molecular subtyping to provide timely characterization of genetic variance among influenza specimens to global partners and global health entities;
- Provided real-time mapping of viral disease outbreaks along with disseminated reports to a wide spectrum of stakeholders.

Although the priority of the DoD is to maintain readiness and protect the health of servicemembers and beneficiaries, the contributions from the AFIOH surveillance program also benefit the greater global health community.

The epidemiological and laboratory components at AFIOH have enhanced their surveillance capabilities by expanding existing infrastructure, developing new processes, and increasing the capacity to effectively monitor for a potential pandemic. The first stage of this effort has been the acquisition of the pandemic influenza preparedness plan. Current efforts have shifted to implementation of new systems and maintenance of newly developed capabilities. Future funding will help sustain the established efforts of the preceding years and will target new efforts to boost military-military and military-civilian relationships in host nations of interest through training, education, and needs assessments.

Surveillance

Active surveillance was performed at sentinel sites around the world, including three of the five DoD overseas laboratories. Sentinel sites were selected according to location and mission. Factors considered in site selection were potential for emergence of new strains, potential for importation of new strains, impact of an outbreak or novel influenza virus on military operations in areas with high troop concentrations, and movement of highly mobile or rapid response units. DoD-GEIS supports sentinel site surveillance by AFIOH by providing key linkages and coordination with international partners.

Sentinel sites were required to institute an active influenza surveillance and identification program (Figure 9). Each site submitted weekly specimens collected from patients meeting the criteria for influenza-like illness (fever of ≥100.5°F and cough or sore throat) along with a completed influenza surveillance questionnaire to provide an epidemiological profile. In the 2006–2007 influenza seasonal year (1 October 2006–29 September 2007), 72 sites located in 42 countries were designated as sentinel sites (50 military sites and 22 non-DoD collaborating sites in host nations).

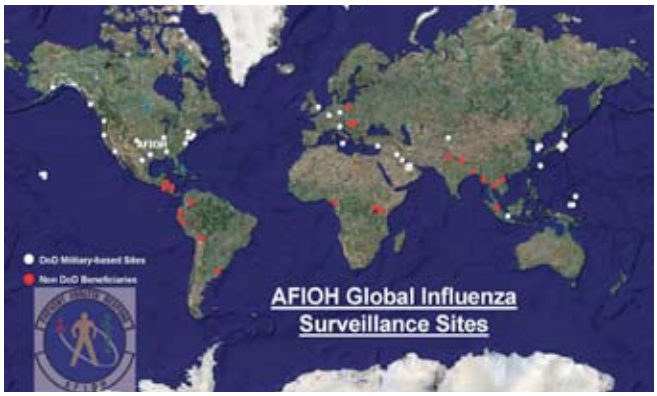


Figure 9. DoD global influenza sentinel surveillance sites, all of which send samples to AFIOH for analysis.

Laboratory

Once received by AFIOH, specimens are screened for influenza A and B using RT-PCR. The original sample is then cultured and examined for the presence of viruses. The most likely isolates are influenza A and B, adenovirus, parainfluenza 1, 2, or 3, enterovirus, and respiratory syncytial virus. Influenza isolates are typed, and all influenza A isolates are then subtyped and further molecularly characterized. All original specimens are archived and kept for requests from DoD partners or the CDC.

All influenza isolates underwent molecular characterization. Genetic sequencing of the hemagglutinin surface proteins was performed on influenza A and B specimens to detect variations from the vaccine component strains. Results are shared with the CDC and are included in the WHO phylogenic representation of circulating strains.

Each year the FDA Vaccines and Related Biological Products Advisory Committee recommends modifications to the Northern Hemisphere influenza vaccine based on the viral strains that circulated during the preceding season. These recommendations are partially based on data provided by AFIOH and the DoD Global Influenza Surveillance Program. The CDC and WHO reference laboratories also contribute data to the committee.

Of the 72 identified sentinel sites, 60% (n = 42) actively participated during the 2006–2007 seasonal year. Note that population sizes may vary at sentinel sites; however, an established relationship is considered valuable despite the expected low yield in specimen submission (i.e., deployed sites). An additional 38 nonsentinel (triservice) sites submitted respiratory specimens to AFIOH.

A total of 5,810 respiratory specimens were collected and processed during the 2006–2007 seasonal year. Specimens submitted by sentinel sites accounted for 64.0% (n = 3,715) of total submissions, and nonsentinel sites submitted 36.0% (n = 2,094) of specimens. Forty-two percent (2,444/5,810) were positive for a respiratory virus; specifically, 19.3% (1,121/5,810) were positive for an influenza virus (Figure 10). Similar to the 2005–2006 seasonal year, influenza A was the predominant influenza type circulating throughout the seasonal year, accounting for 84.8% (951/1,121) of the influenza isolates identified.

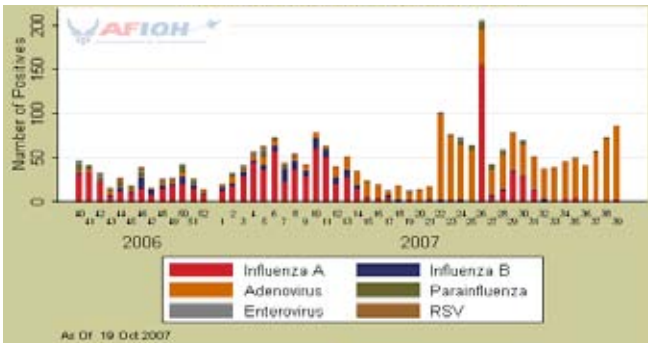
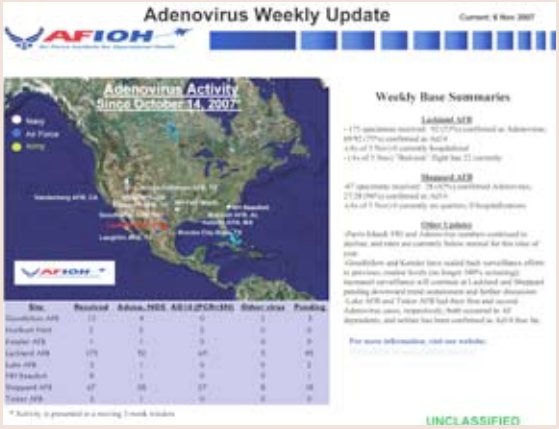


Figure 10. Total positive viral results for AFIOH influenza surveillance, 2006–2007 seasonal year.

AFIOH continues to advance its public health surveillance efforts while working within the constructs of a DoD clinical reference laboratory. Surveillance and disease investigations remain the cornerstones of proper public health preparedness leading up to a pandemic. Risk communication and awareness are crucial given the anticipated enormity of such an event. AFIOH aims to widen the scope of the existing influenza surveillance to better respond to potential threats and better describe viral respiratory diseases within the areas of surveillance.

Cooperation Yields Enhanced Surveillance during Adenovirus Outbreak

In May 2007, AFIOH provided immediate response to an adenovirus serotype 14 outbreak among basic trainees at Lackland AFB that began in March 2007. In collaboration with teams from the CDC, Texas State Health Department, Air and Education Training Command (Randolph AFB, Texas), Walter Reed Army Institute of Research, and other DoD agencies, epidemiology and laboratory staff at AFIOH assisted with more than 10 studies and provided critical analysis and data. This investigation, aided by GEIS funding and the expertise of many GEIS partners, provided further evidence to intensify the effort to reinitiate the adenovirus vaccine among basic trainees.



Weekly report from ongoing surveillance for adenovirus. Weekly reports were distributed to all partners during enhanced surveillance swiftly instituted by GEIS and AFIOH in response to disturbing adenovirus serotype14 outbreak at Lackland AFB in FY07.

Within the first week of the investigation (21–28 May), AFIOH launched an informational website and established an enhanced surveillance network among 12 DoD installations with either secondary training schools or other operations of interest. This surveillance filled a critical gap in assessing the spread of adenovirus 14 among trainees and permanent servicemembers throughout CONUS and OCONUS installations. The enhanced surveillance effort expanded to include 35 DoD installations over 4 months (28 May–30 September 2007), during which AFIOH received and processed 2,144 specimens, identified 950 as adenovirus positive, and identified a subset of 541 as positive for adenovirus 14. AFIOH identified eight installations outside of Lackland AFB with at least one positive adenovirus 14 specimen and reported these findings immediately to the installations and the partners. Weekly reports of activity were distributed through DoD-GEIS, and feedback and support were provided to all installations in the network throughout the enhanced surveillance and thereafter.

Naval Health Research Center

The Naval Health Research Center (NHRC) in San Diego established a Navy Respiratory Disease Laboratory in 1996 to perform epidemiological studies and surveillance of respiratory diseases affecting military personnel. Over the past decade, NHRC has expanded its scope of studies and diagnostics, with an increased emphasis on influenza surveillance. Molecular capabilities have been greatly enhanced, and NHRC has become a leading reference laboratory for respiratory disease within the DoD.

As a respiratory disease reference center for DoD, NHRC has become an important asset within DoD for investigation of infectious disease issues in training centers, deployed forces, and servicemember deaths. Respiratory disease surveillance and research initiatives sponsored by DoD-GEIS at NHRC continue to contribute to force health protection in the United States and abroad. Enhanced and expanded surveillance, increased laboratory throughput, evaluation of new diagnostics, and construction of a BSL-3E (enhanced) laboratory are components of a program valuable to DoD and public health partners that will continue to pay dividends in the future. NHRC provides critical information that is relevant for military operations and for public health and is among the jewels within DoD-GEIS.

Surveillance

NHRC conducted FRI surveillance among basic training, deployed shipboard, and Mexican border populations during FY07. The number of FRI specimens collected and frequency of shipments from eight US basic training centers have been enhanced compared with pre-FY06 levels to provide more robust and timely influenza surveillance. An early season cluster of influenza A/H3N2 was identified at Fort Benning (Georgia) in August 2007. Calculation of the influenza vaccine effectiveness among basic trainees showed that the 2006–2007 vaccine was 87% effective in preventing laboratory-confirmed influenza (Figure 11).

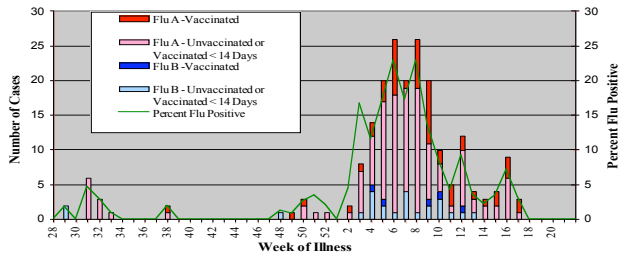


Figure 11. Vaccination status of confirmed influenza cases among military basic trainees, 2006–2007.

Adenovirus types 14 and 21 emerged strongly at several basic training centers, often in conjunction with increased FRI rates and severity of illness, demonstrating the value of surveillance in this population. The ongoing surveillance by NHRC continues to be critical to efforts to reinitiate the adenovirus vaccination program among basic trainees. Surveillance of pneumonia cases is ongoing, and preliminary results indicate that adenovirus, *Mycoplasma pneumoniae,* and *Chlamydia pneumoniae* are the pathogens most commonly associated with pneumonia in otherwise healthy servicemembers.

Shipboard FRI surveillance among the 2nd Fleet (Atlantic), 3rd Fleet (eastern Pacific), and 7th Fleet (western Pacific) since 2003 has identified clusters of influenza cases among sailors aboard many ships after port stops throughout the world, including areas thought to be at increased risk for strains of pandemic influenza. In March 2007, cases of coinfection with both H1 and H3 strains of influenza A were identified among two crew members after port stops in Okinawa (H1 outbreak) and Jakarta, Indonesia (H3 outbreak). Most recently, six influenza A/H3 cases among sailors were documented on a large amphibious ship in late August 2007 after port stops in Papua New Guinea and the Solomon Islands. Isolates from these cases, which would not have been collected without GEIS support, were grown at NHRC and provided valuable strain and sequence information to the global influenza surveillance community. Emphasis on fostering the global influenza surveillance network through GEIS funding was critical to the contribution of NHRC to the community. During FY07, NHRC further expanded shipboard FRI surveillance in the 2nd Fleet and 7th Fleet, and all large deck ships in these fleets now participate.

FRI surveillance along the Mexican border is imperative for the US military because of the proximity of critical bases to the border. Border surveillance was conducted by NHRC at three sites during FY07. Among the 222 patients with FRI who were enrolled in FY07, more than half reported crossing the border within the previous 2 weeks. Thirty-three influenza A and 11 influenza B cases were identified in these populations. Adenovirus, enterovirus, parainfluenza, *Streptococcus pneumoniae*, *Haemophilus* spp., *H. ducreyi*, group A streptococcus, and group C streptococcus were also seen. Evaluation of influenza A rapid antigen test performance in this setting, based on comparison with NHRC laboratory results for the same specimens, showed that the test remains less useful for individual diagnosis than had been hoped.

During FY07 NHRC performed genetic sequencing of more than 200 influenza isolates obtained from the basic training, deployed shipboard, and Mexican border populations. Most influenza A/H3 isolates during the 2006–2007 season differed from the H3 component of the vaccine (A/Wisconsin strain) by three to five amino acids. Findings and isolates were shared with local, state, DoD, and CDC influenza surveillance partners. Evaluation of hemagglutinin sequences (Figure 12) indicated that isolates from these DoD facilities were not of a single lineage except for those from Fort Jackson and Fort Benning.

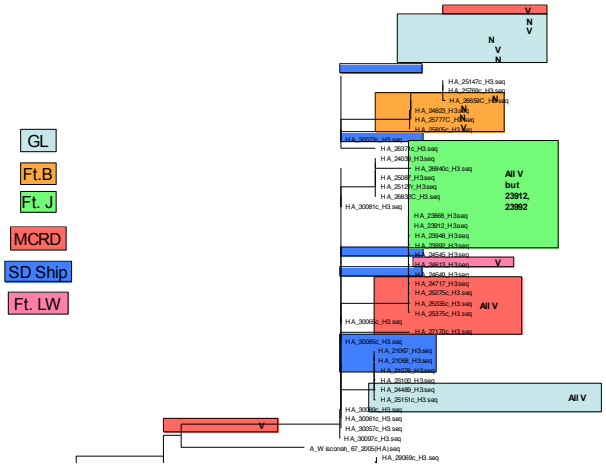


Figure 12. Influenza A/H3 hemagglutinin sequences, 2006–2007. GL, Great Lakes Naval Training Center; Ft. B, Fort Benning; Ft. J, Fort Jackson; MCRD, Marine Corps Recruit Depot; SD Ship, San Diego ship; Ft. LW, Fort Leonard Wood.

Response

NHRC identified an early season cluster of influenza A at Fort Benning in August 2007. Laboratory staff quickly determined that an H3 strain was responsible and that none of the cases had been vaccinated. Information was immediately shared with Fort Benning, DoD-GEIS, and CDC. FRI surveillance was intensified at Fort Benning for several weeks until it was determined that transmission had ceased. Training operations at the base were allowed to continue uninterrupted, in large part because of the epidemiological data provided by NHRC. These cases also represented the first instance of a cluster of influenza H3 cases in the United States this year.

In spring 2007, a large cluster of pneumonia of unknown etiology was reported aboard a large amphibious ship during deployment in the Persian Gulf. Specimens were sent to NHRC while the ship was in transit, and diagnostic testing revealed that *Mycoplasma pneumoniae* was responsible. Results were quickly communicated with the ship and fleet preventive medicine officers, resulting in alteration of plans that would have allowed civilians to join the ship on its return from San Diego to Hawaii.

NHRC detected, reported, and responded to outbreaks of FRI and pneumonia at six basic training centers. Increased sample collection and accelerated testing allowed detection and reporting of results within 7–10 days in most cases. Included in these outbreaks were the emergence of adenovirus serotypes 14 and 21.

NHRC also provided laboratory support for ten fatal and six severe respiratory illness cases during FY07. Most of these were referred through the mortality surveillance program at the AFIP. Key findings included the determination that methicillin-resistant *Staphylococcus aureus* was associated with two deaths among deployed troops and that adenovirus serotype 14 was found in the lung tissue of a basic trainee who died at Lackland AFB. The basic trainee death occurred as part of an emergent outbreak of adenovirus serotype 14 between March and August 2007 (Figure 13). The outbreak involved more than 200 recruits by June 2007 and was associated with severe respiratory disease and numerous hospitalizations. PCR primers and standard operating procedures for adenovirus serotype 14 diagnosis were shared with the reference laboratory at AFIOH, enhancing its local diagnostic capabilities.

NHRC provided weekly updates that included influenza and FRI rate data to surveillance partners throughout the year. Periods of significant FRI rate elevation occurred at six of eight camps under surveillance during FY07. New data-intensive graphics were added to the weekly FRI update in FY07.

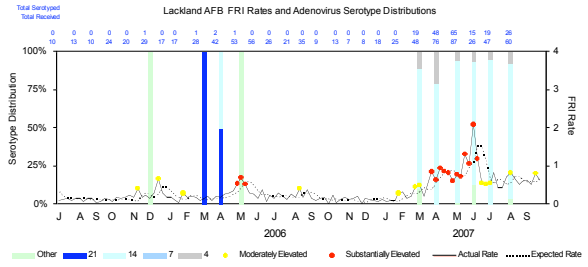


Figure 13. Findings from NHRC investigation of FRI cases at Lackland AFB during FY07 showing outbreak of adenovirus 14, which was associated with one fatality. Before late 1996 adenovirus 14 had not been associated with respiratory illnesses in this hemisphere.

Integration and Innovation

NHRC incorporated the T-5000 (formerly known as TIGER) testing into its surveillance activities. The T-5000 is a high-throughput diagnostic that uses PCR in conjunction with mass spectrometry to rapidly identify viral and bacterial pathogens with high sensitivity and specificity. The system was used to rapidly identify the *M. pneumoniae* in the deployed shipboard cases and was used to supplement standard diagnostics during the investigation of the fatal cases of FRI. The T-5000 at NHRC is one of only two within DoD laboratories.

NHRC and GEIS evaluated the following new influenza diagnostics during FY07.

- Eiken-LAMP. Although able to detect H5 strains with high sensitivity, primers produced random false-positives against clinical samples. New primers are being tested.
- Arbor Vita rapid antigen test. Detected 26 of 28 H5 cases provided by NAMRU-3 in Cairo. No false-positives against clinical samples were seen.
- Meso Scale Discovery electrochemiluminescent system. Performed well against a 100-sample panel of respiratory pathogens. This system will next be tested using clinical isolates at NAMRU-3 in FY08.

The ability and willingness of NHRC to evaluate new diagnostic technologies with a standardized panel of known respiratory pathogens and negative controls are unique within DoD and represent a critical resource for GEIS.

Influenza vaccine effectiveness estimates are generally available only after the influenza season has concluded. During FY07, NHRC collaborated on novel surveillance strategies that utilized web-based information aggregation systems to forecast influenza vaccine effectiveness and avian influenza movement into the United States.

Capacity Building

NHRC completed design and began construction of a new BSL-3E (enhanced) laboratory. By allowing NHRC to grow highly pathogenic influenza strains and other dangerous microbes, this laboratory will provide powerful capabilities for the DoD that are unique within this region. The current schedule calls for the laboratory to be operational in the second quarter of FY08.

NHRC is a member of the CDC Laboratory Response Network for diagnosis of highly pathogenic avian influenza. In a unique agreement with CDC that was

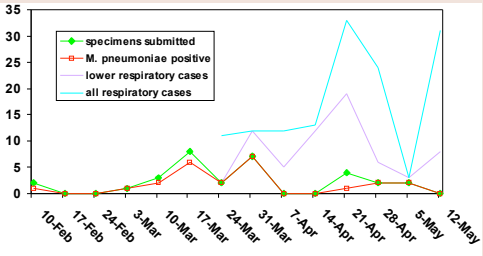
Outbreak of Pneumonia Detected Aboard Navy Ship in Persian Gulf

The NHRC Department of Respiratory Disease Research established shipboard febrile respiratory illness surveillance in the 3rd Fleet (San Diego, CA) in 2002 and in the 2nd Fleet (Norfolk, VA) and 7th Fleet (Yokosuka, Japan) in 2006 with support from DoD-GEIS. NHRC provides participating ships with viral transport media and case data forms and training in the use of each. Ship's medical personnel collect throat swab specimens from sailors meeting the case definition of febrile respiratory illness (fever of ≥ 100.5°F and presence of cough or sore throat). The specimens are stored in an ultralow freezer or liquid nitrogen until they are conveyed to NHRC for laboratory testing. This ongoing surveillance has identified influenza A as the primary pathogen responsible for clusters of febrile respiratory illness that occurred aboard participating ships.

NHRC screens for *Mycoplasma pneumoniae* in febrile respiratory illness specimens. *M. pneumoniae* is a small bacterium that causes pneumonia and other lower respiratory syndromes, such as bronchitis and bronchiolitis, and upper respiratory syndromes, such as pharyngitis and croup. The bacteria are spread via respiratory droplets, and the close confined spaces and shared facilities aboard naval vessels are conducive to its transmission. *M. pneumoniae* has caused epidemics in military populations (e.g., barracks) and causes approximately 20% of community-acquired pneumonias. These infections can mimic viral respiratory syndromes. Most cases can be treated on an outpatient basis.

USS *Boxer*, multipurpose amphibious assault ship.

While deployed in the Persian Gulf in FY07, the USS *Boxer* experienced many cases of lower respiratory illness, most of which were diagnosed as pneumonia via a positive chest X-ray. None of the patients required mechanical ventilation or a medical evacuation, and all responded well to antibiotic therapy.



USS *Boxer* respiratory cases/specimens reported via weekly DNBI reports submitted to NEPMU6, February–May 2007 (no DNBI data were available before 24 March).

After a port stop in Jebel Ali (Dubai, United Arab Emirates), one crewmember reported to sick call on 8 February 2007, met the case definition for febrile respiratory illness, and had a throat swab specimen taken that subsequently tested positive for *M. pneumoniae* at NHRC. The specimen from the next laboratory-confirmed case was submitted on 26 February; the 18-day lapse was consistent with *M. pneumoniae* incubation period, which averages 3 weeks. Of the 31 specimens collected during the early part of this outbreak, 24 tested positive for *M. pneumoniae*. These results were subsequently confirmed by bacteriological culture.

Communication among the *Boxer* medical department, NHRC, and Navy Medicine West preventive medicine staff, including NEPMU5 and NEPMU6, allowed these specimens to be transported by helicopter from the *Boxer* to Pearl Harbor and then express shipped to NHRC in San Diego. Upon receipt, NHRC had results available in fewer than 12 hours. This rapid response provided valuable public health information that was used to inform the decision of whether to allow civilians to board the Tiger Cruise from Pearl Harbor to San Diego. Appropriate precautions were taken in medically screening the crew and civilian guests, who were allowed to participate. Of the 12 specimens collected during the Tiger Cruise, only one specimen tested positive for *M. pneumoniae*.

The presence and support of the NHRC shipboard febrile respiratory illness surveillance program allowed identification of *M. pneumoniae* as the etiologic agent in a timely manner and provided a sound basis for mission-related decisions. Shipboard febrile respiratory illness surveillance continues to be crucial in identifying pathogens that affect the health of deployed military personnel.

developed during FY07, NHRC is also permitted to train and oversee individuals in Laboratory Response Network highly pathogenic avian influenza diagnostics on ships that are part of the FRI surveillance umbrella at NHRC. Personnel on three ships have already been trained, and more ships will undergo training in FY08. These capabilities will, for the first time, provide FDA-approved H5 avian influenza diagnostics to deployed shipboard populations, which will substantially increase support to force health protection. NHRC also leveraged its Pacific Rim surveillance hub in Yokosuka, Japan, to help Naval Hospital Yokosuka and Naval Hospital Okinawa become part of the Laboratory Response Network in FY07. NHRC also provided training, culture media, and rapid point-of-care influenza tests to three clinics that participated in the FRI surveillance project among Mexican border populations.

United States Army Medical Research Institute of Infectious Diseases

DoD-GEIS supports the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) to maintain capabilities in detection and identification of infectious diseases through the development and testing of assays. Collaborations with the DoD overseas laboratories offer USAMRIID scientists unique opportunities to field test assays and provide valuable reagents and expertise to GEIS and USAMRIID collaborators.

Detection and Identification of Infectious Diseases Requiring High Level Biological Containment

During FY07, USAMRIID maintained its diagnostic capabilities with the production of antigens and antibodies for assays in its repertoire and for development of new assays such as Lassa and Crimean-Congo hemorrhagic fever viruses. In support of the DoD diagnostic laboratories, 161 clinical samples were tested for various arthropod-borne and hemorrhagic fever viruses. Notable among these samples were requests from the Armed Forces Medical Examiner to aid in the death investigation of two servicemembers who died in Iraq from a suspected infectious disease cause (sandfly fever virus and Q fever). By utilizing virus isolation techniques and immunodiagnostic and molecular diagnostic assays, USAMRIID attempted to identify the cause of death in both cases. Through continued disease outbreak support, reagents for more than 25,000 diagnostic assays were supplied to the DoD overseas laboratories. In addition, division personnel provided diagnostic expertise and advice to USAMRU-K in Nairobi for the acute febrile illness study about to begin there.

The USAMRIID effort has a direct impact on GEIS response capabilities and is essential for the protection of the warfighter. GEIS diagnostic readiness at USAMRIID is maintained through the constant renewal of diagnostic reagents for testing and development of new and improved assays. Training of military and civilian personnel and organizations in diagnostics is manifested through USAMRIID/GEIS support of the course in field identification of biological warfare agents. GEIS supplies diagnostic reagents, specific agent assays, and additional training and consultation for students and instructors as needed. Through GEIS, USAMRIID maintains the ability to respond to disease outbreaks in the field and/or support collaborators responding to arthropod-borne and hemorrhagic fever virus outbreaks on a global scale.

Pandemic Influenza Surveillance

The influenza A H5N1 subtype, which is responsible for the outbreaks in Asia since 1997, can cause severe illness and death in avian species. The potential for human infection and the growing fear of an avian influenza pandemic illustrate the need for timely and accurate diagnostics to initiate a rapid response. Through the GEIS avian and pandemic influenza effort at USAMRIID, the vital process of evaluating the performance of molecular-based real-time PCR assays available from partner laboratories, commercial sources, and the public domain literature has begun.

Molecular diagnosis of avian influenza, especially as it is related to the military, should be based on detecting both the H5 and N1 specific gene targets within the viral RNA. The identified assays are evaluated using a defined criterion that assesses linearity, limit of detection, inclusivity, and exclusivity for the avian influenza assays. Of critical importance to assay evaluation is the availability of viral RNA to various H5N1 strains and other related virus subtypes.

As a component of the USAMRIID avian and pandemic influenza work, expansion of the influenza virus reference panel that began last year with GEIS support continued. Currently 64 virus subtypes and 30 H5N1 RNAs are in the collection. This well-established, well-maintained, and well-characterized collection of influenza strains is

Collaborative Advanced Testing Capability Standing By

Two deaths believed to be from infectious disease occurred among Army servicemembers in the same region of Iraq during a 5-day period in 2007. The cases had commonalities of time and place, and the possibility of an exposure or outbreak was aggressively explored by the local preventive medicine officer. Clinical features of both cases were respiratory failure and profound thrombocytopenia and leukopenia. The first case was significantly hemorrhagic. Given the high level of concern, when the cases came to the Dover AFB (Delaware) port mortuary for autopsy, the negative pressure isolation room was utilized for the first time, and the medical examiners collected many tissue samples for testing.

Medical evacuation drill during field exercise at Fort Hunter Liggett (California), December 2007.

Immediately after the autopsies were concluded, tissue and blood samples were sent to USAMRIID for extensive viral pathogen testing to identify hemorrhagic fever etiologies and to NHRC for respiratory pathogen exploration. Multiple subspecialists at the Armed Forces Institute of Pathology were consulted who together provided an extensive array of testing and expertise.

Ultimately, the cases were determined to be unrelated, and infectious disease was the cause of death in just one. That case had a non–methicillin-resistant *Staphylococcus aureus* sepsis, thought to have its origin in a grossly infected dermatological lesion discovered at autopsy. The effort demonstrates the capabilities in DoD that have been put in place through DoD-GEIS to rapidly identify deaths caused by numerous infectious agents.

Thus, the link established and supported by DoD-GEIS between the Armed Forces Medical Examiner and USAMRIID to analyze military deaths potentially caused by unusual or highly contagious infectious diseases is working as intended. In this effort, the system was used in direct support of CENTCOM operations. Accordingly, the system is tested and ready to support the investigation of new infectious disease casualties throughout the force worldwide.

essential as a resource and reference for the diagnostic development effort for avian and pandemic influenza and to overall DoD preparedness for pandemic influenza.

Immunodiagnostics are an important component of an integrated diagnostic program. Influenza immunodiagnostics will improve understanding of the annual distribution of the influenza virus worldwide and assessment of vaccine efficacy. Commercial influenza ELISA kits and various antibodies and antigens were tested as a component of the immunodiagnostic effort. Final evaluation of the real-time PCR assays and further immunodiagnostic assay development will continue as reference samples are produced. Additionally, a pyrosequencing assay that predicts the viral strain, clade, receptor binding properties, low- or high-pathogenicity cleavage site, and glycosylation status is being evaluated through GEIS funding.

USAMRIID will continue to establish long-term collaborations with researchers involved in the detection, identification, and pathology of agents with the goal of bringing the most reliable reagents, assays, hardware, and software to the battlefield for the protection of US military forces against avian influenza. Given its unique containment facilities, notably its BSL-4 capability, USAMRIID is uniquely qualified to functionally design and test real-time PCR assays to detect and identify avian influenza.

Naval Medical Research Center

GEIS sponsored the Naval Medical Research Center (NMRC) to continue its work in determining the risk of rickettsial diseases among military populations and to serve as a reference laboratory for the DoD overseas laboratories. Diagnosis of rickettsial diseases can be difficult because symptoms often share characteristics with those of other febrile illnesses.

Rickettsial and related diseases, including epidemic typhus, murine typhus, Rocky Mountain spotted fever, Mediterranean spotted fever, scrub typhus, ehrlichiosis, anaplasmosis, and trench fever, are endemic, emerging, or reemerging in much of the world. For example, *Rickettsia parkeri* was identified at NMRC this year as a pathogen for humans after having been considered for more than 70 years a nonpathogenic commensal of ticks. Antibiotic resistance and prophylaxis breakthroughs have been reported with *Orientia tsutsugamushi*, the agent of scrub typhus in Asia.

The DoD overseas laboratories, supported in part by GEIS, are measuring the extent of these diseases, their threat to military operations, and the emergence of antibiotic resistance. Initial testing of specimens is performed on-site at each laboratory with reagents provided by NMRC. NMRC also provides training to perform the assays and act as a reference laboratory to conduct the confirmatory tests. A need continues for a DoD reference laboratory to confirm serologic and molecular detection results and culture live rickettsiae in BSL-3 laboratories.

The NMRC Rickettsial Disease Research Program is ideal for conducting, training others to perform, and developing diagnostic assays. NMRC personnel are trained in performing serological assays (ELISA, IFA, and rapid flow device), molecular biology assays (PCR, quantitative real-time PCR, and microassays), and isolation techniques (yolk sacs and tissue culture). Two BSL-3 laboratories at NMRC are dedicated to work with rickettsiae. NMRC has developed tests for typhus, spotted fever, and scrub typhus that are certified by the FDA. These include ELISA, Dip-S-Ticks, and reference dose. Previously, the Army Military Infectious Disease Research Program supported the NMRCD reference laboratory functions. However, in recent years their emphasis has shifted to vaccine, drug, diagnostic, design, and development tasks, so GEIS now supports the NMRC reference laboratory functions. GEIS also supports various aspects of rickettsial disease research at the five DoD overseas laboratories. NMRCD has acted as the reference laboratory for these sites, and others, and provides reagents, technical expertise, and training.

Previously developed and optimized serological and molecular genetic assays have been used to detect and characterize rickettsiae and to determine the risk of rickettsial diseases among military populations. The development at NMRC of quantitative real-time PCR assays for the detection of *R. typhi* (murine typhus) and *R. felis* (flea-borne spotted fever) has been utilized to successfully determine the presence of these pathogenic rickettsiae in various flea populations. In September 2006 the NMRC real-time PCR assays (*Rickettsia* genus-specific and tick-borne spotted fever group rickettsiosis-specific) and multilocus sequence typing technique were used to determine that a spotted fever rickettsiosis patient (servicemember) was infected with *R. parkeri*. This case was only the third ever reported of *R. parkeri* associated with human disease even though the agent has been known for more than 70 years as a common tick-associated rickettsia.

To determine the risk of spotted fever group rickettsiosis and human anaplasmosis among US military personnel in general, ~10,000 sera from the DoD Serum Repository were evaluated by ELISA and Western blot. Spotted fever group rickettsiae seropositivity was determined to be 6.0% (95% confidence interval = 5.5–6.4%), whereas *Anaplasma phagocytophilum* seropositivity was only 0.11%. This large study of demographically diverse military personnel showed that a low risk of infection with spotted fever group rickettsiae exists and that the risk is not significantly different from than that reported for US civilians. Moreover, the low risk of *A. phagocytophilum* infection in the military is similar to that seen in civilian populations.

A more specific study was undertaken to determine the risk of rickettsial diseases among US military personnel deployed or stationed in South Korea. Sera from 10,000 US military personnel previously stationed in Korea were assessed for evidence of previous infection with spotted fever, typhus, and scrub typhus rickettsiae. Postdeployment serum samples were identified and provided by the DoD Serum Repository. Approximately 10,000 samples have been tested for antibodies specific for spotted fever group and typhus group rickettsiae and *O. tsutsugamushi* utilizing a screening IgG-specific ELISA protocol. The ELISA antigens were produced in-house, and the postdeployment serum samples were diluted 1:100 and tested

for reactivity to the spotted fever group, typhus group, and *O. tsutsugamushi* antigens. The results showed a seropositivity of 13.1%, 2.4%, and 3.9% for spotted fever group, typhus group, and *O. tsutsugamushi*, respectively. Predeployment sera for those samples screened positive have been requested from the DoD Serum Repository. When these samples are received they will be assessed alongside the corresponding postdeployment sera for evidence of seroconversion and determination of their titers.

New rickettsial assays have been developed to detect *R. parkeri* and *R. africae*, the etiological agents of African tick-bite fever and *Candidatus Rickettsia andeanae*, a newly described rickettsial agent discovered during a febrile illness outbreak investigation in northern Peru. These assays have been optimized, evaluated, and developed by use of plasmid DNA with a target insert for use as a standard and in quantitation assays. The assays have been found to be sensitive and specific using a panel of near- and far-neighbor DNA preparations produced in-house. Validation of the assays with clinical and/or arthropod specimens will have to wait until they have been collected (two studies are scheduled for FY08). Although some of these diseases are no longer classified as *Rickettsia*, NMRC has also produced quantitative PCR assays for other laboratories so that it would have the capability to test for Q fever, Lyme disease, ehrlichiosis, and human granulocytic anaplasmosis and to identify five different tick species (Table 1).

Table 1. Reagents and Assays Produced by NMRC to Diagnose or Detect Agents for Selected Diseases

Disease	Agent	Serology	Assay
Scrub typhus group			
Scrub typhus	*O. tsutsugamushi*	IFA, ELISA, WB	PCR, quantitative real-time PCR
Rickettsioses	*Rickettsia* genus-specific		PCR, quantitative real-time PCR
Typhus group			
Epidemic typhus	*R. prowazekii*	IFA, ELISA, WB	PCR, quantitative real-time PCR
Murine typhus	*R. typhi*	IFA, ELISA, WB	PCR, quantitative real-time PCR
Spotted fever group			
Tick-borne rickettsioses	Group specific	IFA, ELISA, WB	PCR, quantitative real-time PCR
Rocky Mountain spotted fever	*R. rickettsii*	IFA, ELISA, WB	PCR, quantitative real-time PCR
Mediterranean spotted fever	*R. conorii*	IFA, ELISA, WB	PCR, quantitative PCR under optimization
African tick bite fever	*R. africae*	IFA, ELISA, WB	PCR, quantitative real-time PCR
Flea-borne spotted fever	*R. felis*	ELISA	PCR, quantitative real-time PCR
Unknown	*R. montanensis*	ELISA	PCR, quantitative real-time PCR
Unknown	*R. amblyommii*	ELISA	PCR, quantitative real-time PCR
Tidewater spotted fever	*R. parkeri*	ELISA	PCR, quantitative real-time PCR
Unknown	*R. andeanae*	ELISA	PCR; quantitative real-time PCR
Q fever	*Coxiella burnetii*	Under development	PCR; quantitative real-time PCR
Ehrlichiosis and anaplasmosis			
Human monocytic ehrlichiosis	*E. chaffeensis*	IFA	PCR, quantitative real-time PCR
Human granulocytic anaplasmosis	*A. phagocytophila*	ELISA, WB	PCR; quantitative real-time PCR
***Bartonella* group**			
Bartonellosis	*B. bacilliformis*	Under development	PCR
Trench fever	*B. quintana*	IFA	PCR, quantitative real-time PCR
Borrelia			
Relapsing fever	*B. recurrentis*		PCR, quantitative real-time PCR
Lyme disease	*B. burgdorferi*	Commercial assays	PCR, quantitative real-time PCR
Southern tick-associated rash illness	*B. lonestari*		PCR, quantitative real-time PCR

Walter Reed Army Institute of Research

The Walter Reed Army Institute of Research (WRAIR) is a valuable GEIS partner in its efforts to combat one of the GEIS priority surveillance conditions, malaria. GEIS work through WRAIR involves projects on mosquito vector distribution and antimicrobial resistance, and WRAIR heads the GEIS-funded center of excellence for malaria diagnostics in Kisumu, Kenya.

Global Mapping and Modeling of Mosquito Vectors

Modeling for Potential Distribution of Mosquitoes

Ecologic niche modeling can be used to identify areas at potential risk for infectious human diseases in regions important to the military. Modeling can help optimize the use of resources for mosquito vector control and infectious disease prevention via automated forecasting of disease transmission risk. Genetic algorithm and point occurrence data are used to develop models for the major vector species of mosquito-borne human diseases (e.g., malaria and arboviral diseases). Vector occurrence data are available from specimens housed in collections of the Smithsonian Institution and other museums and laboratories. The identities of these specimens were confirmed by morphological and/or molecular techniques. Ecologic distribution parameters (e.g., diurnal range and precipitation) with the greatest effects on the models were determined.

A website at http://www.mapmosquito.org is being developed to host worldwide mosquito occurrence records and mosquito distribution models and prediction maps. A new malaria analysis tool is being developed through DoD-GEIS that will be provide a quick, simple web-based estimation of the risk of malaria for any defined area of the globe, according to the proportion of the area that is predicted to contain the three crucial elements for malaria transmission: humans, malaria parasites, and mosquito vectors.

Modeling Malaria Vectors in South Korea

Data points or occurrence data were obtained from PCR-identified specimen records. Models were prepared for important and potentially important malaria vectors from the Korean peninsula. Figure 14 shows models of potential distribution of known and potential malaria vector species: *Anopheles kleini* Rueda, *A. belenrae* Rueda, *A. lesteri* Baisas and Hu, *A. sinensis* Wiedemann, and *A. pullus* Yamada and related species (i.e., *A. sineroides* Yamada, *A. lindesayi* Giles, *A. koreicus* Yamada and Watanabe).

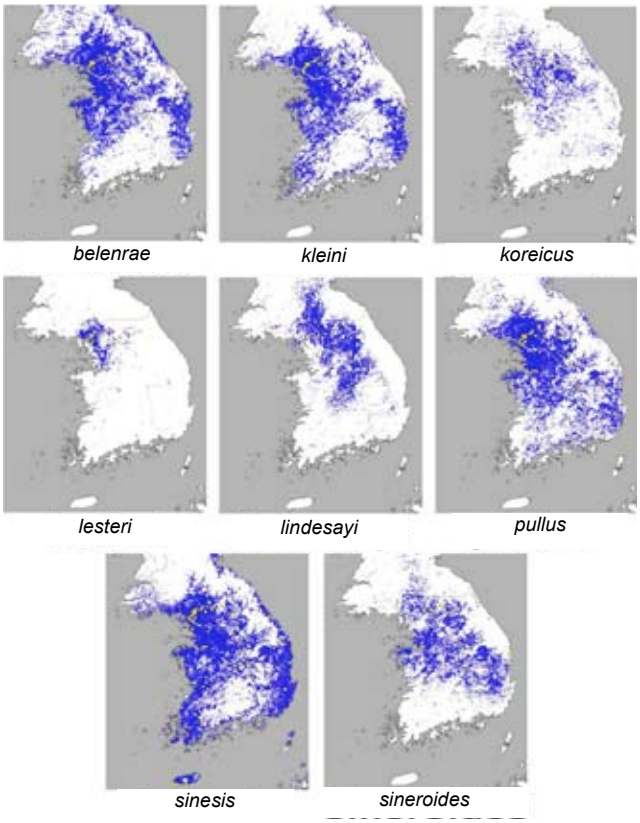


Figure 14. Consensus models of eight *Anopheles* species in South Korea: *A. belenrae* Rueda, *A. kleini* Rueda, *A. koreicus* Yamada and Watanabe, *A. lesteri* Baisas and Hu, *A. lindesayi* Giles, *A. pullus* Yamada, *A. sinensis* Wiedemann, *A. sineroides* Yamada. *Blue areas*, locations where both >9% GARP models and >10% probability from Maxent modeling agree. *Yellow dots,* collection locations used for modeling.

These distribution models proved useful to 2006 and 2007 collection efforts in South Korea that were directed to areas where the models needed more support and where species are predicted to occur but where collections have not been undertaken. The 2006 collections from South Korea have been incorporated into distribution models. To assist future efforts, geocoded satellite images of South Korea and geocoded image files of predicted distribution of the four species could be available for real-time location of predicted mosquito positive areas using the program MacGPS. In addition, Google Earth files, comprising semitransparent images of mosquito

distribution overlayed on satellite images of the Korean peninsula, could be available to assist in locating hotspots in mosquito distribution.

These novel approaches to visualizing mosquito distribution are expected to better enable collectors to ground-truth model predictions and may be extremely useful for sharing this information via the web. Validation of the models in South Korea can further enhance their usefulness in predicting vector distribution. Furthermore, with available occurrence data from South Korea, Japan, and China, prediction models could be prepared for the potential distribution of disease vectors in these countries and their neighbors.

Malaria Drug Resistance Surveillance

WRAIR has established and promoted improved methods for surveillance for malaria drug efficacy at the DoD OCONUS laboratories in recent years. The goal of this surveillance is to document historical and current data on resistance to commonly used antimalarials such as mefloquine, chloroquine, and sulfadoxine-pyrimethamine and on the new drugs and combinations that are being tested in different settings. The malaria drug resistance surveillance resource will permit coordinated analysis of the data and facilitate the recognition of temporal and geographical trends in parasite resistance.

The need for solid evidence on which to base decisions about effective malaria prophylaxis and treatment is acute. Although information from WRAIR and the OCONUS laboratories is reported in quarterly and annual MIDRP-GEIS reports, information from other programs is largely fragmented in journals and meeting reports or in databases to which access is limited. Furthermore, surveillance in general is spotty, and large areas exist where little information is available. Currently, historical or geographic trends in malaria parasite resistance cannot be discerned. As a result, decisions about drug treatment must frequently be based on old, scanty, or no evidence of the probable utility in the country or region at issue. A dynamic web-based database of current information would allow ready access to all available information on drug efficacy for ministries of health and their advisors.

Historical patterns of resistance are known in only a few areas of the world. The speed with which resistance to a particular drug may develop in areas of different transmission and treatment history cannot be extrapolated. To begin to make such generalizations, the speed and pattern of resistance to the same drugs must be tracked in specific regions. The ability to predict the useful therapeutic life of drugs is critical to those recommending contemporary and novel drugs and combinations of drugs for malaria prophylaxis and treatment. GEIS and WRAIR are focussing this surveillance toward the shortfall of information about the development of malaria drug resistance in various parts of the world. The results of a study analyzing two malaria isolates obtained from Marines deployed in Chad are shown in Figure 15.

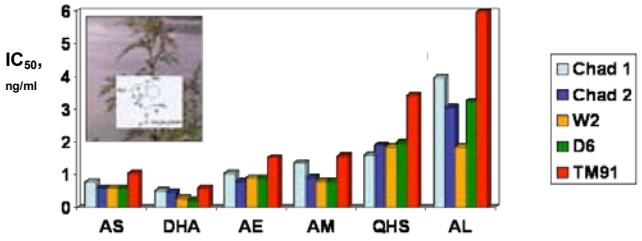


Figure 15. In vitro antimalarial susceptibility study of two *Plasmodium* isolates obtained from Marines infected during operations in Chad (Chad 1 and 2) compared with control isolates (W2, D6, and TM91). Artemisinin (QHS) is derived from *Artemisia annua*. Artesunate (AS) and metabolite dihydroartemisinin (DHA) are the most active. AE, arteether; AM, artemether; AL, artelinic acid.

The WRAIR surveillance for malaria drug resistance involves integration into the Worldwide Antimalarial Resistance Network (WARN), which is supported by the Bill and Melinda Gates Foundation, and allows the fusion of military data from the OCONUS laboratories with civilian data from worldwide sources. Other drug resistance work at WRAIR centers on microscopic identification of malaria, in vitro antimalarial studies, development of PCR identification and speciation of malaria parasites, and genetic analysis of parasites, including identification of molecular markers of drug resistance.

The WRAIR Division of Experimental Therapeutics will continue to support malaria diagnosis at military medical treatment facilities. To expand the GEIS-funded malaria surveillance network, WRAIR is collaborating with CHPPM-West to establish infectious disease surveillance in Central America. WRAIR aspires to expand its service to include in vitro drug susceptibility studies with parasites recovered from infected persons. WRAIR will work closely with WARN to determine the role of GEIS-supported military malaria surveillance network in data collection.

Malaria Diagnostic Center of Excellence

The mission of the malaria diagnostics center of excellence in Kisumu, Kenya, is to ensure valid microscopy to determine the endpoint in clinical trials, to assess new diagnostic methods, and to participate in GEIS-sponsored epidemiology malaria studies. This mission is being accomplished through standardized training, consistent methods documented in standard operating procedures, a critically evaluated rereading paradigm for blood film reading, and objective assessment and documentation of each microscopist's performance. Additional objectives are to train microscopists working in the developing world in the clinical setting, to transfer technology to host countries, and to establish partnerships with similar organizations.

All microscopists working on GEIS projects have been trained and objectively evaluated in microscopy, the gold standard for malaria diagnosis in clinical trials and in emerging infections surveillance. In addition a pilot effort was conducted with 70 individuals to determine the feasibility of and acceptable standards for certification of all microscopists at one of three levels of proficiency. A site inspection checklist has been developed, and inspection of all DoD-GEIS sites in Kenya is underway. Ongoing quality assurance and control will be implemented at all DoD-GEIS sites in Kenya on request by the site. In FY07, 47 microscopists, representing 10 countries, who work primarily in the clinical setting were trained (Table 2). Malaria microscopy is available at the health center level of care in Kenya.

Table 2. Number of Malaria Microscopists Trained, FY07

Country	Number trained
Kenya	19
Tanzania	5
Ghana	9
Burkina Faso	4
Guinea-Bissau	1
Gambia	2
Gabon	2
Nigeria	2
Senegal	2
Malawi	1
Total	47

Rapid diagnostic tests will likely provide an acceptable solution for most malaria diagnosis in Africa, and a training component for rapid diagnostic tests has already been added at the center. Quality control is an ongoing problem with these devices; the CDC has reported difficulty in achieving an accurate diagnosis with rapid diagnostic tests in Tanzania and has had better results in Kenya. The work at the center will help to fill this gap identified by the CDC. The center has recently received approval to collect blood under a second protocol for WHO for quality control. Training microscopists in rapid diagnostic test quality control methods and objectively evaluating the work with known positive and negative tests are planned.

The malaria diagnostics center of excellence supported by GEIS and WRAIR provides a vital platform for malaria microscopy training, which enhances an essential host country medical capability. DoD benefits by gaining the data to evaluate the efficacy of vaccine and drug therapy clinical trials.

Armed Forces Institute of Pathology

Alert Component of DoD Medical Mortality Registry

Since 2001, DoD-GEIS has provided financial and technical support to the Alert Component of the DoD Medical Mortality Registry, The Mortality Surveillance Division is part of the Armed Forces Medical Examiner System at the Armed Forces Institute of Pathology (AFIP). The Mortality Surveillance Division is the only centralized agency in DoD with the mission and authority under federal law (10 USC 1471) to investigate the medical cause of death information for all active duty personnel. The Alert Component actively monitors all active duty deaths in real time for infectious or potentially infectious etiologies, notifies DoD-GEIS in the event of any clusters or unusual types of infections or presentations, and obtains specimens for more extensive testing to identify the agent or agents. Additionally, the Alert Component notifies local preventive medicine and DoD-GEIS personnel of deaths that may require a public health response in a timely enough manner to ensure intervention as necessary.

Program activities consist of 1) the daily collection of mortality information from the Army, Navy, Marine Corps, and Air Force service casualty offices, 2) the collection of death circumstance information from DoD, federal, and civilian investigative agencies, and 3) regular contact with DoD and civilian medical examiners to obtain a medical diagnosis and to request specimen collection and agent-specific testing for infectious agents when appropriate. Additional requests for information

might include medical records from the individual's base or hospital (both at residence and the place of death), autopsy reports, AFIP consultations and toxicology studies, vaccination records, personnel records, legal investigations, safety center and other special investigations, and other sources of eyewitness accounts. A physician individually reviews all complex cases to validate the medical cause of death.

Once gathered and analyzed, the information is provided to various agencies and DoD leadership that can then use it to make changes in policy and procedure based on objective evidence. For each active duty case, the goal is to obtain as complete a file as necessary to determine the medical cause of death. As information is obtained, it is reviewed to extract the relevant medical diagnostic information, risk factors, and circumstances of death, all of which are entered into the DoD Medical Mortality Registry, a searchable database. Finally, the cause of death, comorbid conditions, and ancillary and risk factors are coded and standardized using the *International Classification of Diseases*, 10th Revision. In addition to information on each death, up-to-date military personnel information is obtained from the Defense Manpower Data Center (DMDC), and deployment history is obtained both from the contingency tracking system maintained by DMDC and, in suicides, homicides and potentially infectious diseases where travel history is relevant, telephonically from the unit for validation.

There were 2,174 active duty fatalities during FY07; 37 merited an in-depth review. Eleven of these were determined to have an infectious disease cause with no evidence of an underlying immunocompromised state. Of the 11 infectious disease deaths, two were respiratory, four were sepsis presentations, two were blood-borne pathogens, and three were myocarditis/pericarditis (Table 3). No neurological (meningitic or encephalitic) deaths presented this year.

Table 3. Disease-related Deaths of Active Duty Military Personnel, FY07

Disease category	Total	Agent found (%)	Primary cause of death
Respiratory	2	2 (100)*	Pneumonia (*n* = 2)
Myocarditis	3	0 (0)	Myocarditis (*n* = 1) Myopericarditis (*n* = 1)
Septicemia	4	3 (75)†	Sepsis (*n* = 4)
Bloodborne	2	2 (100)	Hepatitis B (n = 1) HIV (n = 1)
Total	11	7 (64)	

*One death from group A streptococci and *S. aureus*, one from adenovirus.
†One death from group A streptococci, two from *Neisseria*, one pending.

NHRC was consulted in all cases of respiratory disease for which a pathogen was not identified at or before autopsy, and isolates of streptococcus group A were also sent to NHRC for further characterization. AFIP infectious disease, pulmonary and cardiovascular branches, was extensively consulted as part of the process of identifying an infectious etiology when the cause of death was not apparent. USAMRIID was consulted for Hantavirus, arbovirus, and Crimean-Congo hemorrhagic fever testing.

Daily, active surveillance of all deaths has led to a process by which the Armed Forces Medical Examiner, including the Chief of Operations and Investigative Staff, is notified of all deaths in a timely manner, instead of relying on notice from field agents. The result has been a more active role of the Armed Forces Medical Examiners in all cases, sometimes to the point of transferring the body from a civilian facility to a military facility for autopsy. The benefit to DoD is that more thorough investigation is being performed on all active duty deaths than ever before, leading to a full accounting of active duty deaths. DoD-GEIS benefits in that the medical examiners in the Armed Forces Medical Examiner System are aware of the concern regarding vaccine preventable, emerging, and potentially unnatural infections, and they routinely bring any such cases to the attention of GEIS immediately. The medical examiners have changed practice to include saving fresh frozen lung tissue, heart tissue, and blood from cases that have an unclear or infectious cause of death to facilitate PCR testing. Specimens are far more likely to be sent from cases of suspected infectious disease deaths for further microbiological and molecular testing than those from civilian counterparts. Although civilian coroners and medical examiners are not accountable to DoD, AFIP has established excellent working relationships with many of the more active offices and maintains regular communication with them about cases of interest.

DoD-GEIS, as one of the key sponsors of the Mortality Surveillance Division, provided the foundation for the Alert Component, as intended, and for the overall Mortality Surveillance Division. Although the program has expanded well beyond the roots provided by DoD-GEIS, emerging infection surveillance and testing remain, and shall continue to remain, the core of its activities.

DoD Directory of Public Health Laboratory Services

In September 1999, a joint-service Public Health Laboratory Workshop Group identified the absence of clearly defined DoD public health laboratories. The group proposed the development of a DoD directory of clinical tests that are not readily available to many DoD

practitioners. These included tests that are not commonly requested and tests that may be needed during an outbreak or in support of troops deployed to areas of high risk for emerging infectious agents. The 1999 Workshop Group recommended that the AFIP have the mission of implementing and maintaining a DoD directory of special tests, termed a Directory of Public Health Laboratory Services. It also recommended that steps be taken to tie DoD clinical and other laboratories into a virtual Public Health Laboratory network to support DoD beneficiaries globally. A prototype directory of DoD public health laboratory services, developed by GEIS Headquarters, was to be reviewed at the AFIP, updated, and implemented for on-line use. The Armed Forces Epidemiological Board and the DoD-GEIS advisory board subsequently endorsed the project, which was designated the worldwide DoD Directory of Public Health Laboratory Services.

The directory (http://afip-geis.afip.osd.mil) is a compilation of pertinent information available through servers at the AFIP using industry-standard software for its construction, editing, and search capabilities. The directory is linked to the AFIP and GEIS websites and can be found using standard search engines. It contains information for biological agents and corresponding diseases and contact information for CONUS and OCONUS military laboratories that have the capabilities to test for the agents listed. A password is required for access to the directory, and four levels of security are incorporated.

Each agent and disease have a description page containing detailed information such as symptoms, epidemiology, pathogenicity, modes of transmission, communicability, immunization, diagnosis and treatment, and safety precautions. Information regarding influenza viruses and influenza testing is readily accessible through a single keystroke. Illustrative clinical photographs and histological images are provided along with direct links to additional information from the CDC, NIH, and WHO. Laboratory directors can edit their information on-line. The directory contains data for more than 170 infectious agents and more than 130 laboratories and provides links to other websites where pertinent information about the infectious agents and their associated diseases can be found. The directory is password-protected, and laboratory information is only available to appropriate government users. More than 250 users are registered. Of these, approximately 75% are personnel with .mil or .gov addresses. During FY07, the directory website was visited more than 2,500 times. The addition of military environmental laboratories to the website using an Environmental Protection Agency format modified for use by the DoD is an ongoing activity, and nine laboratories representing the Army, Navy, and Air Force are currently listed.

A monthly newsletter is sent electronically to all users. Newsletters contain brief descriptions of relevant news items involving infectious agents along with links to more detailed information. An archive of old newsletters is available on the website, as is a message board through which users can contact the staff. A version of the directory is also available on compact disk and is updated annually. Because there is no global DoD laboratory, these directories serve to unite laboratories for the convenience of the users. The GEIS-supported DoD Directory of Public Health Laboratory Services provides a unique and critical resource for all military medical personnel who have web access throughout the world.

Pacific Air Forces

Building on initiatives begun in FY06, DoD-GEIS supported Pacific Air Forces (PACAF) International Health Affairs as executive agent for PACOM to provide an avian and pandemic influenza rapid response train-the-trainer workshop as part of the WHO avian and pandemic influenza early containment strategy. PACAF also facilitated a biosecurity workshop and technical development subject matter expert exchanges aimed at enhancing early detection and response to infectious disease outbreaks. Countries engaged in these workshops in FY07 included Cambodia, Indonesia, South Korea, Laos, Malaysia, Tonga, and Vietnam. PACAF International Health Affairs also organized training of DoD personnel in the rapid response curriculum to increase the instructor cadre and enhance DoD response preparedness. More than 550 individuals were trained.

PACAF International Health Affairs, on behalf of the PACOM Theater Security Cooperation program, conducted WHO/CDC rapid response train-the-trainer courses for foreign military students and DoD personnel stationed in PACOM. The training encompass three goals:

- Share information on early containment strategies for avian and pandemic influenza;
- Provide an opportunity for medical and nonmedical planning and preparedness for avian and pandemic influenza;
- Provide an opportunity for interagency collaboration for integrated national preparedness for avian and pandemic influenza.

Because this course was designed to train the trainer, students were expected to take the knowledge and skills learned back to their bases and begin instruction at those locales.

The rapid response course was developed based on the CDC/WHO 5-day curriculum that includes lectures and small group breakout workshop sessions. The PACAF rapid response course was given in several variations. The course took 3–5 days, depending on students' background knowledge of epidemiological practice and principles and comprehension of English. The original rapid response training curriculum was modified to meet these requirements and the needs of each country. In addition, the content of the curriculum was slightly modified from the original CDC/WHO curriculum to meet the needs of the military. Didactic lectures on planning, essential services, and a tabletop exercise scenario were added to highlight the similarities and differences between national civilian level planning and military planning. These lectures were intended to facilitate greater civilian-military cooperation.

Although US military facilitators from PACAF were prepared to teach all aspects of the curriculum, in the spirit of partnership and with the desire to meet the goal of interagency collaboration, if a host nation expert was available to teach a module, his or her services were obtained. This served to decrease the barrier of translation and to help demonstrate an inherent host nation ability in pandemic preparedness. Instructors from the US military represented all four services. PACAF also strived for a US government interagency approach by including representation from USAID, CDC, and the Department of Health and Human Services wherever possible. Great effort was made to include individuals from international and nongovernmental organizations as instructors, if they were working in this field.

The principles and practice of rapid response and early containment of a pandemic outbreak have been well received by all military medical and nonmedical personnel with whom PACAF has interfaced. For most of the militaries, pandemic preparation and the roles of the military in early containment had been undeveloped until these workshops were held. Thus PACAF provided a critical piece of avian and pandemic influenza preparedness through DoD-GEIS funding. Without exception, each military realized a requirement for greater depth of planning and preparation to adequately respond to a potential pandemic. All the militaries requested continued assistance with the US military to further develop the capacity to prepare, prevent, and respond to an influenza pandemic.

In the Asia-Pacific region, many potential engagement areas remain for the US military to develop health capacity and build lasting partnerships with the militaries in countries both friendly with and suspicious of the United States. Pandemic influenza preparedness requires increased awareness and continued engagement with these potential partners and represents an opportunity to demonstrate the sincerity of the United States in this area.

Prompt Response by AFIOH to Influenza Outbreak at McMurdo Station, Antarctica

In early December 2006, AFIOH responded to a report of cases of influenza among unvaccinated research personnel working at McMurdo Station, Antarctica. McMurdo Station is a joint research facility between the United States Antarctic Program and the International Antarctic Centre, both operated out of Christchurch, New Zealand. Between 1,100 and 1,500 personnel from around the world, including Air Force servicemembers, work at this isolated station, which creates the opportunity for widely diverse pathogens affecting a small, confined population. Except for US servicemembers, this international group had low vaccination rates for influenza.

After receiving word through PACAF of eight cases testing positive for influenza A on rapid test, AFIOH investigators quickly arranged shipment of specimen collection supplies and shipping materials. Within 4 days of notification, physicians on the ground in Antarctica had taken samples from two acute cases and had the samples en route to AFIOH in San Antonio, Texas. Meanwhile, PACAF worked to get additional influenza vaccines to McMurdo. Both specimens were negative on viral culture, but influenza A H1N1 was detected using real-time PCR. This is the first time that sequenced data from an influenza virus were ever described from the continent of Antarctica and provides an example of how GEIS funding is used to promote direct response to respiratory illness outbreaks at remote sites around the globe.

United States Northern Command

Regional, national, and international planning and response synchronization between the civilian and military sectors will enhance preparedness and response capabilities for an influenza pandemic. To facilitate such cooperation, GEIS supported United States Northern Command (NORTHCOM) to engage with other combatant commands to create a global synchronization plan and to develop a theater-specific plan for NORTHCOM. In conjunction with other federal agencies, NORTHCOM also engaged with Canadian and Mexican counterparts to conduct an historic trinational pandemic influenza conference.

NORTHCOM's unique Defense Support of Civil Authorities mission implies responsibility for close coordination and integration of DoD and civilian planning and response efforts for pandemic influenza as outlined in the National Strategy for Pandemic Influenza (November 2005) and the subsequent Implementation Plan (August 2006).

Based on initial planning efforts, DoD is anticipated to significantly support the primary agencies in the federal government in any response to pandemic influenza, and NORTHCOM will be responsible for coordinating all Title 10 military activity throughout the United States with state and regional efforts. Dedicated pandemic influenza planning efforts in the five Department of Homeland Security and Federal Emergency Management Agency regions will enhance the visibility of regionally specific details that are essential for NORTHCOM to synchronize and integrate into its operations with the local, state, and federal agencies. The incorporation of Canadian and Mexican counterparts will begin to address critical border issues.

NORTHCOM J5 and the NORTHCOM Interagency Coordination Group have hosted pandemic influenza conferences, tabletop exercises, and workshops. Participants have come from NORTHCOM and its subordinate commands and myriad civilian and military partners.

NORTHCOM convened a series of meetings with DoD partners to develop a global synchronization plan and a theater-specific plan and held a series of meetings pertaining to the development of various pandemic influenza CONPLAN documents. During August 2007, the Office of the Command Surgeon in conjunction with NORAD and NORTHCOM Theater Security Cooperation, NORAD-NORTHCOM Interagency Coordination, Department of Homeland Security, Department of Health and Human Services/CDC, Department of State, and the US embassy in Mexico City visited the following Mexican agencies:

- SAGARPA (Department of Agriculture),
- SEDENA (Mexican Army and Air Force),
- Protección Civil (FEMA counterpart),
- SALUD (Ministry of Health),
- SEMAR (Mexican Navy).

Through a series of discussions, these efforts culminated in a trinational (Canada, Mexico, United States) pandemic influenza conference hosted by NORTHCOM 5–6 September 2007 (Figure 16). The first discussion was a senior executive dialogue in July 2007 that led to outreach visits to secure participation by various Mexican agencies. Approximately 80 health representatives and military and civilian leaders from Canada, Mexico, and the United States attended this first trinational conference. Canadian representatives included Foreign Affairs and International Trade Canada, Department of National Defense, and Canada Command. Mexican representatives included SRE (foreign affairs), CISEN (intelligence), SAGARPA, SALUD, SEDENA, SEMAR, and the Mexican embassy in the United States. This meeting constituted the largest exchange with Mexican military and civilian counterparts with NORTHCOM to date. US representatives were from the Department of Homeland Security, Coast Guard, FEMA, Transportation Security Administration, Department of Health and Human Services, CDC, Department of State, DoD, SOUTHCOM, USAMRIID, Joint Task Force-Civil Support, Army North, Air Force North, and various staff divisions of NORTHCOM. Attendees lauded the conference and asked for continued dialogue and exchange.

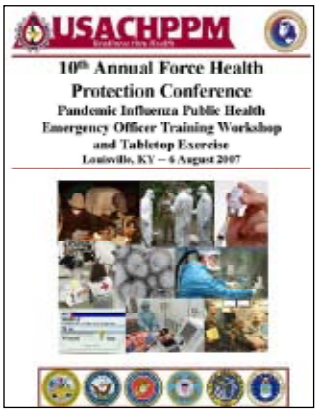
Figure 16. Representatives from Mexican ministry of health (*left*), Foreign Affairs and International Trade Canada (*center*), and US Department of Homeland Security (*right*) during panel discussion at historic trinational pandemic influenza conference, 5 September 2007, sponsored by NORTHCOM and GEIS.

NORTHCOM continues to engage with other federal partners in identifying the next steps toward pandemic influenza preparedness in its area of responsibility. Once planning objectives have been clearly defined with federal partners, NORTHCOM will engage in further dialogue with Canadian and Mexican partners and will continue efforts to improve pandemic influenza preparedness in North America.

United States Army Center for Health Promotion and Preventive Medicine

The United States Army Center for Health Promotion and Preventive Medicine (USACHPPM) includes the Army Medical Surveillance Activity, USACHPPM-Europe (Landstuhl, Germany), and USACHPPM-West (Fort Lewis, WA) as well as the USACHPPM headquarters (Aberdeen Proving Ground, MD). This year, these entities partnered with DoD-GEIS to conduct projects relevant to the MHS including a joint project between USACHPPM-Europe and Landstuhl Regional Medical Center pertaining to influenza surveillance.

DoD-GEIS and CHPPM teamed to host a pandemic influenza workshop at the 10th Annual Force Health Protection Conference in Louisville, Kentucky, on 6 August 2007 (Figure 17). Through a series of presentations and a tabletop exercise, the workshop focussed on training military public health professionals to manage a widespread disease outbreak or another public health emergency using a pandemic influenza scenario. The workshop provided an opportunity to obtain a snapshot of preparedness across DoD at the largest national meeting dedicated to force health protection.



Recognize that pandemic influenza will be a medical problem and a serious operational problem.

Work closely before, during, and after a pandemic with the chain of command and medical staff to maintain readiness.

Communicate with appropriate medical and public health officials on a consistent basis to ensure maximum efficiency of efforts.

Figure 17. Cover of handout for (*left*) and points emphasized at (*right*) pandemic influenza training workshop held during the 10th Annual Force Health Protection Conference.

Army Medical Surveillance Activity

The Army Medical Surveillance Activity (AMSA) was tasked by DoD to operate a medical surveillance system to integrate, analyze, and report information from multiple sources relevant to the health and readiness of military personnel. AMSA conducts comprehensive medical surveillance for the DoD through oversight and management of the Defense Medical Surveillance System (DMSS) and the DoD Serum Repository. The DMSS, the premier DoD epidemiological database, is a longitudinal record of health-related information about servicemembers that is collected from the time they access into the service until they leave and are no longer eligible for care. The DoD Serum Repository is the world's largest serum repository and contains serial specimens from servicemembers. The ability to link the data in the DMSS to the specimens in the repository gives AMSA an unrivaled ability to perform seroepidemiological studies.

Beginning in FY06, AMSA received GEIS funding to establish a center that specializes in surveillance and seroepidemiology for infectious disease with a focus on pandemic and avian influenza. The objectives were to improve surveillance capabilities so that near-real-time serosurveillance for pandemic and avian influenza could occur and to enhance surveillance for other emerging diseases by leveraging the unique serum and data assets of the DoD Serum Repository and DMSS. These assets enable high-quality seroepidemiologic and epidemiological studies to be performed, many of which cannot be performed elsewhere within or outside the DoD. Specific goals for the center were 1) implementation of a system to enable improved serosurveillance for novel and emerging diseases; 2) development, testing, and validation of the ability to conduct detailed seroepidemiologic studies in near real time during a pandemic; and 3) development, testing, and validation of study designs employing DMSS to facilitate the evaluation of the success or efficacy of empiric pharmaceutical or vaccine therapies. In FY07 these efforts were continued and expanded. Six of the projects that are underway or completed follow.

DoD Serum Repository Specimen Processing and Transport Times

During 2006 and 2007, significant investments were made to automate the methods to label and aliquot serum specimens at the DoD Serum Repository. As a result of this work, the number of specimens that can be processed

in a day increased by 40% . In FY07, procedures were begun to decrease delays in archival of serum specimens. When established, this approach is expected to result in a 50% decrease in the time between blood draw and availability of specimens at the repository for study.

Seroprevalence of H5N1 Antibody among Servicemembers Deployed to Countries with Human H5N1 Cases

Data on the number of people that have evidence of H5N1 infection without developing symptoms of severe respiratory tract infection are lacking. Many servicemembers have lived in or deployed to countries with documented H5N1 cases among humans. By utilizing pre- and postdeployment health assessment forms and deployment rosters, AMSA identified a cohort of 1,000 servicemembers that deployed to Thailand, Indonesia, Vietnam, or Cambodia during 2004–2006 when avian and human H5N1 cases were reported among the local populations. AMSA linked the deployment data to appropriate pre- and postdeployment specimens in the serum repository. Hemagglutination inhibition assays and confirmatory microneutralization assays for H5N1 clade 1 and 2 viruses were performed. Results showed that ~1% of the study population was seropositive to H5 antibody before deployment, probably because of cross-reactive antibody. Out of the 1,000 subjects tested, only two were identified who may have seroconverted during deployment to Thailand. Upon further diagnostic testing, these cases of possible seroconversion were determined to likely be due to cross-reactive antibody and were not felt to represent true positives. Overall, a significant risk of H5N1 infection was not found during deployments to countries with human H5N1 activity during this period.

Prolonged Cough in Servicemembers Deployed to Afghanistan

In early 2007, anecdotal reports from US healthcare providers in Afghanistan surfaced that a significant number of US servicemembers were experiencing prolonged episodes of cough. These reports led to the consideration of widespread administration of the new acellular pertussis vaccine. Preventive medicine personnel at CENTCOM and in Afghanistan asked AMSA and GEIS to conduct serological testing to determine the likely etiology to guide vaccine-related policies. A study has been designed that will use pre- and postdeployment serum samples to determine the seroconversion caused by common respiratory pathogens during deployment to Afghanistan. Specifically, seroprevalence of IgG and IgA antibody to *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Bordetella pertussis*, and parainfluenza virus, the seroprevalence of IgG and IgM antibody to adenovirus and respiratory syncytial virus, and the seroprevalence of hemagglutination inhibition antibody to influenza among US servicemembers before and after deployment will be tested by NHRC. The results are expected to inform military vaccination and force health protection policy and should serve as a basis to set priorities among DoD respiratory pathogen research in the future.

Improved Tracking of Influenza throughout Military Health System

Although influenza is a reportable disease within the MHS, relatively few cases actually appear in reportable medical events systems. At the joint influenza surveillance working group annual meeting, it was apparent that tracking influenza infection among MHS beneficiaries must be improved. Clinical laboratory data, electronically captured in HL7 messages, offer the potential to significantly increase the ability to track influenza morbidity among beneficiaries. These data are being developed for incorporation into the DMSS, in collaboration with NEHC and DoD-GEIS. Once this effort is complete, laboratory results from MTFs around the world will be linked to personnel, occupational, health encounter, reportable events, and vaccination data. DoD-GEIS provided equipment to enable this effort that will also increase the number of users that can access the data in the DMSS and streamline reporting of findings.

Hepatitis E

Hepatitis E has been recognized as a threat to military forces since its discovery. Although the seroprevalence in Afghanistan is unknown, the country is thought to be endemic for hepatitis E. With the ongoing deployments of large numbers of servicemembers to this area, the risk continues for sporadic and epidemic hepatitis E infection that could render troops ineffective for combat. A GEIS-supported AMSA study was begun in FY07 that will use pre- and postdeployment serum samples to determine the seroconversion to hepatitis E during deployment to Afghanistan. Specifically, a random sample of 1,500 servicemembers who deployed to Afghanistan from 2002 to 2006 were identified, and their pre- and postdeployment serum samples are being tested at AFRIMS for total Ig and IgM antibody to hepatitis E by ELISA.

This study is expected to provide information about the frequency of infection in troops before and during deployment to Afghanistan and will serve to inform leadership about the risk among troops of hepatitis E infection. This type of information is used by preventive medicine personnel for force health protection programs and will guide future vaccination strategy for deploying forces.

Australian Army Malaria Institute

In an innovative collaboration with AMSA, the Australian Army Malaria Institute in Brisbane, which has researched the treatment and prevention of infectious diseases affecting soldiers throughout Asia, is using extant digitized World War I era medical and administrative records of the Australian Army to create a detailed, prospectively collected history of the 1918–1919 influenza pandemic and its antecedents.

With DoD-GEIS funding, the Australian Army Malaria Institute and the Centre for Military and Veterans' Health, which is affiliated with the University of Queensland, conducted a case-control study of more than 1,200 individuals who died of influenza in the Australian Army in 1918–1919. Similar infantry battalions in France had mortality rates ranging from 0 to 48 per 1,000 soldiers despite the widespread presumption that they were infected by the same influenza virus. This disparity in mortality rates cannot be attributed to quarantine measures or medical care but may be related to preexisting influenza immunity gained earlier in 1918.

The relevance of such historical data in the prepandemic period of the early 21st century concerns definition of the factors that distinguished high and low influenza mortality in infantry battalions, investigation of earlier respiratory epidemics and their possible relationship to the lethal pandemic of October–November 1918, and the geographic tracking of pandemic influenza virus dispersion by military units. Although the next pandemic is certain to be different from that of 1918–1919, the Australian Army records offer indispensable insight into the effect of influenza on military populations that cannot be gained by current investigations.

Historical Data from Australia Used to Assess Impact of Pandemic Influenza on Military Populations

Three influenza pandemics struck during the 20th century: 1918, 1957, and 1968. The 1918 pandemic, which exploded as World War I was ending, was the most devastating, with worldwide deaths estimated by the CDC to be 50 million. Because these pandemics predated relevant scientific advances, current preparations in the military are crippled by lack of reliable data about the effect of pandemic influenza on military populations. This lack is substantial for the 1918 pandemic, both because of its severity and because it occurred before the discovery of viruses as filterable agents.

Military organizations, by their nature, tend to count and recount items of administrative and medical interest. Such detailed records linked to individual soldier records were largely destroyed in the United States by a fire at the National Personnel Records Center in St. Louis in 1973 and in the United Kingdom by the German aerial bombing in 1940–1942. However, such records from the Australian Army from World War I have survived largely intact.

Two nurses with wounded soldier also suffering from influenza Randwick Military Hospital, New South Wales, circa 1919. Masks were worn to protect against transmission of influenza.

DoD-GEIS and AMSA, in conjunction with the Australian Army Malaria Insitute and the Centre for Military and Veterans Health, undertook a massive data management project to recreate the 1918–1919 influenza pandemic in the Australian Army. The goal is to examine antecedents of the disease to determine what information can apply to current pandemic preparations. The Australian Army Malaria Institute traces its origins to World War I when simultaneous epidemics of malaria and influenza halted an entire British Cavalry Corps invasion of Syria.

Continued

Historical Data from Australia, *Continued*

This project has extensively utilized military personnel records maintained and converted into electronic format by the Australian War Memorial and the Australian National Archives. The Australian soldiers were stationed in France along the Western Front and in training camps in the United Kingdom and Middle East from 1914 to 1919. More than 60,000 of the total of 300,000 died from all causes during 1914–1919. Of these 60,000, 6,651 noncombat deaths have been identified, of which ~2,500 were due to influenza/pneumonia, of which 1,237 occurred during the pandemic (October 1918–March 1919). Individual data files have been created for all pandemic influenza/pneumonia deaths as well as random and unit matched controls who survived the war. Data abstracted and entered from the original source documents include demographic, geographic, military organization, and occupation information as well as all hospital admission diagnoses and dates from enlistment to death or discharge.

Preliminary analyses indicate that this historical data set can provide constructive insight into prepandemic events in military organizations. For example, from November 1916 to March 1917, a relatively small epidemic (n = 461 deaths) of lethal respiratory disease described in the records as "purulent bronchitis" killed Australian soldiers in military hospitals in northern France and southern England. The distinct fulminate nature of this disease marked it as novel to the clinicians of the time, and it closely resembled that of the fatal cases during the 1918 pandemic. The failure of the purulent bronchitis to spread generally may not have prevented its seeding the military populations of Europe and suggests that the agent of 1916–1917 may have been a precursor of the 1918 pandemic H1N1 virus.

Members of 1st Australian Field Ambulance in Mericourt, France, 23 August 1918.

Photographs courtesy of Australian War Memorial (awm.gov.au).

A large outbreak of respiratory illness in military units in western Europe during 1918 peaked in June and July and, according to some military authorities, blunted the last German offensives of the war. Few military personnel died during June–July 1918, although sound epidemiological evidence now links this outbreak to the lethal pandemic wave that erupted 4 months later in October–November. Because so few clinical samples from 1918 survive, the best chance of reconstructing the 1918–1919 influenza pandemic experience for study may be epidemiology generated from military records of the time.

USACHPPM-Europe and Landstuhl Regional Medical Center

The United States Army Center for Health Promotion and Preventive Medicine-Europe (USACHPPM-Europe) and Landstuhl Regional Medical Center (LRMC) implemented a GEIS-sponsored program to increase influenza surveillance and reporting in the EUCOM area of responsibility during the 2006–2007 respiratory virus season. This program increased the number of specimens for respiratory viruses in EUCOM three-fold over that in previous seasons.

Military health care providers in EUCOM collected respiratory specimens from patients presenting with the case definition of influenza-like illness: fever of ≥100.5°F/38°C (oral or equivalent) and cough or sore throat of <72 hours duration. Rapid antigen tests were used at the local clinic, and confirmation was made by processing duplicate samples at LRMC using viral isolation techniques and PCR. Influenza virus activity was reported in real time to host nation and US officials. Seven countries participated in this surveillance of military beneficiaries, and 37 MTFs submitted specimens to LRMC. Influenza A/H3N2 was

dominant in EUCOM (~72% of all influenza) and in civilian populations in Europe (~90%). In contrast, influenza A/H1N1 was most common in the United States, constituting 50% of all influenza reported isolates compared with 29% for influenza A/H3N2. Results of influenza surveillance at LRMC for the 2006–2007 season are shown in Figures 18 and 19. This GEIS effort is believed to be the first attempt at population-based regional surveillance in the DoD.

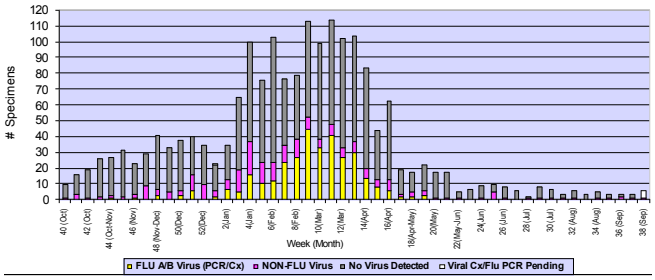


Figure 18. Results from specimens received by EUCOM by week, 2006–2007 influenza season.

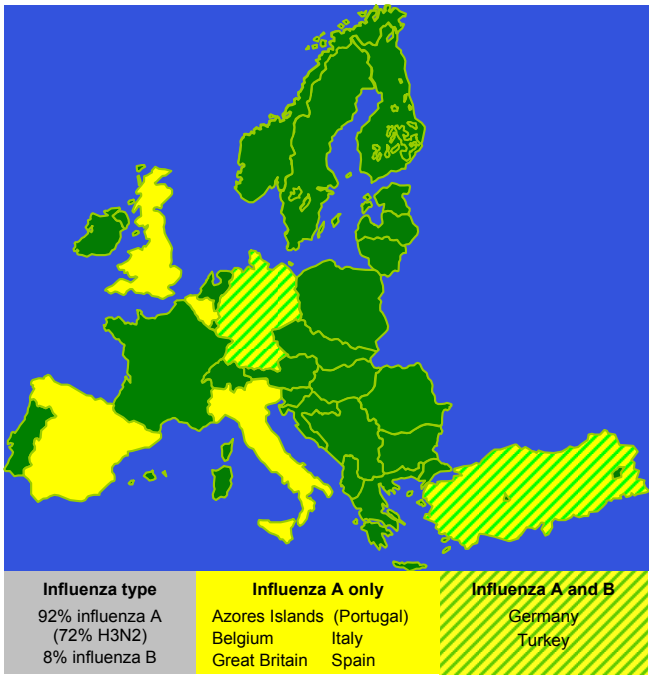


Figure 19. Surveillance by CHPPM-Europe with laboratory support from LRMC indicated influenza A activity separate from influenza A and B, 2006–2007 influenza season. ***Green*****, countries not studied.**

Accomplishments at CHPPM-Europe and LRMC in FY07 follow:

- Increased submission of influenza specimens by roughly three-fold, processing more than 2000 clinical specimens;
- Increased coordination with host nation governments and militaries;
- Formation of partnerships between CHPPM-Europe and AFIOH to ensure long-term program sustainability;
- Real-time reporting of surveillance to EUCOM, AFIOH, and host nations;
- Education and training of more than 600 health care providers, laboratory technicians, and preventative medicine personnel throughout EUCOM regarding influenza surveillance.

USACHPPM-West

Personnel from the United States Army Center for Health Promotion and Preventive Medicine-West (USACHPPM-West) enhanced the ability of the ministries of health of four Central American countries (El Salvador, Guatemala, Honduras, and Nicaragua) to detect infectious diseases through increased laboratory surveillance capabilities. FY07 priorities included transfer of equipment, supplies, and reagents to ministries of health to enable local technicians to screen clinical specimens for infectious agents using PCR.

USACHPPM-West scientists trained ministry of health personnel in the use and maintenance of equipment and reagents and validated PCR protocols. These protocols outlined procedures for assaying clinical specimens for the causative agents of respiratory viruses, leishmaniasis, and enteric infections.

Project officers also continued joint disease efforts that monitored civilian patient populations for the causative agents of influenza-like illnesses, febrile illnesses, enteric diseases, and leishmaniasis. The primary goal of these activities was to assist local health authorities to develop surveillance protocols, procure reagents, and coordinate support from reference laboratories. CHPPM-West performed these projects through funding from DoD-GEIS and the SOUTHCOM J4 Humanitarian Assistance Program.

CHPPM-West FY07 accomplishments follow:

- Provided PCR assays to the ministries of health for influenza A and B and for subtyping influenza A H3N2 and H1N1, adenovirus, rotavirus, and *Leishmania* sp. in skin tissue specimens;

- Provided 87 specimens submitted by the Honduran ministry of health to the DoD influenza reference laboratory at AFIOH where 33 specimens were identified as influenza B/Victoria, influenza H1, influenza H3, respiratory syncytial virus, enterovirus, parainfluenza, and adenovirus;
- Completed evaluation of 40 skin tissue scrapings for leishmaniasis from El Salvador;
- Evaluated 131 fecal specimens from Guatemala and El Salvador for PCR analysis, 38 of which were identified to contain rotavirus;
- Evaluated specimens from patients in Guatemala, Honduras, and El Salvador for influenza-like illness, dengue, and malaria.

Navy Environmental Health Center

The Navy Environmental Health Center (NEHC), which was renamed the Navy and Marine Corps Public Health Center in November 2007, is the medical and deployment health surveillance hub of the Navy. NEHC contributed to the GEIS pillars of surveillance, response, and innovation by improving MHS surveillance capacity in FY07 along with Navy Environmental and Preventive Medicine Units Two and Six.

The flexibility of NEHC to respond to evolving public health demands supports the needs of many GEIS laboratories, whether research, clinical, or operational. Every tool developed though the GEIS-NEHC partnership has been quickly assimilated into the normal operations of Navy public health to create a safer, healthier force.

For 5 years GEIS has supported NEHC in ongoing development of the Health Level Seven (HL7) electronic medical data validation project with the Executive Information and Decision Support Program Office at DoD-Health Affairs. This electronic surveillance project has improved response time for public health inquiries related to the laboratory confirmation of disease, antibiotic-resistant microorganisms, and the estimation of disease burden. In FY06, NEHC established the EpiData Center as a central source for epidemiological support to better understand medical informatics and to develop data tools to support public health policies and programs. To meet privacy and personal health information regulations and laws, all data within the EpiData Center are stored on a secure local area network that is isolated from the web. The EpiData Center expanded in FY07 to meet customer demands for improved access and increased capability.

Public Health Disease Surveillance

The HL7 project was started to reduce the time between the diagnosis and the reporting of a condition of public health importance. Passive surveillance systems, such as medical event and situation reports, provide useful summary case-specific information only when they are actually dispatched and received by the proper health authorities.

The NEHC electronic surveillance system is unique in that it relies on clinical laboratory results as the data source so that confirmed test results are used. NEHC hypothesized that the HL7 data feed from the Composite Health Care System (CHCS) server may provide a more timely and accurate case confirmation if the data were properly transformed and organized. CHCS is an electronic system used in the MTFs to track services related to patient clinical encounters, including outpatient visits, clinic appointments, pharmacy orders and fills, radiology examinations, laboratory test orders and results, and inpatient admissions and discharges. More than 100 CHCS servers distributed worldwide support the MTFs. However, each CHCS server is isolated and cannot communicate with another. Therefore, global collection of laboratory reports from CHCS systems has been a challenge.

HL7 is a national standard messaging format used by health care systems to exchange data (including laboratory results) in support of clinical patient care and health care services. In the MHS, administrative and ancillary services (laboratory, pharmacy, and radiology) associated with inpatient and outpatient visits are electronically tracked in CHCS. Furthermore, each CHCS is programmed to send HL7 messages to a central data repository. In CHCS, an HL7 message is triggered when a laboratory result is certified, medication is dispensed or changed, or a radiology report is verified. An MHS data repository receives HL7 laboratory results from CHCS in real time. With GEIS support, NEHC ensures that these messages are parsed into a database. The message parsing process and database design have been refined and standardized. As a result, these data are used to support critical preventive medicine efforts and programs. NEHC has systematically developed textual tools to abstract and categorize laboratory and pharmacy reports for public health surveillance activities (the radiology data stream

WHONET and HL7 Data Enable Novel Antimicrobial Resistance Surveillance at NEHC

Public health professionals characterize emerging global disease threats. One challenge in this endeavor is to improve treatment and control measures for antibiotic-resistant organisms in medical care facilities. Throughout FY07, laboratory results were used by GEIS partners to support inquiries about antibiotic-resistant organisms at all levels of the MHS. Requests for information came from several commands, including the Navy Bureau of Medicine and Surgery. Among the organisms of interest were *Acinetobacter baumannii* and methicillin-resistant *Staphylococcus aureus*.

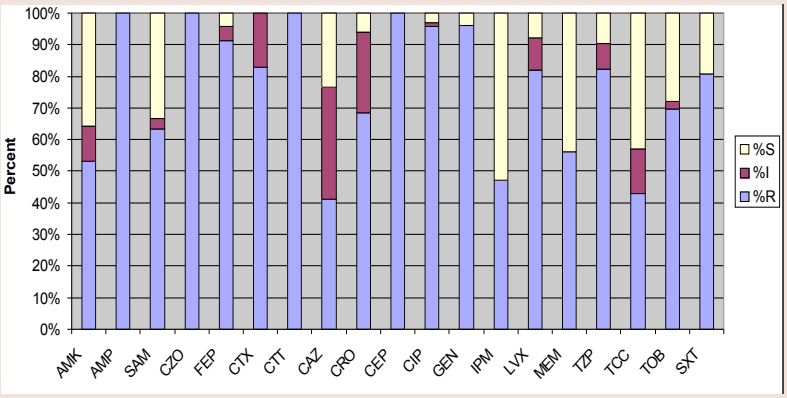
The Health Level Seven (HL7) microbiology data from one Navy MTF, NEHC, were successfully restructured and imported into WHONET using inherent standardization algorithms. From May 2004 to December 2007, data were collected from 7,432 bacteriological isolates (excluding duplicates), of which 1,283 were from blood or cerebrospinal fluid. Rapid analyses, including bacteriology results on pathogens with the corresponding antibiotic sensitivity and resistance data, were conducted to enable management and surveillance of antibiotic-resistant organisms. Reports can be generated quickly by MTFs to address facility-specific concerns and create alerts for organisms of importance such as *A. baumannii* and methicillin-resistant *S. aureus*.

Patient outcomes can be improved at the MTFs by utilizing the restructured microbiology data as a surveillance tool, an important component in the enhanced control of antibiotic-resistant organisms. Data can be viewed by organism, specimen, phenotype, ward, sponsor service, beneficiary type, and/or inpatient or outpatient status. These data can be used at MTFs for trend analysis and early identification of changes in organism-specific resistance patterns. This can assist in providing appropriate drug therapy and revising medications, as warranted, which, in turn, can lead to the following:

- Utilization of fewer antibiotics;
- Reduced transmission of pathogens to other patients;
- Reduced length of illness, hospital stay, and treatment time;
- Fewer secondary infections, complications such as amputations, and mortality;
- Reduced cost.

These data can be used to determine disease burden for many pathogens of interest and can be shared among facilities with similar concerns.

HL7 microbiology laboratory data enhance and significantly improve antibiotic-resistant organism surveillance. Rapid characterization of changes in resistance patterns can be used in surveillance to detect changes in disease trends in a way that hospital records or laboratory tests alone cannot. Early identification of changes in antibiotic resistance patterns has a direct, positive impact on medical readiness, health outcomes, and health care cost.



Resistance profile of isolates positive for *A. baumannii* from blood or cerebrospinal fluid specimens from a single MTF, May 2004–December 2006 (*n* = 79).

is still under development). FY07 GEIS-NEHC projects focused on the identification of influenza cases and the organization of the HL7 microbiology database for identification and tracking of antibiotic-resistant microorganisms. Results from both efforts are promising.

HL7 data strengths:

- Record of certified transactions is structured;
- Data are accumulated at a central repository, providing a single source;
- Data can be linked to a corresponding medical encounter;
- Member's clinical and medical encounter history can be reconstructed;
- Time from transaction certification to availability for analysis is relatively short (1–3 days).

HL7 data limitations:

- Test names and results are nonstandardized;
- Laboratory records reflect those entered at local CHCS server;
- Results for specimens collected and tested at laboratories not affiliated with the MTF are not included (e.g., outside provider);
- Results for specimens collected by the MTFs but referred for outside laboratory testing may not be entered into the CHCS (e.g., specimen sent for testing because of lack of testing capabilities at site).

After identifying these limitations to ensure transparent and accurate analysis, the fundamental HL7 data strengths emerged. These data clearly comprise the sole useable, timely, and centrally located laboratory results for the MHS. HL7 results present significant value to MHS leaders who rely on data-driven decision-making to address pressing military public health concerns.

NEHC continued to expand its experience with HL7 in support of the following projects and inquiries:

- Estimation of the case burden of *Chlamydia* on a single MTF;
- Case identification for influenza, tuberculosis, meningococcal meningitis, dengue, and leishmaniasis;
- Evaluation of commercial and free off-the-shelf software for tracking antibiotic resistance patterns;
- Cancer case validation through pathology reports;
- Case finding for ongoing research projects at a major training MTF, Eastern Virginia Medical School (Norfolk, VA), and USUHS;
- Integration of medical event reports with confirmed laboratory diagnoses.

Pandemic Influenza Surveillance

In FY07, NEHC participated in the Navy Bureau of Medicine and Surgery pandemic influenza workgroups that were tasked with identifying key processes and data gaps, including surveillance and laboratory testing. The work accomplished through the GEIS-NEHC partnership was crucial in determining the state-of-the-science in surveillance of influenza. Based on the experience of NEHC with HL7, standardization of laboratory diagnostic nomenclature for influenza testing was identified as an action item for the DoD Laboratory Working Group. NEHC continues to provide scientific and medical guidance for Navy contingency planners through its increasing understanding and daily use of HL7 as a tool in public health surveillance.

Although many outbreak detection systems use syndromic algorithms as the primary methodology, case identification and tracking are the primary goal of the NEHC pandemic influenza project. An HL7 record is created when a laboratory result is certified, a pharmacy record is closed, or a radiology report is completed. Depending on the type of test or transaction, the time from closing the CHCS record to upload at NEHC may take 1–3 days. Some laboratory tests may take several days or weeks after being ordered to appear in HL7 because the record is created when the record is certified or closed. Tests that require an extended period for completion may be unsuitable for employment in outbreak models that require real-time detection of an outbreak. With the higher utilization of rapid influenza tests, the time delay between diagnosis and surveillance through HL7 could be as short as 1 day but will still lag behind instantaneous notification methods (e.g., phone calls).

These data help illuminate the patient's clinical experience within the MHS. When linked to outpatient and inpatient encounter records, a more comprehensive record of all clinical transactions can be constructed. In FY07, NEHC built on its understanding of the structure and content of HL7 to begin active surveillance of influenza cases. By using a model constructed and tested in previous seasons, NEHC successfully identified positive cases for the 2006–2007 season in a pattern matching

that of the CDC influenza sentinel surveillance work. The progress in laboratory reporting of influenza serotypes was also observed over the last 3 years. In addition to case identification, the HL7 pharmacy database was used to link cases with the prescribing of influenza-specific antiviral medications, specifically amantadine, rimantadine, and oseltamivir phosphate. As understanding of the HL7 databases improves, a more robust case identification process can be developed.

Antibiotic-resistant Organisms

Microorganisms that are resistant to antibiotics pose a severe threat to operational forces and the public. The distinction between hospital- and community-acquired infections continues to be difficult to determine. Development of new antibiotics is dependent on close surveillance of resistant patterns for current drugs. The HL7 microbiology database provides a comprehensive description of the resistance testing conducted in NEHC laboratories, and it has become a primary source for surveillance. NEHC has found that responses to inquiries that concerned antibiotic-resistant microorganisms could take up to several weeks to process using conventional infection control tracking techniques.

NEHC experienced a technological breakthrough in FY07. The primary hurdles to using the HL7 microbiology database for antibiotic-resistant organism surveillance were the nonstandard nomenclature for organisms and drugs and the actual organization of the data within the HL7 data feed message. These barriers required analysts to manually perform searches and validation. When it was discovered that the WHO supported a software program (WHONET) that could read HL7 microbiology data, NEHC began development to restructure the data and create a database that the software could import. In collaboration with a major MTF infection control program, NEHC successfully integrated the requirements for the infection control program with the tools and reports of the software program. NEHC plans to continue development of this application as a tool for MTFs and public health officials.

Navy Environmental Preventive Medicine Unit Two

Preventive medicine personnel at Navy Environmental Preventive Medicine Unit Two (NEPMU2) used GEIS funds for various activities during FY07. In August 2007, NEPMU2 sent a team to educate and establish an influenza-like illness surveillance site in conjunction with AFIOH at the Navy facility at Camp Michaud, Djibouti. MTF personnel (physicians, laboratory, and corpsman) were briefed on influenza surveillance and methods for collection of samples. Contact was established with the host nation ministry of health medical director to facilitate future cooperation and institute a memorandum of understanding to sample the local population, and NEPMU2 personnel were invited to participate in future tabletop exercises to assist cooperative pandemic influenza planning for host government agencies.

Influenza surveillance sites at Navy medical facilities in Rota, Spain, and Sigonella and Naples, Italy, were established or reenergized. Medical personnel at these hospitals were educated about criteria, surveillance efforts, and logistical procedures for submission of samples to be used in the European surveillance system managed at CHPPM-Europe. Standard operating procedures were instituted to ensure continued participation by the hospitals regardless of personnel turnover. Awareness of this training program in the European theater has led to plans to expand this program to African countries given that European naval planning assets will be the initial planners for the new African Command.

Public Health Emergency Officer (PHEO) training has become an important part of NEPMU2 activities. In conjunction with NEHC, NEPMU2 sponsored a 3-day conference for regional PHEOs. GEIS support was used to fund travel for PHEOs from most hospitals in the Navy Medical East (eastern half of the United States and Europe). Navy PHEOs tend to be environmental health officers or physicians with a Master's degree in public health. The intention is to train these individuals, who are officers to assistant installation commanders, in proper response to all hazards, specifically those that are biologic threats. Another focus in training is reducing the long-term effects of pandemic influenza and addressing that threat along with minimizing the morbidity and mortality by instituting nonpharmacologic interventions including quarantine, isolation, and protective sequestration. Those who attended also received risk communication training and briefs on current influenza activities and surveillance.

NEPMU2 is also a partner with NHRC on shipboard febrile respiratory illness programs (Figure 20). Shipboard visits were conducted on aircraft carriers and amphibious ships to educate medical departments and establish collection and processing procedures for specimens. Ships deploy for up to 7 months and store specimens onboard. NEPMU2 maintains supplies for delivery to ships and picks up collected specimens for shipment to NHRC. Fleet liaison and support are integral to NEPMU2 and provide research units a single point of contact for engaging shipboard activities and maintaining a presence at the deck plate.

Figure 20. With large crews in close quarters, aircraft carriers (*top*) serve as effective influenza surveillance sites before sailors return home after deployment (*bottom*).

GEIS funds supported participation by NEPMU2 personnel at the annual GEIS influenza surveillance meeting in San Diego, the PHEO training at the Army force health protection meeting in Louisville, Kentucky, and the semiannual force health protection working group for EUCOM regarding PHEO training and European surveillance. All these meetings and conferences allowed NEPMU2 physicians to engage with the continually advancing surveillance networks and to be aware of new training activities for public health management in pandemics and other disasters.

NEPMU2 is one of the primary units within DoD that works at the unique interface between research activities and operational support. The activities of the unit involve emergency infectious disease training, information dissemination, and operational support in the form of respiratory disease surveillance in deployed forces. The partnership between NEPMU2 and GEIS places DoD personnel at lower risk from infectious diseases and enhances pandemic influenza preparedness on multiple levels in the military.

Navy Environmental Preventive Medicine Unit Six

Febrile respiratory illness constitutes the most significant contributor to lost operational work time in PACOM. Pacific Fleet experienced three separate outbreaks of febrile respiratory illness aboard ships in the summer of 2007, two of which were traced to index cases acquired while visiting liberty ports. Surveillance for respiratory diseases is essential for understanding baseline rates of illness and incidence rates that exceed the baseline. Consistent surveillance also provides insight into which respiratory pathogens are in circulation in a given location at a given time. Armed with this knowledge, commanders can better protect the health of warfighters through preventive measures and countermeasures.

Over the past 4 years, Navy Environmental Preventive Medicine Unit Six (NEPMU6) has worked in conjunction with AFIOH and GEIS to extend respiratory illness surveillance efforts to civilian partner sites throughout the western Pacific (Figure 21) and to enhance sites already in operation. In FY07, NEPMU6 established three new surveillance sites: one each on the islands of Tinian and Rota in the Northern Mariana Islands and one in Koror, Republic of Palau. These new partner sites, as well as enhancement of an existing site on Saipan (Northern Mariana Islands), improve the understanding of the circulating respiratory pathogens in areas of the western Pacific of significance to US citizens and military personnel traveling abroad.

This year, NEPMU6 identified three influenza outbreaks in the Northern Mariana Islands using rapid, handheld influenza assays. The outbreaks were interdicted with the deployment of antivirals and community-wide home-based voluntary quarantine of healthy contacts of cases, combined with rapid identification of illness in family and work contacts of the initial cases. Additionally, a respiratory disease database was created for the Marianas that incorporated clinical and laboratory information from febrile respiratory illness cases for 1998–2007. The information will be used by component commanders to protect forces in the Mariana region, and the partnership with the Northern Mariana Islands fosters a closer working relationship for DoD in the region. NEPMU6 will continue to establish new surveillance sites to improve force health protection and public health capacity in the PACOM area of responsibility.

Figure 21. Western Pacific region in which GEIS partners conduct infectious disease surveillance in support of PACOM.

Brooke Army Medical Center

DoD-GEIS supports Brooke Army Medical Center (BAMC) to continue its work as a center of excellence for leptospirosis and to develop active surveillance for acute febrile respiratory disease. Through collaborative projects developed with the DoD overseas laboratories, BAMC actively supports the GEIS pillars of surveillance, response, integration, and capacity building.

With its central location at Fort Sam Houston (Texas), BAMC hosts a large volume of military troops and their dependents as well as wounded servicemembers returning from Iraq and Afghanistan. Considering the global scope of operations for the US military, this patient population is of particular interest for epidemiological surveillance of infectious diseases.

Surveillance

BAMC continues to assist in the surveillance for leptospirosis at the DoD overseas laboratories. The center for leptospirosis has performed and provided expert interpretation of the current gold standard, the macroscopic agglutination test, for many febrile illness surveillance studies performed overseas because the center is located within the DoD reference laboratory for leptospirosis diagnosis. In addition, BAMC provides technical expertise in the diagnosis of leptospirosis, including currently evaluated PCR molecular probes, genetic fingerprinting with pulsed field gel electrophoresis, and culture techniques. These capabilities have allowed numerous cultures obtained from NAMRU-3 (Egypt) and AFRIMS (Thailand) to be identified. The PCR technology previously transferred by BAMC to NAMRU-3 continues to enhance the epidemiological work underway in Egypt. As more cultures and serum samples are acquired throughout the world, the BAMC center of excellence for leptospirosis is developing a repository for rapid comparison among newly recovered strains. This work has augmented collaboration with the CDC leptospirosis diagnostic facility.

Work with AFRIMS has established the presence of leptospirosis in Nepal using an investigational hepatitis E vaccine study population. This effort, which began with specimens collected by WARUN, highlights the possibilities of dual infections of leptospirosis and other pathogens and the continued recognition of the global impact of leptospirosis. The international collaborative programs at BAMC also include a GEIS study in Thailand with AFRIMS assessing the presence of leptospirosis in civilian children, an underevaluated population. In addition, a large repository of serum from various animals in Thailand is being evaluated for serological evidence of ongoing infection or colonization, especially as it relates to other human leptospirosis studies. Ongoing studies elsewhere include performance of macroscopic agglutination tests for fever studies underway in Peru.

Response

GEIS work with diagnostic and clinical treatment strategies is ongoing at BAMC. In vitro antimicrobial susceptibility testing of clinical and laboratory isolates from around the world was recently completed to assess differences in resistance panels. This work revealed no difference in resistance between clinical and laboratory isolates, which supports the continued effort by BAMC to design alternative treatment strategies that include agents that are safe during pregnancy and for children, because results with one strain should be applicable to strains from around the world.

Drug testing in animal models has revealed that azithromycin is an extremely active agent against leptospirosis. Azithromycin has recently been shown in small studies by other investigators to be effective in humans. Work with other agents that are typically used in developing regions and not the United States are underway, including the assessment of chloramphenicol at international laboratories.

Integration

The GEIS center of excellence in leptospirosis has set a high priority on working with the DoD overseas laboratories and supporting their fever studies and clinical trials. The primary emphasis is to develop useful diagnostic strategies, including macroscopic agglutination tests and molecular testing. Diagnostics, especially for the field, are critical to force health protection. The development of probes that can identify species of *Leptospira* will also enable a more rapid epidemiological characterization of samples from febrile illness cases. The accuracy of the probes will continue to be confirmed with the

technology being developed at BAMC. In addition, the ongoing worldwide collection of leptospire isolates will enable BAMC to create a repository of pathogens for future work transitioning from epidemiologically based to patient-based strategies that can be implemented at the time of diagnosis. Animal studies continue to be performed to refine molecular diagnosis so that the best platforms are available for movement into clinical or research settings. In addition, joint work with industry has fostered renewed development of rapid diagnostic kits for point of care diagnosis.

Capacity Building

Many strategies developed through GEIS at BAMC allow the overseas laboratories to streamline their techniques for evaluation of leptospirosis in their respective regions. Establishing pulsed field gel electrophoresis has enabled better characterization of isolates, which enhances the current knowledge of leptospirosis strains circulating in the world. BAMC and GEIS are developing a deeper collaboration with the CDC to establish a combined repository and fingerprint database for *Leptospira* species. This powerful tool will merge the *Leptospira* detection capabilities of the foremost civilian laboratory interested in leptospirosis with the DoD surveillance and response network.

Systematic Active Disease Surveillance in Patients Admitted for Acute Febrile Respiratory Illness

BAMC is well equipped to perform diagnostic testing and is a premier site for sample collection and evaluation of patients presenting with acute febrile respiratory illness. Its close proximity to AFIOH enables collaboration in projects beneficial to the DoD and the field of febrile respiratory illness. GEIS is funding BAMC to develop a system to detect clusters of unusual respiratory illness at the medical center. BAMC will collect specimens from patients with acute febrile respiratory illness and will deliver the samples to AFIOH for analysis. The intent is to link patient symptoms with laboratory results to detect any increase in influenza-like illness within the medical center. Once this system is operational at BAMC, the goal is to apply it at all MTFs. Objectives of the project follow:

- To identify any patient admitted to an MTF with acute febrile respiratory disease in near real time and facilitate the appropriate diagnostic evaluation;
- To provide a mechanism to identify and quantify (in near real time) the number of patients admitted to an MTF for a concerning complex of symptoms that could be consistent with pandemic influenza;
- To collect data on the clinical course and outcome of the most severe cases of influenza (patients requiring admission to intensive care units, cardiac care units, or medical wards) and attempt to correlate the severity of disease with possible molecular features of the influenza isolate;
- To collect clinical samples from patients identified as having influenza to assess host factors relevant to clinical response.

During FY07, BAMC-GEIS personnel developed several protocols approved by the institutional review board to enhance the surveillance of respiratory diseases at this tertiary care center. A blood and tissue storage bank, approved by the institutional review board, is available to store samples from patients with a febrile respiratory illness. Patients who volunteer to participate have serum and respiratory samples collected, tested, and archived for future testing or research. BAMC also developed a protocol to survey patients with an exacerbation of chronic obstructive lung disease for respiratory viruses. These patients are known to be at higher risk for respiratory viral infections and may have more severe disease. These samples are also eligible for the tissue archive, should the patients volunteer to participate.

Further progress is being made in rapid diagnostic testing of respiratory samples. BAMC-GEIS personnel have partnered with an industry collaborator to provide a new diagnostic platform for the analysis of respiratory samples. This diagnostic platform is based on a custom microarray electrochemical device that can test for multiple respiratory pathogens in a single pass. BAMC will work to evaluate this system concurrent with ongoing surveillance protocols.

BAMC-GEIS personnel are beginning collaborations with NHRC in San Diego to provide clinical samples for testing on the T-5000 diagnostic platform. These pilot studies will allow clinical samples to be collected and tested from a range of tissue types and disease states with the ultimate goal of developing a useful method of analyzing respiratory samples from patients suffering from febrile respiratory disease with an unknown pathogen.

National Naval Medical Center

DoD-GEIS supported the National Naval Medical Center (NNMC) to undertake preventive measures to reduce *Acinetobacter* infections at NNMC and to participate in a multicenter investigation of multidrug-resistant *Acinetobacter* infections in military medical centers. The emergence and spread of antimicrobial resistance create a significant national and international problem and affect treatment at many medical centers throughout the military.

Nearly 18,000 US military personnel have been wounded in action while serving in Operation Enduring Freedom and Operation Iraqi Freedom (Figure 22). Wound infections have been a frequent complication of these injuries but have not been thoroughly characterized. As in all wars, wound infections caused by Gram-negative organisms, including *Acinetobacter calcoaceticus-Acinetobacter baumannii* complex (*Acinetobacter*), *Pseudomonas aeruginosa, Klebsiella* sp., and *Escherichia coli*, have been common in Operation Iraqi Freedom and Operation Enduring Freedom. However, the acquisition of multidrug-resistant isolates appears to be significantly increased in Iraq and Afghanistan compared with that in past wars. The reasons for this problematic increase are unclear.

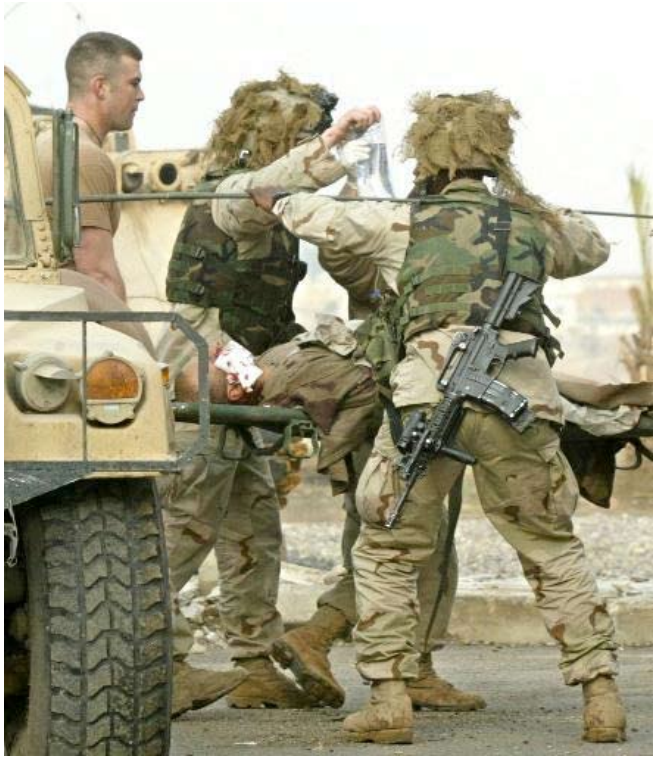


Figure 22. Soldiers of 4th Infantry Division evacuate wounded near Tikrit, Iraq.

Acinetobacter is a bacterial colonizer frequently acquired by US Marines and soldiers deployed to Iraq and Afghanistan. The wounds resulting from war injuries frequently involve traumatic amputation, large soft tissue defects, and skeletal trauma with exposed bone, all of which present an ideal setting for colonization by bacteria and wound infections. After injury, wounded soldiers colonized with *Acinetobacter* are medically evacuated to tertiary medical centers such as NNMC and Walter Reed Army Medical Center (WRAMC) for definitive care. NNMC, WRAMC, and other military facilities in the United States have documented nosocomial spread of *Acinetobacter* from hospitalized wounded soldiers to noncombat patients. Nosocomial infections in US civilian hospitals caused by *Acinetobacter* have also increased over the last few years, so vigilance and strengthened infection control efforts in all healthcare settings are important.

Acinetobacter can clinically manifest as nosocomial bacteremia, pneumonia, meningitis, and surgical wound infections. Nosocomial *Acinetobacter* bacteremia alone has a mortality rate of 19–44%. At 44%, *Acinetobacter* has the third highest crude mortality among intensive care unit infections. Nosocomial bloodstream infections with Gram-negative pathogens were more frequently observed in the intensive care setting and with mechanical ventilation, and ~30% of the isolates of *A. baumannii* strains were resistant to four or more antibiotics. Further susceptibility profiles of *A. baumannii-calcoaceticus* complex to amikacin, ampicillin/sulbactam, ciprofloxacin, gentamicin, imipenem/cilastatin, and piperacillin/tazobactam showed >90% susceptibility when isolated from healthy individuals but was only 50% for isolates from inpatients. Given this evidence for nosocomial spread, NNMC implemented infection control policies and appropriate antimicrobial use guidelines such as modifying periprocedure antibiotics with amikacin during wound debridement in burn patients or limiting the use of carbapenems to treat other bacterial infections to prevent propagation of further resistance.

Despite the unexplained increase in multidrug-resistant organisms isolated from wounded military personnel, surveillance that routinely includes characterization by molecular techniques has not been established in any MTF. Molecular genotyping of these isolates would enhance infection control monitoring of personnel wounded in the Middle East and the possible nosocomial transmission of these organisms within NNMC.

Characterization of the multidrug-resistant organisms via genotyping will lead to strategies for employing antibiotics and isolation practices at both the individual patient and guideline levels. The ability to identify clonal multidrug-resistant outbreaks creates the opportunity for targeted infection control measures in inpatient wards.

Strategies implemented as a result of this study include increasing contact and droplet precautions for patients identified with *Acinetobacter* infection or colonization. The data were also used to justify an increase in nursing staff at NNMC, which allowed wards to dedicate nurses to individuals on droplet or contact precautions. A corresponding increase in housekeeping staff led to more thorough cleaning of patient rooms and wards. Having dedicated staff for patients on precautions helps prevent the transmission of *Acinetobacter* to those patients who are not on precautions. Furthermore, the number of antimicrobial soap dispensers was increased in wards and patient rooms.

Through the first 6 months of 2006, nosocomial transmission of *Acinetobacter* at NNMC occurred at a rate of two to three per month, with a peak of seven in June. Identifying the outbreak and using the enhanced infection control measures reduced the cases of multidrug-resistant *Acinetobacter* to less than one case per month on average through the end of 2006 and into early 2007.

GEIS also initiated the first multicenter study to begin to genetically characterize and track patterns in the strains that cause *Acinetobacter* wound infections; the centers participating in the study are NNMC, WRAMC, and BAMC along with WRAIR. Through this collaboration, pulsed field gel electrophoresis protocols and analysis have been standardized among NNMC, WRAMC, BAMC, and WRAIR. This system will allow the identification of common genotypes of *Acinetobacter* among facilities, suggesting the acquisition of infection or colonization before a patient's arrival at an MTF, and help track strain patterns that may change over time.

GEIS and NNMC have instituted surveillance of multidrug-resistant organisms within each MTF, and clonal outbreaks of *Acinetobacter* have been identified. The highly effective infection control strategies, some of which were implemented as a result of this study, that led to the reduction of nosocomial transmission of these organisms at NNMC can be used elsewhere. Using this model of molecular epidemiology at all military medical centers could profoundly improve patient care of active duty and beneficiary populations. This public health approach to characterizing the strains of *Acinetobacter* that cause these infections is expected to lead to better control and decreased morbidity and mortality through better understanding of the genetic relationships among these organisms.

18th Medical Command

Surveillance systems operated by the 18th Medical Command (MEDCOM) with GEIS assistance allow United States Forces Korea (USFK) to collect and assess disease nonbattle injury (DNBI) data associated with anticipated exposures and to rapidly deploy and implement appropriate countermeasures. DNBI surveillance that includes historical and geographical analyses in conjunction with vector-borne disease and human surveillance is important to the identification of DNBI risks and the development of mitigation strategies.

The mountainous topography and isolated river valleys of Korea create the potential for focal transmission of malaria, arbovirus infections, and other tick-, mite-, and rodent-borne diseases. Rice is the primary crop, and the low-lying flooded fields provide abundant mosquito habitats that result in large populations of the malaria and Japanese encephalitis virus vectors. In addition, tall grass regions bordering the hills, mountains, and farmlands provide a fertile environment for the Hantaan virus reservoir, *Apodemus agrarius*. Human populations are often centered in villages, towns, and cities within the valley and river systems, a situation that is unlike that in other regions in Asia where families reside on the land that they farm. Both Republic of Korea and US military bases are frequently associated with these clustered civilian populations. This arrangement creates areas of dense populations, which can increase and magnify the risks of infectious disease transmission. Travel outside these areas of concentrated populations compromises containment of focal disease transmission, especially for avian influenza, which occurred sporadically throughout Korea during the winter and early spring of 2006–2007. The nature of the geography of Korea puts USFK military and civilian populations at risk for infectious diseases (e.g., malaria, Japanese encephalitis, and scrub typhus) to which they are not normally exposed in the United States.

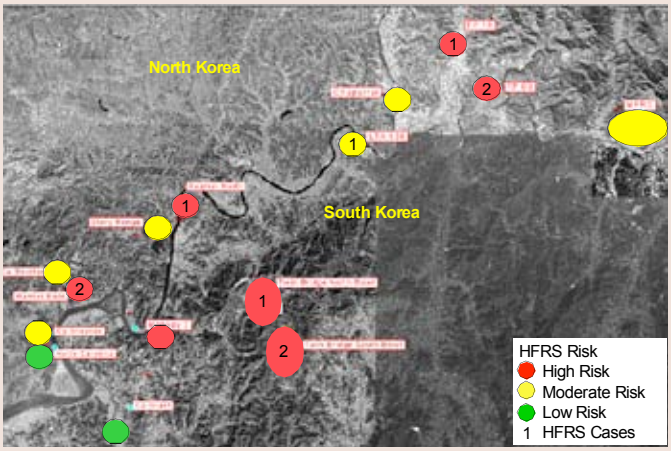
The Office of the Deputy Chief of Staff, Force Health Protection, 18th MEDCOM, Seoul, Korea, is responsible for the surveillance of vector-borne and infectious diseases and other DNBIs among military, civilian,

and family member populations assigned to Korea. 18th MEDCOM collaborates with Korean counterparts to share disease surveillance information and analysis of data important to USFK leadership and works with local university professionals to conduct vector-borne disease surveillance. 18th MEDCOM also collaborates with US agencies to provide assays for identification of pathogens to determine infection rates in arthropod, rodent, and insectivore populations. These collaborative efforts, supported by DoD-GEIS, to gather and analyze data associated with DNBIs are key to maintaining troop readiness, planning, and education to ensure that preventable diseases are minimized among all USFK populations.

In collaboration with the Korean CDC and other Korean agencies, 18th MEDCOM conducts current and historical analyses of endemic, reemerging, and newly described human pathogens throughout Korea, including those that cause malaria, Japanese encephalitis, Hantavirus pulmonary syndrome, scrub typhus, leptospirosis, murine typhus, ehrlichiosis, anaplasmosis, and spotted fever group *Rickettsia*. Monitoring vector- and rodent-borne diseases is increasingly important in DNBI risk analysis for the development of mitigation strategies.

Avian and human influenza surveillance is of primary concern to USFK. Since the advent of recent human cases of the H5N1 strain of avian influenza around the

Locations of Hantavirus Threat to USFK Identified



Hantavirus risk assessment of US and Republic of Korea training sites near demilitarized zone. *Numbers*, number of Hantavirus cases associated with each training site. HFRS, hemorrhagic fever with renal syndrome.

Each year >400 cases of Hantavirus pulmonary syndrome are reported among Korean civilians. Although few relative to the entire population of Korea, these cases indicate that Hantaviruses pose a serious health threat to USFK personnel given the high morbidity and mortality (3–10%) associated with the infection and because medical assets may be limited during hostilities. Air evacuation of patients with a hemorrhagic syndrome is known to increase mortality.

During armistice, the sites of Hantavirus transmission where USFK personnel trained were determined, and the environmental factors that were responsible for transmission were identified. This work led to the development of environmental and human behavior mitigation strategies to reduce risks. Rodent behaviors and distributions vary by species, which increases the need to identify geographical and seasonal distributions and ecological parameters to develop health risk assessments. Hantaan virus poses the most serious infectious disease threat to USFK personnel while training in the field. Seoul virus poses a less serious threat in the garrisons.

Rodent-borne disease surveillance in FY07 by GEIS and 18th MEDCOM identified high rates of Hantavirus infection (Hantaan virus) at selected US military training sites. Based on rodent carriage and counts of human cases of Hantavirus pulmonary syndrome, risk assessments were developed. As a result of nucleotide sequencing of a portion of the Hantavirus genome from Hantaviruses isolated from rodents and USFK patients, the location of transmission was identified. Because the incubation lag in four patients in 2005 exceeded 20 days, the location of transmission could not be assumed to near the clinic where the patient appeared. The sequence data compiled in this effort allows investigators to determine the location of transmission to develop a more accurate analysis for disease risk and mitigation.

world, Korea has experienced two human outbreaks as the result of bird migrations: one during late winter-early spring of 2003–2004 and one in 2006–2007. In both outbreaks, coordination with the Korean CDC provided USFK with timely updates and information that were important to quell concerns among USFK populations. Through GEIS, 18th MEDCOM gave data to the Korean CDC, along with guidelines for properly handling and cooking chicken meat and instructions to avoid open air markets selling fowl, to people in the outbreak areas, which included USFK personnel because some of the areas were near US military installations. The rapid action of the Korean ministry of health in culling birds at or near infected farms and placing bird handlers (cullers) on antivirals greatly reduced the spread of avian influenza, resulting in no symptomatic cases among the exposed population (several asymptomatic cases were seen). By March 2007, no more avian influenza outbreaks were reported among farmed birds in Korea. Nevertheless, the Korean ministry of health monitors avian influenza in migrating bird populations and uses this information to inform the public of potential outbreaks during the winter/spring. Sharing these data with USFK is essential to maintain an informed USFK public and ensure that military medical personnel are prepared to meet the challenges of human outbreaks that may extend to the USFK community.

In addition to its effort with avian influenza, 18th MEDCOM works closely with the Eighth United States Army to ensure that military personnel are vaccinated against human influenza and to conduct surveillance for human influenza at the 121st Combat Support Hospital and widely dispersed outlying health clinics of the 168th Medical Battalion—a total of five health facilities. Korean CDC data showed that differences in the distribution of human influenza strains were evident in Korea this year. Thus, influenza surveillance at these widely separated military medical facilities, combined with ongoing DoD influenza work through AFIOH and sentinel Air Force and Navy sites (e.g., Osan Air Base and Kunsan Air Base in South Korea and Air Force and Navy sites in Japan), will capture distribution differences of circulating influenza viruses throughout the peninsula and indicate timelines when influenza viruses appear and/or rates increase. These data can be used, in conjunction with hospital admissions, to educate the population and increase vaccination rates to reduce the impact of disease and admissions to the 121st Combat Support Hospital.

Through DoD-GEIS, 18th MEDCOM conducts critical surveillance, including human and vector/reservoir aspects of surveillance for vector-borne and infectious diseases in Korea. Highlights of FY07 DoD-GEIS work at 18th MEDCOM follow:

- Identification of new species of mosquitoes that are important in the analysis of malaria and its distribution in Korea;
- Identification of new Hantaviruses among distinct rodent reservoirs;
- Identification of a new and novel Hantavirus in a shrew;
- Development of methods to identify the location of transmission of Hantaviruses in humans as a result of spatial differences in the virus genome;
- Logging of new records of a tick species in Korea;
- Determination of the distribution of human influenza strains (among the Korean population);
- Determination of ecological relationships of avian influenza and the potential impact of avian influenza on USFK populations;
- Determination of the incidence of symptomatic *Chlamydia* in USFK populations and delivery of a proposal to determine rates of asymptomatic *Chlamydia* rates among female soldiers upon reception to Korea;
- Coordination with the Korean National Institutes of Health, Korean CDC, various universities, and US institutions to understand the dynamics of disease vector and infectious human pathogens in Korea;
- Acquisition of modular BSL-3 laboratory to provide high containment laboratory capability on the Korean peninsula.

DoD-GEIS also guides and assists in conducting vector and infectious disease surveillance that benefits Korea and other areas where servicemembers are deployed or assigned. For example, ~60% of the malaria cases in Korea become symptomatic >6 months after infection, creating a circumstance in which many cases are exported to other areas, e.g., the United States, Iraq, and Afghanistan. In coordination with the Army Medical Surveillance Activity, DoD-GEIS supports the tracking and reporting of cases of malaria throughout the Army that are attributed to exposure in Korea.

Office of the Assistant Secretary of Defense for Health Affairs

To respond effectively to emerging infectious disease epidemics and bioterrorist attacks, the MHS is refining techniques to detect, validate, characterize, and even predict outbreaks at the earliest opportunity. In FY07, the Office of the Assistant Secretary of Defense for Health Affairs assembled a methods development team to conduct these activities and established a consortium with DoD-GEIS partners, including the Johns Hopkins University Applied Physics Laboratory, Naval Environmental Health Center, and AFIOH, to share surveillance approaches.

The capabilities and areas for improvement of the MHS global surveillance system, ESSENCE, were evaluated. The evaluation involved comparison of ESSENCE with national and regional civilian surveillance systems that suggested new directions for ESSENCE enhancement.

The Office of the Assistant Secretary of Defense for Health Affairs also laid essential groundwork for incorporation of laboratory and radiology data into ESSENCE by mapping data codes against existing ESSENCE categories for patient syndromes. Full integration of these data into ESSENCE will provide military health personnel with powerful new capabilities to detect and investigate outbreaks. These improvements in ESSENCE will position DoD to recognize outbreaks of infectious disease at the onset of the eruption of the disease and therefore enable the MHS to respond and prevent severe damage to operational readiness for US forces.

Uniformed Services University of the Health Sciences

DoD-GEIS funds tropical medicine training for uniformed personnel through an agreement with the Uniformed Services University for the Health Sciences (USUHS). This training program primarily supports the GEIS pillar of capacity building, although the training contributes to surveillance, integration, and response. The training serves the educational needs of medical students, residents in various specialties, infectious disease fellows, master and doctoral candidates, and junior staff in each uniformed service. Through this program, GEIS is addressing the lessons learned in Vietnam, as described in *Internal Medicine in Vietnam,* the authoritative US military medical history of the Vietnam conflict.

> Several lessons are to be learned from the [fevers of unknown origin] experience in Vietnam. First, a nucleus of tropical disease experts should be maintained from one generation to the next, as should an awareness of the major tropical diseases that might be encountered on future ventures into tropical countries. Second, worldwide tropical disease problems should be monitored so that one can accurately predict which diseases might be encountered in various areas of the world. Third, ongoing medical research studies in the less developed countries should be supported. These can contribute to eradication of such diseases in those countries. Finally, properly equipped laboratories for the study of tropical disease should accompany initial military units into all tropical environments so that unfamiliar medical problems can be recognized early and preventive measures instituted.[1]

The GEIS training program at USUHS is preparing practitioners so that 1) they will encounter fewer unfamiliar medical problems and 2) they can plan and execute diagnosis, treatment, prevention, and future research for problems that are unfamiliar. Trainees are required to have one learning objective each for clinical tropical medicine, surveillance, and research in a developing country setting, all of which address virtually all the lessons learned in Vietnam.

GEIS values a university that is involved in the training program. The strength of this association lies in the ability of the faculty to contribute to educational needs assessment and curriculum development. Faculty members can match applicants' educational interests with the activities of the DoD overseas laboratories. Thus, GEIS can more strongly develop an integrated system utilizing

[1] Deller JJ Jr. Fever of undetermined origin. In *Internal Medicine in Vietnam, Volume II: General Medicine and Infectious Diseases*, edited by AJ Ognibene and O Barrett Jr.Washington DC: Office of the Surgeon General and Center of Military History, United States Army, 1982.

different partners to address military medical needs. This integration can include, for example, having USUHS Master of Tropical Medicine and Hygiene degree candidates and the laboratories mutually assist each other by having the students working at the laboratories to complete their required projects and practicums on activities of importance to the laboratories; allowing a student with particular laboratory or language skills to have a rotation unique to those skills; and/or helping primary care specialty residents match their budding interests with appropriate laboratory projects and staff.

Through this program, GEIS is helping to solve the problem of inadequate training in tropical medicine among US practitioners that was recently expressed by the Global Network for Neglected Tropical Disease Control: "Training opportunities in clinical tropical medicine, parasitology, laboratory diagnostics, vector control, and public health practices are especially depleted and portend a lost generation of experts in these areas."[2] GEIS, USUHS, and the DoD overseas laboratories are helping train substantial numbers of professionals in precisely these areas.

Outbreaks of tropical disease, including malaria and cutaneous leishmaniasis, have occurred in military operations in recent years. The GEIS training program at USUHS is preparing officers for current real-world military operations, and many of its funding recipients have already deployed and contributed to global military operations. During FY07, 34 uniformed officers received training through this program. Eight medical students with prior service, and therefore exempted from the required line unit experience for rising second year medical students, participated in a structured rotation in Peru based at NMRCD. These students became part of the US embassy's immediate response to the magnitude 8.0 earthquake that struck near their location in August 2007 during the training rotation.

One student who rotated to USAMRU-K through the GEIS training received two awards: the USUHS Public Health Service Surgeon General Award, given to the graduating public health service medical student most exemplifying academic achievement, military medical professionalism, and commitment to enhancing the mission and goals of his or her service, and the Captain Richard R. Hooper Memorial Award, given to the graduating medical student exhibiting exceptional promise in preventive medicine.

The GEIS training has furthered the corporate knowledge of uniformed health professionals by giving students hands-on experience with expert staff. As awareness of the program continues to spread, training opportunities and research collaborations around the world will increase, all to the benefit of the US military.

Center for Disaster and Humanitarian Assistance Medicine

GEIS has a collaborative relationship with the Center for Disaster and Humanitarian Assistance Medicine (CDHAM) to maintain and build relationships within the DoD and with other organizations active in disease surveillance and rapid response. In 2006, DoD-GEIS requested that the CDHAM assist the geographic COCOMs in concept development, planning, and execution of education and training programs to support the respective requirements for influenza surveillance and response. The CDHAM responded by working with the COCOMs to develop project proposals that would direct their focus on the needs of each command while meeting the objectives of the National Strategy for Pandemic Influenza.

In FY07, the CDHAM worked with the COCOMs to plan and execute education and training activities while ensuring that national and COCOM objectives were met. Additionally, the CDHAM provided technical assistance by reviewing the strategic settings of the regional COCOMs, analyzing operational and contingency plans, evaluating those plans against the National Strategy for Pandemic Influenza, and providing recommendations to improve preparedness and response activities. CDHAM assisted in the design, development, scheduling, logistics management, and execution of education and training venues or COCOM-supported regional conferences directed at preparedness, surveillance, and response efforts within EUCOM (Albania and Germany)

[2] Hotez PJ. Should we establish a North American school of global health sciences? *Am J Med Sci* 2004;328:71–7.

and SOUTHCOM (Central America and Caribbean). Further initiatives were designed and planned for all five COCOMs to begin execution in FY08. During FY07, CDHAM accomplished the following with GEIS support:

- Under the auspices of EUCOM, conducted a seminar for the Albanian ministry of health and ministry of defense in surveillance, diagnosis, preparedness and response to an outbreak of avian and/or pandemic influenza.
- In collaboration with SOUTHCOM, planned, organized, coordinated, and executed two pandemic influenza conferences and tabletop exercises, one for South and Central American countries and one for countries of the Caribbean.
- Provided a subject matter expert in pandemic influenza to develop and facilitate a tabletop exercise for annual conference of the EUCOM surgeon.

GEIS support of the COCOMs continues through the CDHAM effort. By building capacity within each region through information sharing, information technology, laboratory enhancement, and training, GEIS can gain and expand knowledge on regionally specific issues related to influenza and other potential infectious disease threats.

DoD Overseas Laboratories

Naval Medical Research Unit No. 2 (Jakarta, Indonesia)

Naval Medical Research Unit No. 2 (NAMRU-2) has been at the forefront of surveillance in the region of the world hardest hit by the highly pathogenic avian influenza virus H5N1. GEIS-funded projects at NAMRU-2 have been highly instrumental in characterizing and mitigating regional infectious disease threats and assisting developing countries to build investigative and diagnostic infrastructures for effective outbreak surveillance throughout Southeast Asia. Through the establishment of an extensive network of collaborative relationships, NAMRU-2 has assisted countries most vulnerable to new or reemerging pathogens by developing state-of-the-art laboratories and disease surveillance programs. NAMRU-2 has been especially involved with the diagnosis, surveillance, and identification of H5N1 strains.

NAMRU-2 continued to monitor the spread of influenza-like illnesses through its extensive network of collaborating hospitals in Laos, Cambodia, and Indonesia. During FY07 NAMRU-2 tested specimens from 4,568 influenza-like illness patients in Indonesia alone (Figure 23). Positive blood or respiratory samples are shipped (when possible) to the CDC for verification and genetic sequencing and for assay and vaccine development. Data are shared with the Indonesian ministry of health and WHO.

Figure 23. Study sites for NAMRU-2 (*red star*) influenza surveillance throughout Indonesia.

With GEIS support, NAMRU-2 upgraded equipment to conduct on-site genetic sequencing to detect potential pandemic mutations and increase the volume of specimens that can be tested with real-time PCR. The multiplex assay system, Luminex xMAP, is now fully deployed in Laos and has assisted the National Center for Laboratory and Epidemiology in its surveillance for influenza-like illness, including highly pathogenic avian influenza. The Luminex system was used during investigation of two human cases of H5N1 influenza in Laos. Three collaborating hospitals have been added to the influenza-like illness study in Laos: Champassack, Luangnamtha, and Savannakhet. These provincial hospitals will comprise a network of collaborating centers across the country from north to south. The Luminex system is a promising new diagnostic platform for respiratory disease at MHS sites such as NHRC and military medical centers. GEIS funding for the NAMRU-2 work on the Luminex respiratory panel is helping purchase and support this cutting-edge technology for overall Luminex deployment that will bring a level of diagnostic standardization to laboratory medicine for the entire US military.

NAMRU-2 has been extensively involved in Cambodia with the establishment of a new laboratory in Phnom Penh. NAMRU-2 has collaborated extensively with the Cambodian ministry of health and two major referral hospitals (Chey Chummas and Oudoung), and several catchment area clinics have joined as collaborators. For the upcoming year, NAMRU-2 intends to expand sentinel site surveillance to two additional referral hospitals and embedded clinics. The laboratory is averaging 20 specimens per day. This includes throat and nasal swabs for influenza-like illness, stool/rectal swabs for diarrhea, and blood for blood culture on all participates. Pathogens have been identified through many assays: serology, direct via nucleic acid assays, and bacterial culture.

In addition to surveillance studies in humans during FY07, NAMRU-2 implemented a study to examine the seroincidence of H5N1 in humans and the seroprevalence of H5N1 in animals. This study is innovative in that no other epidemiological prospective study of H5N1 influenza transmission among adults exposed to poultry residing in H5N1 endemic areas in Asia has ever been conducted. Recently, international leaders in public health have called for such epidemiological studies to be performed before either nationwide vaccination or chemoprophylaxis is undertaken.

Civilian and military operations in Southeast Asia continue to benefit from GEIS-supported NAMRU-2 surveillance projects for malaria and diarrheal diseases. Malaria and diarrheal diseases widely affect civilian populations and are leading infectious disease threats to the US military. NAMRU-2 began using established WHO protocols for measuring the in vivo efficacy of standard antimalarial drugs for infections caused by *Plasmodium falciparum* and

P. vivax in Cambodia and Indonesia. In Kampot Province in Cambodia, NAMRU-2 continued in vivo drug efficacy studies of the current first-line regimens for *P. falciparum* and *P. vivax* malaria, mefloquine-artesunate and chloroquine, using a standard WHO protocol.

In Indonesia, NAMRU-2 conducted preliminary epidemiological characterization of sites for future in vivo efficacy trials on the islands of Sumba and New Guinea. In Sumba, two large-scale cluster-sampling malaria prevalence studies were completed that estimated malaria prevalence in the West Sumba District of East Nusa Tenggara Province (population ~380,000) in Indonesia. NAMRU-2 conducted separate surveys in the rainy season and the dry season. As part of this survey ~9,000 samples were collected at 45 sites that will allow the measurement of the prevalence of known malaria drug resistance markers across West Sumba. These results will identify localities where emerging drug resistance may be a problem and where in vivo efficacy studies would be useful. In the third quarter preliminary malaria mass blood surveys were conducted near Jayapura, in Irian Jaya on New Guinea, to identify sites for further in vivo efficacy studies (Figure 21).

In addition to on-site field studies NAMRU-2 also began using mathematical modeling of competition between drug-sensitive and drug-resistant malaria under different treatment regimens and transmission intensities to identify parasitological and epidemiological factors that favor either the maintenance of a stable equilibrium between resistant and sensitive strains or the spreading to a fixation of resistance. NAMRU-2 researchers will develop models making different assumptions about the relative fitness of sensitive and resistant strains in the presence or absence of drug. Models will then be correlated with secular trends of drug resistance on published data from Africa and Southeast Asia. The fitted models will be used to determine which parameters are most important for determining rapid spread of resistance and will attempt to identify the corresponding epidemiological factors that predict the rapid spread of resistance.

Across Indonesia, NAMRU-2 characterizes diarrhea etiologies among children seeking healthcare at either the clinic or hospital level. The surveillance of enteropathogens (bacterial, viral, and parasitic), antimicrobial resistance among bacterial isolates, and changes in antimicrobial resistance over time stratified by geographic region remains important for the government of Indonesia. This information is used, in conjunction with that of other surveillance systems, to set policy on pediatric diarrheal disease.

The major bacterial pathogens recovered from NAMRU-2 diarrheal etiology surveillance are *Shigella* sp., *Campylobacter* sp., *Salmonella* sp., *Aeromonas* sp., *Plesiomonas* sp., *Vibrio* sp., pathogenic *Escherichia coli*, and a low number of miscellaneous bacterial organisms. Of note regarding antimicrobial resistance among bacteria has been the discovery of high-level fluoroquinolone resistance among *C. jejuni*, with nearly 80% demonstrating this resistance phenotype. The recovery of *V. cholera* O1 and O139 has been alarming, although no detectable outbreak(s) have been identified; sporadic cases across the multiple sites have been recovered. The antimicrobial resistance patterns of *V. cholera* have also shown increasing resistance to several antibiotics that are used as primary and secondary treatments.

A highlight of the diarrheal etiology surveillance has been the discovery of a high prevalence of rotavirus infection among pediatric samples (~60%). Rotavirus among children is not surprising of itself, but this finding may help the government of Indonesia and the ministry of health develop Indonesia's vaccination strategy. This report is the first to describe the genotype distribution of rotavirus and the identification of G9 in Indonesia. The relevance of this discovery is directly related to the recently licensed rotavirus vaccine formulations that do not include the G9 genotype, which brings the efficacy of these vaccines into question for use among Indonesian children.

A second notable achievement of the diarrheal etiology surveillance was the recovery of viable human influenza (H1N1 and H3N2) virus among children with diarrhea and respiratory symptoms. In an area of significant H5N1 activity among poultry and humans, this study has shown that human and avian influenza may be transmitted via the oral/respiratory or fecal route. That influenza among poultry is an enteric-associated infection is well established. Therefore, highly pathogenic avian influenza may be associated with diarrhea disease among infected humans. This information adds value to the understanding of the vaccine-preventable diarrheal illness.

In collaboration with GEIS, NAMRU-2 fully implemented the Early Warning Outbreak Recognition system (EWORS) in Laos. EWORS is an innovative syndromic surveillance system for early detection of disease outbreaks that was developed and successfully implemented in Indonesia with partial GEIS funding and in collaboration with the CDC. In Indonesia this system has successfully transitioned to the ministry of health and continues to provide valuable information as a tool to respond to disease outbreaks. In Laos the system is located at hospitals throughout the country with information being directed to the Center for Laboratory and Epidemiology

where it is analyzed and then disseminated back to the participating hospitals. Early results indicate that this system successfully correlated with the results of diagnostic testing during recent influenza-like illness outbreaks in Indonesia.

In continued support of the GEIS pillars of cooperation, capacity building, and integration, NAMRU-2 shared its results, resources, and expertise with collaborators from regional ministries of health and with other branches of the US military. Conferences and publications along with close information sharing with GEIS mean that data are shared with the scientific community and the DoD.

The GEIS-supported work of NAMRU-2 continues to contribute to the understanding of disease threats in this region. This knowledge furthers science, helps regional government health agencies, and supports US government and military entities, notably PACOM. GEIS has facilitated the rapid identification of human influenza A H5N1 infection along with numerous other infectious diseases of importance to the US military. Innovative studies have increased the understanding of emerging and reemerging pathogens, their vectors, and their environment. The use of dried blood spot collection of clinical samples has the potential to facilitate large-scale screening efforts by simplifying shipping of specimens and allowing centralization of laboratory activities in an efficient and cost-effective manner. Implementation of dried blood spot collection procedures will provide increased surveillance coverage in areas of the world that are hard to reach.

Naval Medical Research Unit No. 3 (Cairo, Egypt)

Core GEIS FY07 funding at Naval Medical Research Unit No. 3 (NAMRU-3) was applied to 13 projects, most of which were continued from the previous year. Additional supplemental funding for pandemic and avian influenza was aimed at sustaining surveillance and response capacities built in FY06 and increasing geographic coverage. The collective results of the GEIS projects (Figure 24) led to the development and/or strengthening of regional capacities to accurately detect and define emerging/reemerging diseases, epidemiological trends, and sensitivity/resistance profiles as they may affect operational forces in CENTCOM and EUCOM areas of responsibility.

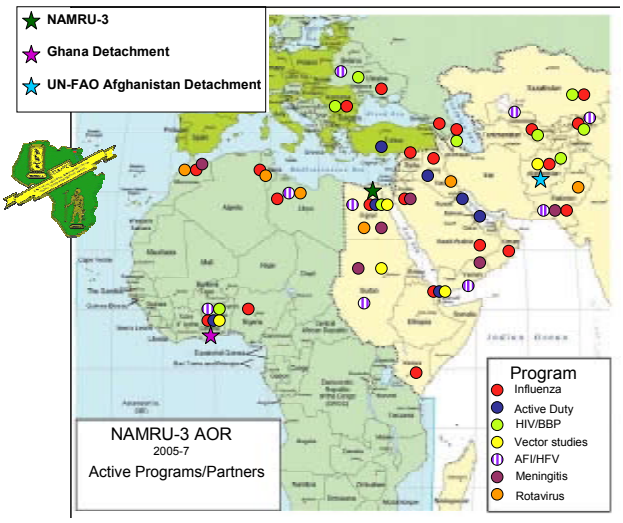


Figure 24. GEIS-funded programs at NAMRU-3 within CENTCOM, AFRICOM, and EUCOM areas of responsibility (AOR). HIV/BBP, human immunodeficiency virus/ blood-borne pathogens; AFI/HFV, acute febrile illness/hemorrhagic fever virus.

Surveillance for influenza and other respiratory viruses in the Middle East, Africa, and eastern Europe is a primary focus of the NAMRU-3 Viral and Zoonotic Disease research program. In FY07, NAMRU-3 continued its support of the WHO regional influenza surveillance network in the Middle East, eastern Europe, the central Asian republics, and Africa. The primary objective is to obtain representative samples of circulating influenza strains by targeting regions underrepresented in the global influenza surveillance network. Secondary objectives include capacity building in targeted regions through provision of training, equipment, and supplies; support for collecting specimens from patients with influenza-like illness; outbreak support; and reference laboratory support to WHO, DoD, and respective ministries of health. All influenza isolates collected were shipped to the CDC for inclusion in the seasonal vaccine decision-making process. GEIS and NAMRU-3 trained 41 scientists from 11 countries in the laboratory diagnosis of influenza. These efforts directly translate into a more robust and comprehensive regional influenza surveillance network for GEIS.

NAMRU-3 continues to support collaborating laboratories in Afghanistan, Jordan, Ghana, and Libya that were established by FY06 GEIS funding. This support is critical as each establishes first-time national influenza centers. NAMRU-3 also assists other regional partners by providing reagents, supplies, and shipping containers to facilitate specimen collection and transport to the NAMRU-3 reference laboratory.

As the WHO regional influenza reference laboratory and WHO reference laboratory for diagnosis of influenza A/

H5 infection, NAMRU-3 continues to proactively support all countries in the region where troops are currently deployed (e.g., provide reagents, consumables, personal protective equipment, and shipping containers for specimen collection and movement). From Egypt, 141 human specimens were received for influenza A/H5N1 reference testing, and 26 specimens tested positive for H5N1. H5 reference testing was performed on 459 animal specimens, with 92 positive for H5N1 from Afghanistan, Egypt, and Ghana.

Monitoring the emergence of avian influenza strains, especially highly pathogenic avian influenza in bird populations, is essential for the prevention of pandemic influenza. Egypt is a waypoint for migratory birds transiting from Europe and Asia to Africa. With GEIS support, NAMRU-3 performs surveillance for influenza in migratory birds through collaborations with Ukraine, Egypt, and Kenya. For the 2006–2007 season, NAMRU-3 collected 4,404 specimens from migratory birds from these three countries, of which 243 (5.5%) were positive for influenza A. Through this project, many strains were isolated, including H1N1, H5N2, H6N2, H7N1, H7N7, H9N2, H10N1, H10N7, and H11. These data support the need for ongoing surveillance to define other reservoir species and their individual migratory patterns.

Influenza and other respiratory diseases are not the only subjects of GEIS work at NAMRU-3. Hemorrhagic fever viruses, arboviruses, and tick-borne pathogens produce serious clinical disease and epidemic outbreaks and are considered potential bioterrorism agents. NAMRU-3 conducted surveillance for these agents in Kyrgyzstan, Yemen, Sudan, Ukraine, and Uzbekistan. This surveillance provided data on the presence of these diseases in civilian populations and on the geographical distribution and ecology of the diseases, thereby allowing effective control programs to be developed by the respective ministries of health. An additional benefit was the ability to test several newly designed molecular-based diagnostic tests for viral hemorrhagic fever viruses, arthropod-borne encephalitis viruses, and tick-borne diseases in a relevant clinical setting. The field testing of diagnostic assays for these viral pathogens is of great importance to force health protection and is a unique function performed by NAMRU-3 with GEIS support.

During FY07, NAMRU-3 continued its mission to provide epidemiological/laboratory support, training, and diagnostic capacity building in the Middle East and Georgia (Figure 25). As part of its regional strategy, more than 15 training workshops on epidemiology and laboratory procedures were conducted for bacterial pneumonia, hospital-acquired infections, acute febrile illness, and bacterial meningitis surveillance. More than 75 scientists from four countries, both on and off-site, attended. Training topics included good laboratory practices, quality control/quality assurance, diagnostics to determine bacterial etiologies, procedures related to surveillance activities, and molecular characterization of selected human pathogens. Minor equipment and supplies were procured for regional collaborators at more than 30 hospitals in support of GEIS surveillance. These activities have substantially increased the capacity of regional partners in the CENTCOM, EUCOM, and AFRICOM areas of responsibility to determine disease burden of certain illnesses and to confirm diseases and outbreaks using laboratory-based data.

Figure 25. Laboratory capacity building in Afghanistan supported by NAMRU-3 and GEIS. *Top,* conventional AB 7300 and RAPID PCR machines; *bottom*, technician preparing sample for PCR testing.

In support of Operation Iraqi Freedom, NAMRU-3 provided diagnostic and molecular characterization during an outbreak of cholera that began in Iraq in August 2007.

Samples were collected from civilian personnel in Iraq. Participation was crucial in confirming serotype distribution and relatedness among isolates and in elucidating the antimicrobial resistance patterns. Critical supplies and reagents were provided to the Central Public Health Laboratory in Baghdad so that laboratory services could continue in the affected regions. Bacterial isolates were analyzed by pulsed-field gel electrophoresis molecular genotyping and DNA sequence analysis of species-specific genes and multilocus sequence typing. These analyses demonstrated that the cause of the outbreak was primarily a single strain of type 01 Inaba El Tor. Further collaboration is ongoing with scientists at the Naval Research Laboratory (Washington, DC) and the CDC to better understand the epidemiology of this outbreak.

In continued support of public health in Egypt, GEIS established a nosocomial surveillance system for bloodstream infections at high-risk wards in three university hospitals and completed an acute febrile illness study. The high infection rates and the high antimicrobial resistance pattern identified in these studies demonstrate a need for continuous healthcare infection surveillance systems in Egyptian hospitals. High levels of antimicrobial resistance emphasize the need to develop effective hospital policies regarding antibiotic use. High infection rates in hospitals with no infection control programs stress the importance of expanding infection control programs in all Egyptian hospitals.

NAMRU-3 formed a military infectious disease and operational health surveillance network from existing field sites in Turkey, Qatar, and Djibouti at which surveillance for infectious diseases and other health problems is conducted among deployed US military personnel in northern Africa, the Middle East, and throughout CENTCOM. The creation of this network reflects a new strategy for NAMRU-3 to maximize its field assets to respond to emerging, reemerging, and endemic diseases that are present in theaters of operation and in areas that are strategically important to the United States and that threaten military personnel. NAMRU-3 will likely sustain, if not augment, resources and personnel for these surveillance activities for the foreseeable future. The NAMRU-3 surveillance network standardizes, coordinates, and centralizes all activities and provides coordination among DoD collaborators at various military medical treatment facilities.

The surveillance activities performed within the network include case surveillance study, serosurvey study, and a self-completed deployment survey. At the time of the creation of the network, NAMRU-3 was conducting GEIS surveillance at the following sites in direct support of the combatant commands:

- Camp As Sayliyah, Qatar (CENTCOM Forward Headquarters);
- Marine Corps Air Station Al Asad, Iraq;
- Camp Arifjan, Kuwait;
- Incirlik Air Base, Turkey;
- Multinational Force & Observers, Egypt (two camps on the Sinai Peninsula);
- Rhein-Main Air Base, Germany;
- Exercise Bright Star, Egypt.

GEIS continued to support NAMRU-3 to serve, in collaboration with the WHO, as the regional reference laboratory for rotavirus surveillance in the Eastern Mediterranean Region. In this capacity, NAMRU-3 participated in four training missions during 2007, including the first regional rotavirus genotyping training held for Egypt, Iran, Libya, Morocco, Pakistan, and Tunisia in February at NAMRU-3 and a training workshop for the Iraq rotavirus surveillance network held in Amman, Jordan. Activities planned for the upcoming year were discussed at the rotavirus regional laboratory directors meeting held outside Stockholm in June and include the following: development of a multilocus sequence typing method for rotavirus isolates, comparative analysis of enzyme immunoassay to latex agglutination and immunochromatographic methods for the detection of rotavirus, and expansion of the network to additional countries, including Afghanistan, Djibouti, and Lebanon. Partnerships established through GEIS between host nation scientists and NAMRU-3 showcase the international role of Navy medicine in establishing strong research programs in the region and serve as a platform for future collaborations with those scientists.

NAMRU-3 outbreak responses, capacity building, and surveillance have resulted in a better knowledge of globally important pathogens, and host nationals have been trained to provide a first response to an array of microbial problems. This work, made possible through GEIS, improves understanding of disease and increases the capacity to limit the severity of future outbreaks.

Naval Medical Research Center Detachment (Lima, Peru)

As a crucial DoD-GEIS asset in Latin America, the Naval Medical Research Center Detachment (NMRCD) conducts infectious disease surveillance and response in nearly all countries of South America and several in Central America. Activities are coordinated with SOUTHCOM and relevant US government agencies such as US embassies and USAID.

Two cornerstone capabilities at NMRCD that are provided by GEIS are outbreak detection and response. These involve training, microbial agent identification, and communicable disease control and prevention. Although its response efforts have been mainly in Peru, NMRCD responded to a large dengue outbreak in Paraguay.

NMRCD and GEIS have developed a broad array of projects that provide surveillance data for the most militarily relevant infectious diseases in Latin America. Surveillance extended into 14 countries in Latin America, with the notable exceptions of Brazil and French Guiana, and some countries in Central America that have traditionally been covered by CHPPM-West.

The addition of pandemic influenza funding has allowed the rapid expansion of a network of laboratory-based strain surveillance for influenza that is unparalleled in Latin America. This effort has strengthened regional biosecurity and has built significant capacity within the countries where this network is established. NMRCD has also undertaken several epidemiologically based influenza projects that have added to the knowledge about influenza patterns in the tropics.

Alignments

DoD-GEIS and NMRCD continue to have close relationships with SOUTHCOM. NMRCD actively pursues coordination with the Command Surgeon and follows guidance from that office concerning high priority countries. Colombia continues to be the country of highest interest for the SOUTHCOM. As soon as an agreement is signed between the US Navy Bureau of Medicine and the Colombian government, NMRCD will start the following projects in Colombia:

- Electronic surveillance for the Colombian military, which has been approved;
- HIV and sexually transmitted diseases surveillance at several sites;
- Influenza surveillance expansion;
- Parasitic infections monitoring, primarily malaria and leishmaniasis.

NMRCD is planning to expand surveillance efforts in Ecuador, Bolivia, Paraguay, and Uruguay. Although a formal biodefense program does not exist, NMRCD has continued to assist the Peruvian ministry of health with identification and characterization of dangerous, naturally occurring pathogens. This project has been leveraged through funding from the Department of Homeland Security and the Naval Medical Research Center. Specimens of cutaneous anthrax, bubonic plague, brucellosis, and Venezuelan equine encephalitis have been collected, characterized locally, and sent to the United States for further advanced testing.

GEIS and NMRCD have continued to build partnerships with many US government agencies and entities to help create a network of complementary efforts rather than competing or duplicating efforts. NMRCD works intimately with GEIS in the region on the following initiatives:

- Drafting an agreement with the Pan American Health Organization that will serve to formalize the relationship and improve coordination;
- Developing an electronic disease surveillance hub for Latin America in Lima;
- Presenting work on Alerta DISAMAR and EWORS in a syndromic surveillance conference in Thailand sponsored by GEIS.

NMRCD continues to support the annual humanitarian missions of Operation New Horizons (United States Army, Southern Command) in the form of diagnostic laboratory support and assistance with outbreak management.

GEIS funded several training programs at NMRCD for US and Peruvian military personnel and sponsored the formal partnership with USUHS for the military tropical medicine course. In this course, US military medical students and physicians in training at USUHS learn tropical medicine that will prepare them for service overseas.

In the nonmilitary setting, NMRCD continues to coordinate efforts with the CDC Global Disease Detection Laboratory in Guatemala City, Guatemala, particularly for

training in outbreak detection and response and influenza surveillance. Two NMRCD staffmembers were sent to Guatemala in November 2006 to participate as faculty in an avian influenza outbreak response conference, which was offered to all the countries in Central America. USAID has seen the value in the NMRCD training platform, which has resulted in collaboration to replicate this outbreak response training throughout the region. Collaborations with the Pan American Health Organization and several ministries of health have been strengthened by the training in outbreak management. NMRCD has continued to work with scientists and epidemiologists from the Peruvian ministry of health, Navy, and Army to build collaborations and respond to outbreaks of infectious disease. NMRCD has leveraged the talents and projects of several local and US academicians to enhance surveillance on emerging infectious diseases.

Overview of Projects

The GEIS effort at NMRCD represents a coordinated effort to provide comprehensive emerging infectious disease surveillance for South America. Each program at NMRCD has GEIS projects, including virology, bacteriology, parasitology, entomology, and emerging infections. Assets from each program are leveraged to assure flexibility, efficiency, and a maximum return for investment of time, personnel, and other resources. For example, the same physician is used to recruit patients for febrile illness surveillance, influenza surveillance, and bacterial enteric pathogen surveillance. A central supply system and common shipping of samples and reagents have created an efficient and logical system that optimizes performance and return. Additionally, the upgrade of the NMRCD BSL-2 laboratory to BSL-3, completed this year with GEIS funding, will enhance the capability of NMRCD to identify highly pathogenic organisms in the SOUTHCOM area of responsibility.

Infectious disease surveillance has markedly expanded in the area of influenza, currently the greatest emerging pandemic threat. NMRCD has conducted respiratory disease surveillance since 2000, and in FY07 has vastly increased the capacity for laboratory detection and the scope of collection areas. In addition to standard respiratory viral culture and identification by PCR techniques, NMRCD has expanded sequencing capability through the addition of another automatic sequencer and personnel trained in this field. More than 1,600 respiratory samples were submitted, with an isolation rate from respiratory samples (yield) of over 36%. Isolates are now collected from 57 sites in 10 countries throughout South and Central America. Most sites are in Peru ($n = 25$), and the others are in Argentina, Bolivia, Ecuador, El Salvador, Honduras, Nicaragua, Paraguay, and Venezuela. These samples are characterized in Lima by their hemagglutinin subtype, and a portion is sequenced and novel results entered into GenBank. Through collaboration with AFIOH and the CDC, potential candidate vaccine strains are included in the annual vaccine development process.

Febrile illness surveillance for novel pathogens continued and leveraged the increased number of sites for respiratory disease surveillance. NMRCD continues to isolate novel viruses and has the most comprehensive collection of dengue isolates in South America. Dengue 3 was the predominant isolate this year, but dengue 2 seems to be reemerging, which may indicate the possibility of an outbreak of dengue hemorrhagic fever. In addition to dengue, which was the most frequent isolate, Venezuelan equine encephalomyelitis, Caraparu, Tacaribe, and rabies viruses were identified through febrile illness surveillance. The febrile illness surveillance collected more than 2,200 specimens in FY07, with an isolation rate of 27%. These were collected from Ecuador, Peru and Bolivia, and surveillance will be expanded by further leveraging the respiratory illness surveillance sites. In addition to the current battery of viral testing, new techniques for identification of rickettsia and leptospirosis were pioneered and have been implemented.

The bacteriology program at NMRCD has continued to work primarily on enteric pathogen resistance patterns and conducts surveillance for brucellosis and sexually transmitted infections. This year, a continued trend of increasing resistance among many of the enteric bacteria, especially *Campylobacter* species, was found. Concerning fluoroquinolones, over 90% of *Campylobacter* isolates are now resistant to ciprofloxacin, rivaling and surpassing the same trends found in other regions of the world such as Southeast Asia. Luckily, the rates of resistance among isolates of *Shigella* and *Salmonella* to azithromycin remain low. Surveillance continues among Peruvian military populations and among travelers and US embassy personnel. For sexually transmitted infections, molecular technology is used to track fluoroquinolone resistance among *Neisseria gonorrhea* and *Treponema pallidum*. A novel method to isolate *Brucella* more rapidly has been optimized, and this accomplishment has resulted in a publication. NMRCD is working with several local epidemiology groups to transfer this technology to increase detection of this dangerous pathogen among local hospitals. Naturally occurring isolates of dangerous agents such as *Bacillus anthracis and Yersinia pestis* continue to be collected and characterized and used to build the specimen repository.

The parasitology program has been successful in studying antimalarial resistance mechanisms via molecular methods. Pioneered at NMRCD, these methods have been

exported to India, Brazil, WRAIR, and USAMRU-K. Active and passive surveillance for *Plasmodium falciparum* and *P. vivax* drug resistance is being conducted via molecular markers and multilocus sequencing analysis to identify polymorphisms and populations of parasites that carry signatures indicative of resistance. As requested by SOUTHCOM, rates of *Leishmania* in Colombia are being studied. This is a significant issue for US and Colombian government forces involved in the war on narcotics. Molecular methods to differentiate between New World *Leishmania* species have been developed and have been exported to Colombia and WRAIR. NMRCD continues to study *Cyclospora cayetanensis*, specifically its effect on Peruvian military recruits and risk factors among expatriates and others for acquisition of this gastroenteric pathogen.

Among the most critical capacities of NMRCD is the ongoing ability to conduct comprehensive outbreak investigations. An outbreak response team has been developed that includes a CDC staff member, laboratory technicians, and a Peruvian physician. Formal and informal advice and laboratory support are provided as requested, and full epidemiological teams have been deployed to respond to requests for assistance. Outbreak responses have often involved the resources of multiple departments and significant collaborations with the ministry of health and regional health directorates. NMRCD has provided any or all of the following: epidemiological consultation, fieldwork, laboratory assistance and training, supplies and media, and relevant scientific expertise.

FY07 outbreak responses included field deployments to Paraguay to respond to a large dengue outbreak and, within Peru, 25 cases of fatal rabies, five influenza outbreaks among Peruvian military populations, a Venezuelan equine encephalomyelitis outbreak in Iquitos, and widespread mumps outbreaks throughout Lima and other Peruvian cities. NMRCD also responded to an outbreak of diarrhea at the US embassy among the kitchen staff and Department of State personnel as well as numerous outbreaks of diarrhea of various etiologies throughout Peru. An example of an epidemic curve from one of the respiratory illness outbreaks is shown in Figure 26.

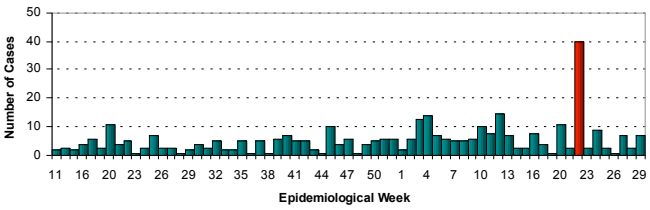


Figure 26. Cases of acute respiratory illness on San Lorenzo Island, 2006–2007, showing influenza outbreak in May 2007.

Contingency operations were important this year, with the largest earthquake in 30 years (magnitude 8.0) striking the central coast of Peru in August. Through DoD-GEIS funding and NMRCD flexibility, field laboratories were set up within 48 hours of the disaster, and deployed teams of epidemiologists, scientists, laboratory technicians, and physicians were deployed to the affected region for 1 month after the earthquake. NMRCD assisted the Peruvian CDC teams with surveillance for infectious diseases, humanitarian assistance, needs assessments, and laboratory diagnostics. This cooperation likely led to the much improved relationships with the ministry of health agencies that were evident after the earthquake.

Formal classroom training in outbreak investigation continues to be a GEIS priority at NMRCD. In FY07, public health officials were trained in Peru, Argentina, Chile, and seven Central American countries. NMRCD has collaborated with the CDC laboratory in Guatemala to teach outbreak response as it relates to pandemic influenza in Guatemala and Panama and has assisted SOUTHCOM in pandemic influenza conferences in Panama and on the island of Curacao. Many NMRCD scientists and senior laboratory technicians teach these courses. NMRCD continues to collaborate with the Pan American Health Organization and the ministries of health to share costs for these courses and ask them to provide instructors and tutors. The methodology and experience of teaching this course to more than 1,300 Latin American public health officials were recently published and have resulted in many requests for further training, most recently an invitation to Manaus, Brazil. This is a significant feat, because NMRCD has not been able to work in Brazil for over a decade. NMRCD continued to use video- and teleconference capabilities this year, which allowed distance learning within and outside Peru, including clinical tropical medicine and epidemiology training opportunities. NMRCD supports other courses such as biostatistics, bioethics, and, at the Naval Medical Educational Training Command, military tropical medicine.

Electronic surveillance programs have been extremely successful at NMRCD. GEIS projects at NMRCD have been recognized by the Institute of Medicine and the International Syndromic Surveillance Conference as novel and noteworthy. These projects address all the GEIS goals and include Alerta DISAMAR for transmissible disease and outbreak notification and EWORS for timely outbreak detection. Alerta DISAMAR has been consolidated within the Army and was optimized in the Navy. New disease nonbattle injury data have been added to Alerta DISAMAR, which has given the Peruvian military its first estimates of the burden of disease with respect to this category. Alerta DISAMAR continues to

NMRCD Provides Swift Initial Response after Earthquake

On 15 August 2007, a magnitude 8.0 earthquake struck near Pisco, Peru, devastating this town of 116,000 people and leaving more than 500 people dead and tens of thousands displaced. The earthquake was the worst humanitarian crisis in Peru in 30 years.

With the use of DoD-GEIS contingency funds, NMRCD deployed teams of epidemiologists to the area and set up a field laboratory to provide diagnostic aid to the Peruvian ministry of health. Within 12 hours of the earthquake, NMRCD provided the US embassy with the first reliable on-the-scene needs assessment, allowing proper allocation and distribution of relief supplies and personnel by the embassy. The NMRCD epidemiological teams assisted the Peruvian ministry of health in creating a simple yet effective infectious disease surveillance system and helped in the continual public health evaluation of the many displaced persons camps throughout the region. NMRCD personnel were colocated with Peruvian ministry of health personnel for more than 4 weeks after the disaster and contributed to local laboratory capacity through the donation of basic equipment, supplies, and laboratory training.

Aftermath of earthquake in Pisco, Peru. *Top*, water bladder (*foreground*) and displaced persons camp. *Bottom*, NMRCS epidemiology team at site of destroyed hospital.

detect numerous outbreaks, the most significant of which were several influenza and mumps outbreaks. These efforts have led to timely awareness within the Peruvian Navy of disease outbreaks and enhanced cooperation between its health services and NMRCD research support. Use of Alerta DISAMAR has resulted in the training of more than 1,000 Peruvian military public health and medical personnel in epidemiology, a significant achievement in a developing country. Leveraging GEIS support and SOUTHCOM support, NMRCD has undertaken to spread Alerta DISAMAR to five South American countries: Colombia, Ecuador, Bolivia, Paraguay, and Uruguay. This ambitious expansion will be implemented per SOUTHCOM priorities and will potentially create the only regional surveillance network that utilizes the same system. All components of the system are developed, and NMRCD is only waiting for the international agreements to be signed.

EWORS continues to function in Peru, with two sites continuing to report from Tumbes and seven sites from Lima. NMRCD has partnered with NAMRU-2 and the Johns Hopkins University Applied Physics Laboratory to optimize the automated analysis of this system, and a self-analysis of the system has been conducted. The daily operations have been turned over to the Peruvian ministry of health, which has chosen to incorporate EWORS into its national reporting system in the next 2 years.

Armed Forces Research Institute of Medical Sciences (Bangkok, Thailand)

GEIS work continued to expand at the Armed Forces Research Institute of Medical Sciences (AFRIMS) in terms of programs and regions covered. Although much of this growth was driven by the congressional supplemental funding for pandemic and avian influenza, GEIS funds were also used to support antimalarial drug resistance surveillance, enteric illness etiology and sensitivity determination, encephalitic and febrile illness characterization, institutional laboratory and human capacity building, and international collaboration building.

Surveillance

Influenza

The AFRIMS influenza surveillance program provides rapid diagnostic kits and specimen collection and transportation capabilities to practitioners seeing patients within the AFRIMS-GEIS surveillance network. In Nepal, the Philippines, and Kamphaeng Phet, Thailand, AFRIMS has developed laboratories that can perform

PCR diagnostics. Confirmatory testing and further characterization are accomplished at the AFRIMS central respiratory laboratory facilities in Bangkok. All samples are transported to AFIOH, where further molecular characterization is undertaken, and a select number are sent to the WHO Collaborating Centre at the CDC headquarters. This system provides on-site, clinically relevant information, in-country diagnostic testing for host nation action, confirmatory testing within the region, and inclusion in the DoD Global Influenza Surveillance System and WHO FluNet programs.

Influenza surveillance at AFRIMS is active throughout Nepal, in the Philippines, in Kamphaeng Phet, and at six Royal Thai Army hospitals with significant cross-border traffic. These Royal Thai Army sites are using a mass tag diagnostic system new to AFRIMS this year; this technology, developed at Columbia University, allows testing for 30 respiratory pathogens with one sample. In Nepal, the Walter Reed/AFRIMS Research Unit-Nepal (WARUN) continues to serve as the reference laboratory for the National Public Health Laboratory and runs sentinel influenza surveillance sites in the Kathmandu Valley. AFRIMS performs surveillance at US embassies in Bangladesh, Burma, India, Laos, Malaysia, Mongolia, Nepal, Pakistan, Philippines, Sri Lanka, Thailand, and Vietnam. Collectively in FY07, the GEIS/AFRIMS influenza surveillance projects yielded more than 1,000 respiratory samples from more than 20 sites in seven countries. This effort represents more than double the number of samples collected by AFRIMS last year and enhanced awareness of the prevalence of influenza globally. Virus isolation results are shown in Figure 27.

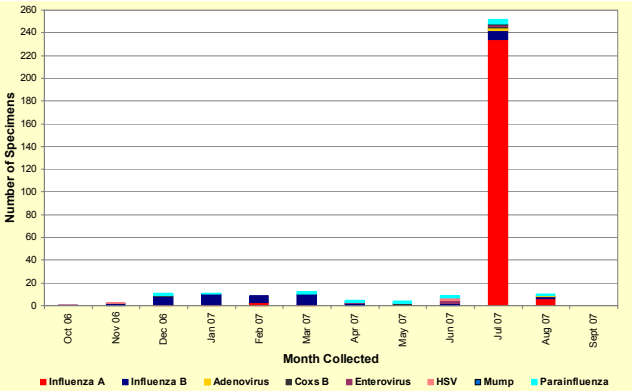


Figure 27. Number and types of viruses found in human specimens collected during GEIS influenza surveillance at AFRIMS, 2006–2007. As happened last year, a large outbreak of influenza A occurred in July in Nepal.

Antimalarial Drug Resistance

The AFRIMS Department of Immunology operates an antimalarial drug resistance surveillance program that gives decision-makers timely information on resistance to currently used antimalarials. In one project the presence of antimalarial resistance markers to artesunate and mefloquine in *Plasmodium falciparum* infections in Bangladesh is being determined.

This year the troubling reports of artemisinin failures along the Thai-Cambodian border continued, and the comprehensive surveillance of artemisinin efficacy there by GEIS/AFRIMS is ongoing. A study in Battambang Province in western Cambodia demonstrated a 28-day cure rate for artesunate of 93.3% vs. 100% for quinine-tetracycline. Two patients had parasites resistant to artemisinin, a finding based on clinical response, parasite clearance time, and in vitro drug sensitivity and pharmacokinetic data. Although the number of patients with artemisinin resistance is fortunately low, the presence of resistant parasites demonstrates the value of GEIS surveillance and the need for follow-on aggressive studies of the rate of increase, geographical extent, and potential genetic markers so that this emerging problem can be contained.

Enterics

The Department of Enterics performs surveillance for the causes of diarrheal illness and antimicrobial susceptibility patterns in Asia. In the past year, AFRIMS collected more than 3,400 stool samples from ill patients in Phnom Penh, at two sites in the Maldives, at three sites in Nepal, and in five regions in Thailand. Samples from an equal number of healthy controls were also collected. *Campylobacter*, *Salmonella*, *Shigella*, and enterotoxigenic *Escherichia coli* (ETEC) were identified from cases in significantly higher rates than controls, although pathogens are frequently isolated from asymptomatic controls. In the Maldives and Nepal, *Vibrio cholera* is an important pathogen, as is *Aeromonas* in the Maldives and rotavirus in Nepal. Most *Campylobacter* isolates are resistant to ciprofloxacin in Thailand and Nepal but are less resistant in Cambodia. Most ETEC and *Shigella* isolates are resistant to trimethoprim-sulfamethoxazole in Thailand and Cambodia, but ETEC is still susceptible in Nepal. Resistance to ampicillin was surprisingly low in Thailand and Nepal.

Febrile and Encephalitic Illnesses

The Department of Virology completed laboratory testing of 260 cases of dengue-like syndrome in Manila; 232 (89%) were positive for dengue with all four serotypes circulating, and the majority (74%) was dengue 3. Acute secondary dengue infection accounted for 76% of cases, and dengue hemorrhagic fever was the predominant clinical diagnosis (47%). Surveillance will expand to Cebu, Philippines, next year.

AFRIMS and Royal Thai Army Continue Influenza Surveillance along Thai Border

Royal Thai Army surveillance network. *Blue stars*, border sites with Royal Thai Army facilities; *yellow circles*, sites at which surveillance is conducted.

At the request of the Royal Thai Army, AFRIMS and GEIS are providing ongoing assistance in enhancing the Royal Thai Army influenza surveillance and response system that was established through AFRIMS, with GEIS support, beginning in 2002. Through this network of surveillance sites, the seasonal and regional etiology of respiratory disease can be determined; the outbreak response capability is enhanced; and clinical samples can be safely and appropriately collected.

The system is based in 34 Royal Thai Army hospitals, 10 of which are in rural areas with high traffic near the Thai border with Burma, Malaysia, Laos, and Cambodia. The hospitals serve the military and the surrounding local civilian populations and offer the opportunity to collect samples in areas where influenza strains are emerging. Among the efficiencies of this system is that soldiers (i.e., individuals without medical experience) can collect the data, thereby providing needed medical training for military personnel. The surveillance also contributes to security against intentionally caused outbreaks, the symptoms of which may resemble those of influenza.

At six of the ten border sites, AFRIMS trained staff in good clinical practice, outbreak recognition, subject recruitment, data collection, sample processing and shipment, and use of the influenza rapid test. AFRIMS provided each site with a freezer, refrigerator, safety cabinet, and centrifuge. At all sites, adults who present with a history of fever and cough, sore throat, or runny nose are invited to participate and provide written informed consent. Respiratory samples are taken and tested on-site with a rapid test for influenza A and B. All samples are then sent to AFRIMS for real-time PCR testing for influenza A H1, H3, H5, H7, and H9 and influenza B and, if positive, for genotyping, viral isolation, and genetic characterization. AFRIMS recently acquired mass tag PCR capability that allows 30 respiratory pathogens to be tested with one sample, at an estimated cost of <25¢ per pathogen tested.

In the mass tag system, genetic material is amplified through PCR using domain-specific tagged primers. The genetic material is cleaved off the tag, leaving the final sample biologically safe and able to allow detection of the pathogen by spectrometric analysis. The respiratory mass tag panel can test for seven elements of influenza A viruses, influenza B, both genotypes of respiratory syncytial virus and human metapneumovirus, enterovirus, adenovirus, three strains of coronavirus (including the causative agent of SARS), five subtypes of human parainfluenza virus, *Chlamydia pneumoniae, Mycoplasma pneumoniae, Streptococcus pneumoniae, Legionella pneumophila, and Haemophilus influenzae.*

From March to September 2007, 216 samples were collected, and rapid tests found six influenza A and four influenza B positive. PCR for influenza of 39 of the samples revealed four positive for influenza A/H3. Testing with mass tag will commence in FY08. FY07 funding has allowed collection to begin at six sites, and expansion to 12 sites is planned for FY08.

In August 2007 the Royal Thai Army bestowed on the influenza surveillance program the honor of being an official project in the celebration of the Auspicious Occasion of His Majesty the King's 80th Birthday Anniversary.

Samples Collected through Royal Thai Army Surveillance, March–September 2007

Active study site	Mar	Apr	May	Jun	Jul	Aug	Sep	Total
Fort Mengraimaharat Hospital	13	3	4	6	0	6	25	**57**
Fort Supphasitthiprasong Hospital	0	1	5	3	13	11	19	**52**
Fort Surasinghanath Hospital	0	0	3	8	3	7	7	**28**
Fort Surasi Hospital	4	1	5	1	0	8	15	**34**
Fort Khetudomsak Hospital	1	5	0	7	8	6	4	**31**
Fort Ingkayutthaborihan Hospital	0	1	9	1	0	1	2	**14**
Total	**18**	**11**	**26**	**26**	**24**	**39**	**72**	**216**

AFRIMS performed retrospective testing of 300 Japanese encephalitis negative sera from an outbreak of encephalitis in Nepal to determine the etiology. Cases were tested for dengue, chikungunya, malaria, brucellosis, leptospirosis, and West Nile virus. Over 50% were positive for leptospirosis, whereas dengue, chikungunya, and brucellosis were found infrequently. None were positive for malaria or West Nile virus. This study demonstrated that, contrary to previous thought, leptospirosis is a significant cause of encephalitis. The infections are probably due to high rates of water contamination, but other causes must be considered during an outbreak.

Response

For the fourth consecutive year, WARUN investigated an outbreak of influenza-like illness among political refugees from Bhutan who are living in camps in eastern Nepal. Influenza A/H1N1 was isolated in July 2007. The strain that caused this outbreak has a mutation pattern that differentiates it from the 2007–2008 vaccine strain; a similar pattern was seen between the 2006–2007 and 2007–2008 vaccine strains. Four isolates have additional mutations that are being analyzed. Results of this outbreak investigation were presented at the American Society of Tropical Medicine and Hygiene meeting in November 2007.

GEIS/AFRIMS investigated an encephalitis outbreak in Nepal and a febrile illness outbreak in Bhutan, both of which were caused by dengue virus. AFRIMS also responded to an outbreak of an unknown illness in Sri Lanka and determined that chikungunya was the cause. The first confirmation that an outbreak of diarrhea in Bharatpur, Nepal, in September 2007 was caused by *V. cholera* was made by WARUN.

Capacity Building

Significant laboratory capacity development by GEIS occurred at AFRIMS over the past year. The largest is the completion of the AFRIMS BSL-3 laboratory, which is undergoing regulatory testing and is expected to be operational in 2008. The addition of this facility will immensely expand the capabilities of researchers at AFRIMS, and elsewhere as needed, to work with highly pathogenic organisms in Thailand. AFRIMS also has real-time PCR capability in its veterinary BSL-3 facility in Bangkok, which greatly enhances the available scope of zoonotic illness surveillance programs.

WARUN continues to be the premier reference laboratory in Nepal and provides diagnostics and training to the National Public Health Laboratory. In FY07, GEIS facilitated the acquisition of ELISA, real-time PCR, and microbiology capacity at WARUN in addition to blood culture capabilities that allow improved diagnostics of febrile illness cases.

Two AFRIMS field sites, one in Kamphaeng Phet and one in Cebu, now have real-time PCR capabilities that 1) augment the reach of DoD surveillance in these critical regions for infectious disease development and 2) decrease the time to provide results to public health practitioners. This capacity is especially important in Kamphaeng Phet, because cases of avian influenza have occurred in this province.

Training is performed continuously at AFRIMS. Laboratory personnel from WARUN, Cebu, and Kamphaeng Phet have been trained in new influenza primers and protocols for real-time PCR. AFRIMS continues to serve as a training site for US military and civilian medical students, residents, and infectious disease fellows pursuing careers in tropical medicine and research.

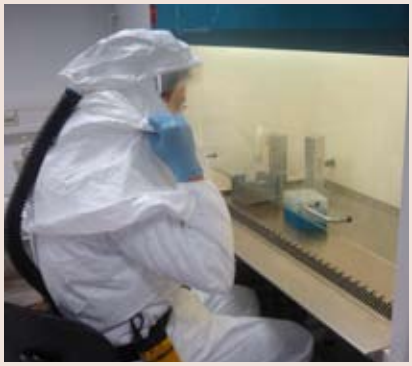
United States Army Medical Research Unit-Kenya (Nairobi, Kenya)

Measured expansion characterized GEIS work at United States Army Medical Research Unit-Kenya (USAMRU-K) in FY07. Two active protocols, human influenza sentinel surveillance and entomological surveillance for arboviruses, continued, and the number of surveillance sites and specimens collected increased.

GEIS helped lead the NAMRU-3 migratory bird avian influenza surveillance in Kenya. The research activities of enterics and malaria drug resistance surveillance were reinitiated after shifts in personnel and resources. GEIS also was integral in the massive US government interagency effort to assist the Kenyan government response to the Rift Valley fever virus epidemic of 2006–2007. In addition, the GEIS surveillance network, which provides an essential platform to conduct surveillance case finding and specimen collection in the diverse epidemiological regions of Kenya, increased from five to ten active collection sites. This expansion of activities was buttressed by the willingness and the ability of GEIS to collaborate with

Biosafety Laboratory Capacity Enhanced in Military

In the event of a viral disease pandemic, biosafety containment laboratories are critical for isolation and characterization of the causative virus. DoD and GEIS recognized that biosafety level 3 (BSL-3) infrastructure within DoD needed to be improved and in FY06 began to invest supplemental funding to create new BSL-3 facilities at Landstuhl Regional Medical Center (Germany), AFRIMS (Thailand), NHRC (San Diego), 18th MEDCOM (Korea), and NMRCD (Peru).



Technician donning power air purifying respirator in new BSL-3 laboratory at Landstuhl Regional Medical Center.

Given its duty as the primary military medical center in Europe for the wounded evacuated from Operation Iraqi Freedom and Operation Enduring Freedom, Landstuhl has been made a focal point for influenza surveillance and diagnostics for the EUCOM area of responsibility. To improve its capability in influenza, existing laboratory space at Landstuhl is being renovated and upgraded to accommodate BSL-3 work.

BSL-3 containment laboratory nearing completion at AFRIMS (Bangkok, Thailand).

Thailand has had 25 cases of H5N1 influenza disease and 17 deaths as of November 2007 and is a neighbor of Vietnam, which has had the second highest death toll (n = 46) from H5N1. To improve DoD and GEIS resources in this region, a new BSL-3 facility is under construction at AFRIMS. The ability to analyze and contain virulent strains such as H5N1 or SARS coronavirus near the geographical source rather than transporting specimens to a distant laboratory with BSL-3 capability hastens identification in an outbreak. It also facilitates improved diagnostic capability and training while streamlining the processes of public health surveillance and response to emerging infectious diseases.

NHRC is one of two CONUS-based influenza reference laboratories in DoD (AFIOH is the other) and is responsible for population-based surveillance on recruit training bases, aboard ships, and along the Mexican border. The new laboratory under construction at NHRC will have BSL-3E (enhanced) capability and will be the second DoD containment laboratory at which highly pathogenic avian influenza A strains can be grown. At present among CONUS DoD laboratories, H5N1 is grown only at USAMRIID.

BSL-3E laboratory under construction at NHRC in San Diego, March 2007.

GEIS contributed funds to allow completion of a longstanding effort to purchase and place a modular BSL-3 laboratory at 18th MEDCOM, which will finally provide much needed containment laboratory space on the Korean peninsula. At NMRCD in Lima, GEIS helped fund an upgrade and renovation of the existing BSL-2 laboratory to BSL-3.

Having BSL-3 capability at these five locations that combined span four continents will shorten the time necessary for critical specimens to be evaluated and shared with appropriate national and international laboratories and for effective control measures to be put in place. Additional laboratory capacity substantially increases the work that can be accomplished within DoD and will directly support the services and the missions of EUCOM, PACOM, and NORTHCOM, while reinforcing US government programs. By reducing the workload on existing DoD facilities, these new laboratories will also enhance laboratory capability throughout the DoD, notably surge capacity during the next pandemic.

NMRCD (Lima, Peru) laboratory upgraded from BSL-2 to BSL3 in operation.

multiple partners including other USAMRU-K investigators, other US government agencies, and Kenyan governmental entities such as the ministry of health. Capacity building was an important component of the Kenyan GEIS program and culminated in the week-long First Annual GEIS Training Conference held in July in Kilifi.

Surveillance

USAMRU-K and GEIS have led the development of the national influenza sentinel surveillance network in Kenya. This effort was made in collaboration with the Kenyan ministry of health, the Kenya Medical Research Institute (KEMRI), and the CDC International Emerging Infections Program in Kenya. The number of surveillance sites within the GEIS network increased from two to eight hospitals during FY07. Laboratory diagnoses are conducted at the Kenya National Influenza Center, which is now fully renovated and equipped and actively managed by GEIS in conjunction with KEMRI. Screening is conducted by real-time PCR, and all samples are isolated by laboratory staff for multiple viral causes of respiratory disease. In the first year of the surveillance program, 2,675 respiratory specimens were obtained; 37.1% of these tested positive for influenza by PCR. Among these PCR-positive specimens, 75% were influenza A viruses and 25% were influenza B viruses; 2.1% of the influenza A viruses were subtyped, revealing 8.3% as influenza A viruses similar to A/New Caledonia/20/99 (H1N1) and 91.7% similar to A/New York/55/2004(H3N2) viruses. Twenty-four isolates of influenza B were subtyped and found to be antigenically similar to B/Malaysia/2506/2004 belonging to B/Victoria lineage. This is the first time that H1N1 and H3N2 viruses have been isolated and reported in Kenya.

Mosquito- and tick-targeted arbovirus surveillance provides the earliest evidence of transmission in an area, identifies the potential risk to humans, and allows emergency control operations to be set in motion well in advance of epidemics. By determining the genetic diversity, evolutionary trends, and spatial distribution of arboviruses circulating in Kenya, GEIS is evaluating the role of mosquito and tick species in the maintenance, transmission, and dissemination of relevant arboviruses.

In FY07, GEIS and the Entomology Program expanded vector collection from four to ten study sites representing coastal, western, central, and northeastern Kenya. Standard mosquito and tick collection methods were used, and insect species identification was performed in the field. In the course of 21 field visits, more than 50,000 mosquitoes and 15,000 ticks were collected despite a massive shift in resources and personnel to the Rift Valley fever virus epidemic response effort. Twelve virus strains have been isolated and partially characterized from mosquitoes including Usutu virus, three Flavivirus strains most similar to Kamiti River virus, two strains of Babanki virus, and one Sindbis virus. Ten virus strains have been characterized from 993 tick pools including Dugbe-like strains and several unknown strains that are being analyzed at USAMRIID. Characterization is ongoing.

Migratory bird surveillance to survey for avian influenza in Kenya languished during the 2006–2007 season because of management issues and resource allocation to the Rift Valley fever virus response. The USAMRU-K GEIS program volunteered to assist NAMRU-3 in reinvigorating sample collection, and 399 samples were collected: 44 (11.2%) tested positive for influenza A by PCR. Subtyping was conducted by NAMRU-3 at the end of FY07, and more aggressive surveillance is planned with USAMRU-K involvement for the 2007–2008 migratory season.

After nearly 2 years of inactivity in enterics surveillance at USAMRU-K, diarrhea specimens were collected from 581 patients younger than age 5 throughout FY07 at four surveillance sites. Pathogenic *Escherichia coli* comprised 173/581 (29.7%), *Salmonella* 3/581 (0.005%), *Shigella* 54/581 (9.3%), and *Campylobacter* 7/581 (0.073%). The enterics study team also tested for antibiotic resistance and promptly reported results to the field sites. This information was vital in treating persistent cases and invariably saved lives.

GEIS successfully moved the entire malaria drug resistance laboratory to Kisumu, The laboratory has adopted new nonradioactive technology and has started to screen fresh samples. A new protocol that includes an in vivo therapeutic monitoring component will soon be implemented to map the antimalarial resistance patterns in Kenya.

Response

In November 2006, increased Indian Ocean temperatures caused El Nin o-like weather patterns throughout Kenya that resulted in wide-scale flooding in Northeast Province. This flooding led to a dramatic increase in the mosquito vector population and subsequent fatal Rift Valley fever virus transmission among livestock and humans in the province's primarily pastoralist Somali population in December 2006. By May 2007, the epidemic caused more than 1,000 human cases and 300 human deaths

in Kenya, Tanzania, and Somalia. The USAMRU-K GEIS program was a significant component of the US government agency effort in supporting the Kenyan government's epidemic response. In late September/early October 2006, 2 months before Rift Valley fever cases were reported, the location and nature of this outbreak were pinpointed by the GEIS-NASA remote sensing model. Model predictions were updated frequently during the epidemic to guide response efforts by the government of Kenya, CDC, and WHO. Kenya ministry of health officials were alerted, and actions were taken to mitigate the outbreak (e.g., by limiting human contact with potentially infected animal tissues) and to warn nearby nations and the WHO.

USAMRU-K and GEIS coordinated and led the entomologic surveillance effort (Figure 28). Over more than 595 trap nights, ~297,000 mosquitoes were collected, and a subset (n = 164,626) was identified to species. Of these, 72,058 were pooled into 3,003 pools and tested for Rift Valley fever virus, and 77 pools were positive by RT-PCR.

Figure 28. Technicians examine tissue culture cells for Rift Valley fever virus growth.

GEIS funded and led part of a larger case-control study initiated in January 2007 in three Kenyan provinces to examine risk factors for severe disease caused by Rift Valley fever virus versus mild or subclinical disease and for Rift Valley fever virus infection versus noninfection. Further analysis is pending.

Capacity Building

GEIS-sponsored personnel completed three master's degrees and one doctoral degree in FY07 at USAMRU-K. After a 2-year moratorium on additional education funding, a new competitive scholarship program for GEIS-funded staff was implemented, and four scholarships were awarded. In addition, GEIS sponsored and conducted other training opportunities through USAMRU-K. This commitment to education culminated in the week-long First Annual GEIS Training Conference held in July in Kilifi, at which more than 50 personnel working on GEIS activities participated in more than 30 hours of expert and peer-led education in basic science, quality assurance and control, safety, and surveillance protocols. Other training opportunities for individuals on staff included Good Clinical Laboratory Practices training in Thailand and Good Clinical Practices training in Kenya.

NAMRU-3, USAMRU-K, and CDC Battle Rift Valley Fever

Mosquito trapping in Kenya during Rift Valley fever outbreak.

Within just 30 hours of receiving a request for assistance from USAMRU-K, CDC, and the Kenyan ministry of health, NAMRU-3 deployed an entomology and mobile real-time PCR laboratory to Garissa District, Kenya, to combat Rift Valley fever in late December 2006. NAMRU-3 was asked to assist with investigations into mosquito vectors responsible for the outbreak and to provide rapid PCR-based diagnostics based on the forecast generated as a result of the NASA remote sensing model.

Work began shortly after the team arrived in Garissa, in eastern Kenya, on 31 December. The Garissa site served as headquarters for an array of multinational investigations and services: NAMRU-3, USAMRU-K, CDC, Kenyan ministry of health, and Médecins Sans Frontières (nongovernment organization). Field assets and programs based in Garissa included blood and serum testing for suspected human cases, mass cattle immunization, receiving center/isolation ward for cases (provincial hospital), daily public health briefings for multinational response, mosquito surveillance, vector control and identification, and virus isolation activities.

Early mosquito surveys netted an abundance of floodwater Aedes mosquitoes, primarily A. mcintoshi and other Aedes (Ochlerotatus) species. A. mcintoshi is believed to be a major contributor in the genesis of Rift Valley fever outbreaks. Floodwater mosquitoes are capable of transovarial transmission, and eggs are extremely resistant to desiccation (they have been shown to remain viable for several years). Consequently, flooding after a drought can start the cycle moving again. Most Aedes mosquitoes have a strong feeding preference for large mammals such as cattle, which develop high viremias and serve as amplifying reservoirs after being infected by mosquitoes or ticks. Culex mosquitoes begin breeding several weeks after the emergence of Aedes mosquitoes, eventually surpassing Aedes in numbers as time passes, and are believed to be important vectors in prolonging outbreaks. Species of Culex that were caught include C. univittatus, C. bitaeniorhynchus, and C. poicilips, all of which also feed on cattle but are more likely than Aedes mosquitoes to feed on humans.

New cases of Rift Valley fever began to appear to the south on the Kenyan coast after the first week of January 2007. In hopes of increasing the chance of collecting virus-infected mosquitoes, the team moved by road 10 hours south to the coastal town of Kilifi, where mosquitoes were trapped 11–16 January 2007. The team set up a laboratory at the Wellcome Foundation in Kilifi, from which operations were launched. The Wellcome Foundation is colocated with the provincial hospital. As human cases were positively identified at the hospital, the team was given patient residency information and then trapped intensely in these villages, particularly around homes where cases occurred. The mosquito fauna in this area were much different from those in the bush, with C. pipiens, A. penibaensis, and Anopheles gambiae frequently caught.

Over a 10-day period in Garissa, 70,000 mosquitoes were trapped, and many larval breeding sites were located (producing Culex mosquito larvae). Far fewer mosquitoes were caught in Kilifi, probably ~3,000 in 4 days. Mosquitoes were separated by species using the keys of Edwards (1941) and pooled into groups of 25 for virus detection. Efforts at both locations uncovered six mosquito species identified as Rift Valley fever carriers, including two species not previously implicated.

Continued

Rift Valley Fever, *Continued*

The objective of the response was to augment the CDC laboratory effort underway and to provide material and subject matter expertise. Reagents to perform 400 real-time PCR reactions to detect Rift Valley fever were prepared, and supplies for 250 RNA extractions were packed. Equipment at the mobile laboratory, which was hosted by the Kenyan CDC and USAMRU-K, consisted of a rapid real-time thermocycler and two Pelican cases (24 × 24 × 19″) containing reagents, support equipment, and consumables. The mobile laboratory also provided direct support to the General Hospital in Garissa, where an isolation ward for severe cases was created, and results were provided within 3 hours of specimen receipt.

The field-basing of real-time PCR during the outbreak allowed rapid processing and analysis of blood and serum while minimizing sample degradation. The data collected in the field provided, for the first time, a correlation between amount of Rift Valley fever RNA detected and the severity of the cases for samples collected ~3 days after the onset of symptoms. Furthermore, real-time PCR testing, in conjunction with IgM and IgG ELISA, provided a platform to clinically measure the kinetics of Rift Valley fever infection. The complete results of this work are being prepared for publication.

The initial laboratory confirmation was from a specimen obtained in a border area near Somalia, which was also affected, but surveillance capability there was limited by political turmoil and military action. Rift Valley fever continued to affect Kenya, Uganda, Somalia, and Sudan through the winter of 2007.

The contribution of GEIS is its long-term support of the NASA project and programs at USAMRU-K and NAMRU-3. In addition, as the outbreak was underway, Headquarters alerted DoD, the services, and those responsible for risk assessment for deploying our overseas forces.

Technicians at USAMRU-K separating and grouping trapped mosquitoes by species during response to 2006–2007 Rift Valley fever outbreak in East Africa.

Nonmilitary Organizations

National Aeronautics and Space Administration

DoD-GEIS and the National Aeronautics and Space Administration (NASA) use detailed analyses of satellite vegetation and related derived global climate data sets for remote monitoring of climatic conditions and ecological dynamics associated with vector-borne disease outbreaks. These analyses of global climate conditions provide on-demand information for primarily DoD-GEIS vector-borne disease monitoring activities worldwide. In addition, remote monitoring can be used for non–vector-borne diseases. This capacity to give early warning of outbreaks in regions where DoD personnel are or may be deployed, such as East Africa and the Arabian peninsula, enhance force health protection.

The Global Inventory Mapping and Monitoring System group at NASA Goddard Space Flight Center (Greenbelt, MD) produces and compiles long time series measurements of vegetation and rainfall, global sea surface temperature, and outgoing longwave radiation. These data sets are used in remote monitoring of climatic conditions through anomaly analyses associated with the emergence of disease vectors. Identification and mapping of risk areas involve tracking and computation of a persistence index of above normal vegetation conditions that are associated with above normal rainfall with a focus on regions endemic for Rift Valley fever. Global scale indicators of interannual climate variability, such as El Niño Southern Oscillation, are monitored to guide personnel in areas that could be affected by extreme climatic events, such as floods or drought, that might affect vector emergence and dynamics.

NASA prepared a global outlook and assessment advisory of disease outbreak risk under developing El Niño Southern Oscillation for 2006–2007. NASA disseminated the advisory, or alert, to the DoD-GEIS global laboratory network as early warning information. Unusually wet and dry conditions were forecast, depending on the geographic location, both of which could result in environmental factors favorable for different diseases in defined areas. This year, the prediction for Rift Valley fever in Kenya was accurate; not all the forecasts were so clearly on target. Most importantly, early warning of unusually favorable conditions for disease occurrence and spread were provided to public health authorities.

In Indonesia, Malaysia, Thailand, and most of the islands of southeast Asia, an increase in dengue fever transmission caused by drought conditions was forecast. The drought would 1) increase water storage around houses, which would lead to elevated *Aedes aegypti* populations, and 2) elevate ambient air temperatures, which would reduce the extrinsic incubation period for the virus in vector mosquitoes and consequently increase vectorial capacity. The advisory also predicted an increase in the incidence of respiratory illness because of haze from uncontrolled burning of tropical forests that occurs during extreme drought.

An outbreak of dengue hemorrhagic fever that occurred in Indonesia in early 2007 was characterized by the Indonesian government as "an extraordinary situation." Additionally, in March 2007 Thailand reported an increase in respiratory illness and issued alerts owing to haze from uncontrolled burning of tropical forests caused by extreme drought that occurred in early 2007. Air quality was recorded at 240–290 $\mu g/m^3$ in the northern provinces of Chiang Mai, Mae Hong Son, and Lamphun (120 $\mu g/m^3$ is considered hazardous).

In coastal Peru, Ecuador, Venezuela, and Colombia, an increased risk of malaria caused by elevated *Anopheles* vector populations was forecast. The mosquito populations were forecast to develop when various types of immature habitats flood after heavy rainfall that follows a period of drought. No reports of increased malaria transmission were received in FY07.

In Bangladesh and coastal India, an increased risk of cholera caused by elevated sea surface temperatures and an inland incursion of plankton-laden water rich in *Vibrio cholerae* was forecast. In addition to elevated sea surface temperatures, heavy rains wash nutrients into waterways and may trigger plankton blooms. Cholera cases were reported in and around Delhi in May 2007. Extensive flooding occurred in Bangladesh and parts of India in October and November 2007, and outbreaks of diarrhea and cholera were reported in Bangladesh and India, respectively, in November 2007.

In southwestern United States, an increased risk for Hantavirus pulmonary syndrome and plague was forecast for the year given elevated rodent populations caused by heavy rainfall. One human case was reported in Colorado in April 2007, which is more than would normally be expected at that point in a normal year. New Mexico reported one case of Hantavirus pulmonary syndrome, and the number of deer mice there increased.

In northeastern Brazil, increased dengue fever and respiratory illness were forecast to result from drought conditions. An elevation in dengue transmission was reported in Brazil from January to April 2007 that was 20% over that in the same period in 2006.

In East Africa (Ethiopia, Kenya, Somalia, and Uganda), an increased risk for Rift Valley fever and malaria was forecast to result from elevated mosquito vector populations. In addition, the incidence of cholera was forecast to increase after flooding that would follow heavy rainfall in dry land areas. Above normal rainfall in October–December 2006 in most of Kenya and Tanzania ranged from 50 to 200 mm/month above normal. Increased numbers of cholera cases were reported in Somalia, Djibouti, Kenya, and Tanzania in the first half of 2007. Rift Valley fever was confirmed in patients from Garissa District in North Eastern Province, Kenya, in late December 2006. Significant Rift Valley fever activity was also reported in Somalia in early 2007 and Tanzania through at least May 2007. By February 2007, Rift Valley fever cases in humans had been reported in Somalia, other parts of Kenya, and Tanzania, confirming the accuracy of the NASA remote sensing forecast.

Early warning satellite vegetation index and rainfall products were provided to USAMRU-K, WHO, the Food and Agriculture Organization of the United Nations (FAO), and CDC as an alert to conduct field investigations in regions at risk for Rift Valley fever in East Africa from October 2006 to May 2007 (Figure 29). Based on the early warning advisories of the elevated risk of a Rift Valley fever outbreak, DoD-GEIS and USAMRU-K initiated entomological surveillance in Garissa District in early December 2006, a few weeks before reports were even received of unexplained hemorrhagic fever in humans, which were confirmed as Rift Valley fever later that month. The outbreak affected most of the Horn of Africa countries including Somalia, Kenya, and Tanzania, with human cases reported over the region from December 2006 to May 2007 (Figure 30).

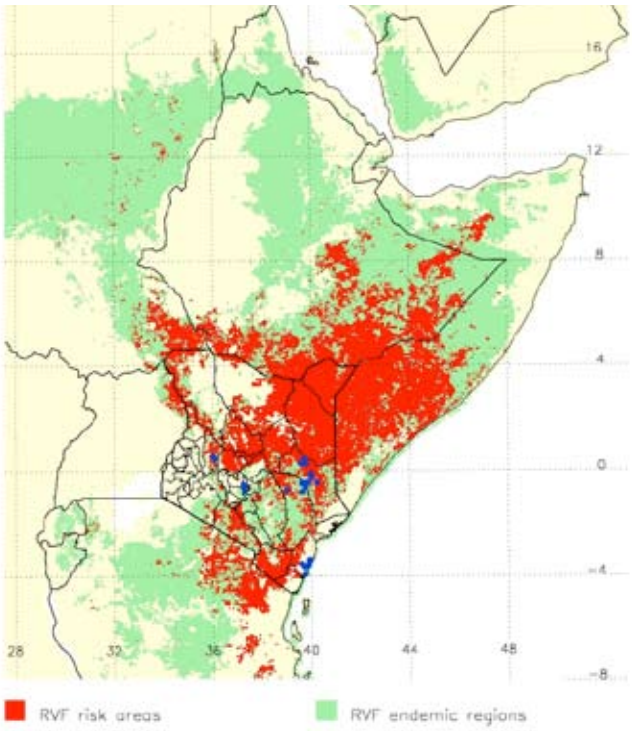


Figure 29. Rift Valley fever risk map for January 2007. ***Blue dots*****, locations where GEIS and USAMRU-K team initiated entomological surveillance in December 2006.**

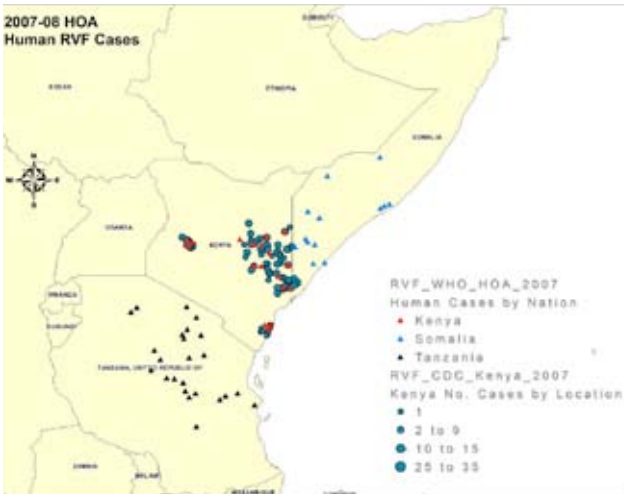


Figure 30. Distribution of human cases of Rift Valley fever (RVF) over Horn of Africa (HOA) for December 2006–May 2007 (data from WHO and CDC).

Early warning satellite vegetation index and rainfall data were provided to NAMRU-3, WHO, and FAO that showed elevated risk of conditions for Rift Valley fever activity over the western Arabian Peninsula in April 2007. Increased monitoring of the situation and intensified surveillance were initiated by in-country staff of the USDA-Animal and Plant Health Inspection Service. No

disease was reported in the region, but risk remained high because of environmental conditions, the outbreak in the Horn of Africa, and another outbreak occurring in Sudan in the fall of 2007.

Anomalously elevated rainfall, vegetation, and Rift Valley fever risk were detected in Sudan starting in July 2007. Warnings were issued to NAMRU-3, WHO, and FAO, and increased surveillance was instituted. NAMRU-3 confirmed a Rift Valley fever outbreak in October 2007, and transmission continued into December 2007, although release of information to the public on the outbreak has been limited. WHO and FAO are actively participating in the Sudan response efforts and receive updated satellite data via the GEIS website and directly.

Monthly electronic reports on Rift Valley fever monitoring were also provided to WHO and FAO in support of continental efforts to monitor and suppress Rift Valley fever activity. Rift Valley fever risk maps are published for continental Africa, Madagascar, and the Arabian Peninsula for global public dissemination through the DoD-GEIS website: http://www.geis.fhp.osd.mil/GEIS/SurveillanceActivities/RVFWeb/indexRVF.asp

Collaborators used the information provided by NASA in surveillance of Rift Valley fever activity to institute mosquito control measures where needed. Project staff members have been invited to support other programs and institutions interested in the use of remotely sensed data for vector-borne disease surveillance. These groups include WHO, USDA-Animal and Plant Health Inspection Service, World Organization for Animal Health, and the USDA-led interagency Rift Valley fever working group.

Johns Hopkins University Applied Physics Laboratory

GEIS efforts at Johns Hopkins University Applied Physics Laboratory (JHU/APL) were a continuation of work that began in FY06 in two areas: an evaluation of Early Warning Outbreak Recognition System (EWORS) and continued development of the pandemic influenza policy model (PIPM). The goal of both projects is to improve GEIS surveillance and response systems through infectious disease modeling.

EWORS Evaluation

With the goal of enhancing the ability of resource-limited countries to detect emerging infectious diseases in a timely fashion, DoD-GEIS and JHU/APL have participated in an evaluation of EWORS. In FY07, JHU/APL conducted site visits to Laos and Peru to determine which aspects of existing systems are successful and where improvements could be made. The evaluation team comprised personnel from NAMRU-2, NMRCD, JHU/APL, and DoD-GEIS. Given the inherent differences among countries, the characteristics of an effective surveillance and response system will vary greatly among locations. Consequently, JHU/APL developed a disease model to be incorporated into EWORS that borrows epidemiological features from the PIPM, which JHU/APL and GEIS developed last year.

JHU/APL and DoD-GEIS were also invited to the Philippines to assess that country's ability to host an enhanced electronic surveillance system based on EWORS. As a result of this site visit, the team proposed a pilot project that will introduce enhanced data collection and analysis via an electronic surveillance system. If successful, the potential exists to duplicate this application at additional sites within the Philippines and in other countries.

Pandemic Influenza Policy Model

PIPM is a collaborative modeling effort among DoD-GEIS, JHU/APL, and the Fort Leonard Wood (Missouri) Medical Department Activity. Many helpful simulations exist for pandemic influenza surveillance and response in civilian populations. However, the mission-oriented nature and the structured social composition at military installations result in pandemic influenza intervention strategies that are different from those appropriate for civilian populations. The strategies can even differ significantly among military bases.

Tailored for the military, PIPM is a web-based, user-configurable, installation-specific, tool to allow military public health emergency officers to evaluate intervention strategies and enable a quick response. Innovative features in the PIPM include 1) expanding the mathematics

of prior stochastic models using social network epidemiology and a user-friendly graphical user interface, 2) using DoD personnel databases to accurately characterize the population at risk, and 3) incorporating possible interventions (e.g., the pneumococcal vaccine) not examined in previous models.

PIPM is available to DoD public health planners and responders. Although primarily a tool to assist with pandemic influenza detection and response, PIPM can accommodate other novel respiratory pathogens. The PIPM incorporates key disease transmission variables found in existing models constructed for civilian use and many variables that are unique to DoD resulting from training missions, deployments, and other activities not found in the civilian sector.

The JHU/APL disease model is intended for application on a much larger scale than PIPM and will apply agent-based modeling only to the infected individuals and their contacts. The end-stage capability will be a stand-alone tool to examine the effectiveness of large-scale policy decisions such as global travel restrictions or the installation of EWORS in additional provinces in Laos or at the district level.

Outputs from the model include epidemiological curves showing projected disease propagation through a particular military installation, projected morbidity and mortality, and projections of green/yellow/red operational readiness. Military planners can use the PIPM to evaluate the impact of a pandemic on their populations and their operational readiness. By altering inputs in successive runs of the model, i.e., changing possible interventions, the user can assess the impact of interventions on disease progression and operational readiness.

Ongoing Work

Through JHU/APL and AFRIMS, DoD-GEIS plans to continue the EWORS evaluation to develop and implement an electronic surveillance capability for use in the Philippines and other identified sites and to modify the existing model for additional countries. Existing collaborations will be leveraged to improve the PIPM, to create a website, to work on the visualization of disease propagation within the PIPM simulation, and to ingest DoD population data to create the population at risk with greater fidelity. DoD-GEIS also intends to generalize the PIPM for use at bases other than Fort Leonard Wood and with services other than the Army, explore methods to output one prioritized set of interventions to optimize the probability of a specified outcome for a given scenario, and develop a suite of templates for other respiratory pathogens of interest.

Countries or Locations with GEIS Activities in FY07

Afghanistan
Albania
Antarctica
Argentina
Australia
Azerbaijan
Bahrain
Bangladesh
Belarus
Belgium
Bhutan
Bolivia
Burkina Faso
Burma
Cambodia
Cameroon
Canada
Chile
Colombia
Cote d'Ivoire
Cuba
Djibouti
Ecuador
Egypt
El Salvador
Ethiopia
Gabon
Gambia
Georgia
Germany
Ghana
Guam
Guatemala
Guinea-Bissau
Honduras
Hungary
India
Indonesia
Iran
Iraq
Italy
Japan
Jordan
Kazakhstan
Kenya
Kuwait
Kyrgyzstan
Laos
Lebanon
Libya
Malawi
Malaysia
Maldives
Mexico
Mongolia
Morocco
Nepal
Nicaragua
Nigeria
Northern Mariana Islands
Oman
Pakistan
Palau
Palestine
Panama
Papua New Guinea
Paraguay
Peru
Philippines
Poland
Portugal
Qatar
Saudi Arabia
Senegal
Singapore
Somalia
South Korea
Spain
Sri Lanka
Sudan
Syria
Tanzania
Thailand
Tonga
Tunisia
Turkey
Uganda
Ukraine
United Kingdom
United States
Uruguay
Uzbekistan
Venezuela
Vietnam
Yemen

Publications, Presentations, and GenBank Submissions

Publications

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GenBank Submissions

MD Saad submitted the following for the hemagglutinin gene of influenza A virus strains from Egypt.

1. DQ435200; Influenza A virus (A/domestic cat/Iraq/820/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|89275862|gb|DQ435200.1|[89275862]. 2006.

2. DQ435201; Influenza A virus (A/domestic goose/Iraq/812/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|89275864|gb|DQ435201.1|[89275864]. 2006.

3. DQ435202; Influenza A virus (A/human/Iraq/207-NAMRU3/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|89275866|gb|DQ435202.1|[89275866]. 2006.

4. DQ447199; Influenza A virus (A/chicken/Egypt/960N3-004/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|90025360|gb|DQ447199.1|[90025360]. 2006.

5. DQ666146; Influenza A virus (A/Djibouti/5691NAMRU3/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|109727317|gb|DQ666146.1|[109727317]. 2006.

6. DQ835389; Influenza A virus (A/goose/Iraq/812NAMRU3/2006(H5N1)) neuraminidase (NA) gene, partial cds; gi|110227238|gb|DQ835389.1|[110227238]. 2006.

7. DQ835390; Influenza A virus (A/cat/Iraq/820NAMRU3/2006(H5N1)) neuraminidase (NA) gene, partial cds; gi|110227240|gb|DQ835390.1|[110227240]. 2006.

8. DQ837587; Influenza A virus (A/Chicken/Egypt/5610NAMRU3-F3/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|110333722|gb|DQ837587.1|[110333722]. 2006.

9. DQ837588; Influenza A virus (A/Chicken/Egypt/5611NAMRU3-AN/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|110333724|gb|DQ837588.1|[110333724]. 2006.

10. DQ837589; Influenza A virus (A/Chicken/Egypt/5612NAMRU3-S/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|110333726|gb|DQ837589.1|[110333726]. 2006.

11. DQ837590; Influenza A virus (A/Turkey/Egypt/5613NAMRU3-T/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|110333728|gb|DQ837590.1|[110333728]. 2006.

12. EF061116; Influenza A virus (A/Egypt/12374-NAMRU3/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|116248058|gb|EF061116.1|[116248058]. 2006.

13. EF200512; Influenza A virus (A/Egypt/14724-NAMRU3/2006(H5N1)) hemagglutinin (HA gene) gene, partial cds; gi|121483685|gb|EF200512.1|[121483685]. 2006.

14. EF200513; Influenza A virus (A/Egypt/14725-NAMRU3/2006(H5N1)) hemagglutinin (HA gene) gene, partial cds; gi|121483687|gb|EF200513.1|[121483687]. 2006.

15. EF222322; Influenza A virus (A/Egypt/14725-NAMRU3/2006(H5N1)) neuraminidase (NA) gene, complete cds; gi|122913044|gb|EF222322.1|[122913044]. 2006.

16. EF222323; Influenza A virus (A/Egypt/14724-NAMRU3/2006(H5N1)) neuraminidase (NA) gene, complete cds; gi|122913046|gb|EF222323.1|[122913046]. 2006.

17. EF222324; Influenza A virus (A/Egypt/12374-NAMRU3/2006(H5N1)) neuraminidase (NA) gene, complete cds; gi|122913048|gb|EF222324.1|[122913048]. 2006.

18. EF382359; Influenza A virus (A/Egypt/0636-NAMRU3/2007(H5N1)) hemagglutinin (HA) mRNA, complete cds; gi|124244205|gb|EF382359.1|[124244205]. 2007.

19. EF382360; Influenza A virus (A/Egypt/0636-NAMRU3/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|124244207|gb|EF382360.1|[124244207]. 2007.

20. EF441276; Influenza A virus (A/chicken/Egypt/1078-NAMRU3/2006(H5N1)) hemagglutinin (HA) gene, complete cds; gi|126015349|gb|EF441276.1|[126015349]. 2006.

21. EF441277; Influenza A virus (A/chicken/Egypt/1079-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|126015351|gb|EF441277.1|[126015351]. 2007.

22. EF441278; Influenza A virus (A/chicken/Egypt/1080-NAMRU3/2006(H5N1)) hemagglutinin (HA) gene, complete cds; gi|126015353|gb|EF441278.1|[126015353]. 2006.

23. EF441279; Influenza A virus (A/chicken/Egypt/1081-NAMRU3/2006(H5N1)) hemagglutinin (HA) gene, complete cds; gi|126015355|gb|EF441279.1|[126015355]. 2006.

24. EF441280; Influenza A virus (A/chicken/Egypt/1300-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|126015357|gb|EF441280.1|[126015357]. 2007.

25. EF441281; Influenza A virus (A/duck/Egypt/1301-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|126015359|gb|EF441281.1|[126015359]. 2007.

26. EF469650; Influenza A virus (A/chicken/Egypt/1129N3-HK9/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|134251779|gb|EF469650.1|[134251779]. 2007.

27. EF469651; Influenza A virus (A/chicken/Egypt/12378N3-CLEVB/2006(H5N1)) hemagglutinin (HA) gene, complete cds; gi|134251781|gb|EF469651.1|[134251781]. 2006.

28. EF469652; Influenza A virus (A/chicken/Egypt/12379N3-CLEVB/2006(H5N1)) hemagglutinin (HA) gene, complete cds; gi|134251783|gb|EF469652.1|[134251783]. 2006.

29. EF469653; Influenza A virus (A/chicken/Egypt/1889N3-SM26/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|134251785|gb|EF469653.1|[134251785]. 2007.

30. EF469654; Influenza A virus (A/chicken/Egypt/1890N3-HK45/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|134251787|gb|EF469654.1|[134251787]. 2007.

31. EF469655; Influenza A virus (A/duck/Egypt/12380N3-CLEVB/2006(H5N1)) hemagglutinin (HA) gene, complete cds; gi|134251789|gb|EF469655.1|[134251789]. 2006.

32. EF469656; Influenza A virus (A/duck/Egypt/13010N3-CLEVB/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|134251791|gb|EF469656.1|[134251791]. 2006.

33. EF469657; Influenza A virus (A/duck/Egypt/1888N3-SM25/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|134251793|gb|EF469657.1|[134251793]. 2007.

34. EF469658; Influenza A virus (A/goose/Egypt/13009N3-SM2/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|134251795|gb|EF469658.1|[134251795]. 2006.

35. EF469659; Influenza A virus (A/chicken/Egypt/1891N3-CLEVB/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|134251797|gb|EF469659.1|[134251797]. 2007.

36. EF469660; Influenza A virus (A/chicken/Egypt/1892N3-HK49/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|134251799|gb|EF469660.1|[134251799]. 2007.

37. EF486240; Influenza A virus (A/chicken/Egypt/1129N3-HK9/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037015|gb|EF486240.1|[134037015]. 2007.

38. EF486241; Influenza A virus (A/chicken/Egypt/12378N3-CLEVB/2006(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037017|gb|EF486241.1|[134037017]. 2006.

39. EF486242; Influenza A virus (A/chicken/Egypt/12379N3-CLEVB/2006(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037019|gb|EF486242.1|[134037019]. 2006.

40. EF486243; Influenza A virus (A/chicken/Egypt/1889N3-SM26/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037021|gb|EF486243.1|[134037021]. 2007.

41. EF486244; Influenza A virus (A/chicken/Egypt/1890N3-HK45/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037023|gb|EF486244.1|[134037023]. 2007.

42. EF486245; Influenza A virus (A/chicken/Egypt/1891N3-CLEVB/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037025|gb|EF486245.1|[134037025]. 2007.

43. EF486246; Influenza A virus (A/chicken/Egypt/1892N3-HK49/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037027|gb|EF486246.1|[134037027]. 2007.

44. EF486247; Influenza A virus (A/duck/Egypt/12380N3-CLEVB/2006(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037029|gb|EF486247.1|[134037029]. 2006.

45. EF486248; Influenza A virus (A/duck/Egypt/13010N3-CLEVB/2006(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037031|gb|EF486248.1|[134037031]. 2006.

46. EF486249; Influenza A virus (A/duck/Egypt/1888N3-SM25/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037033|gb|EF486249.1|[134037033]. 2007.

47. EF486250; Influenza A virus (A/goose/Egypt/13009N3-SM2/2006(H5N1)) neuraminidase (NA) gene, complete cds; gi|134037035|gb|EF486250.1|[134037035]. 2006.

48. EF535817; Influenza A virus (A/Egypt/1394-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843655|gb|EF535817.1|[145843655]. 2007.

49. EF535818; Influenza A virus (A/Egypt/1604-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843657|gb|EF535818.1|[145843657]. 2007.

50. EF535819; Influenza A virus (A/Egypt/1731-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843659|gb|EF535819.1|[145843659]. 2007.

51. EF535820; Influenza A virus (A/Egypt/1902-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843661|gb|EF535820.1|[145843661]. 2007.

52. EF535821; Influenza A virus (A/Egypt/2256-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843663|gb|EF535821.1|[145843663]. 2007.

53. EF535822; Influenza A virus (A/Egypt/2321-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843665|gb|EF535822.1|[145843665]. 2007.

54. EF535823; Influenza A virus (A/Egypt/2331-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843667|gb|EF535823.1|[145843667]. 2007.

55. EF535824; Influenza A virus (A/Egypt/2616-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843669|gb|EF535824.1|[145843669]. 2007.

56. EF535825; Influenza A virus (A/Egypt/2620-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843671|gb|EF535825.1|[145843671]. 2007.

57. EF535826; Influenza A virus (A/Egypt/2621-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|145843673|gb|EF535826.1|[145843673]. 2007.

58. EF624250; Influenza A virus (A/chicken/Ghana/3158-NAMRU3/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|148628582|gb|EF624250.1|[148628582]. 2007.

59. EF624251; Influenza A virus (A/chicken/Ghana/3159-NAMRU3/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|148628584|gb|EF624251.1|[148628584]. 2007.

60. EF624252; Influenza A virus (A/chicken/Ghana/3160-NAMRU3/2007(H5N1)) neuraminidase (NA) gene, complete cds; gi|148628586|gb|EF624252.1|[148628586]. 2007.

61. EF624253; Influenza A virus (A/chicken/Ghana/3158-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|148628588|gb|EF624253.1|[148628588]. 2007.

62. EF624254; Influenza A virus (A/chicken/Ghana/3159-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|148628590|gb|EF624254.1|[148628590]. 2007.

63. EF624255; Influenza A virus (A/chicken/Ghana/3160-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, complete cds; gi|148628592|gb|EF624255.1|[148628592]. 2007.

64. EU095023; Influenza A virus (A/Egypt/2991-NAMRU3/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147971|gb|EU095023.1|[156147971]. 2006.

65. EU095024; Influenza A virus (A/Egypt/2992-NAMRU3/2006(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147973|gb|EU095024.1|[156147973]. 2006.

66. EU095025; Influenza A virus (A/Egypt/2629-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147975|gb|EU095025.1|[156147975]. 2007.

67. EU095026; Influenza A virus (A/Egypt/2630-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147977|gb|EU095026.1|[156147977]. 2007.

68. EU095027; Influenza A virus (A/Egypt/2631-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147979|gb|EU095027.1|[156147979]. 2007.

69. EU095028; Influenza A virus (A/Egypt/2750-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147981|gb|EU095028.1|[156147981]. 2007.

70. EU095029; Influenza A virus (A/Egypt/2751-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147983|gb|EU095029.1|[156147983]. 2007.

71. EU095030; Influenza A virus (A/Egypt/4081-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147985|gb|EU095030.1|[156147985]. 2007.

72. EU095031; Influenza A virus (A/Egypt/4082-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147987|gb|EU095031.1|[156147987]. 2007.

73. EU095032; Influenza A virus (A/Egypt/4226-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147989|gb|EU095032.1|[156147989]. 2007.

74. EU095033; Influenza A virus (A/Egypt/6251-NAMRU3/2007(H5N1)) hemagglutinin (HA) gene, partial cds; gi|156147991|gb|EU095033.1|[156147991]. 2007.

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Acronyms

AFB	Air Force base
AFIOH	Air Force Institute for Operational Health
AFIP	Armed Forces Institute of Pathology
AFMIC	Armed Forces Medical Intelligence Center
AFRICOM	United States Africa Command
AFRIMS	Armed Forces Research Institute of Medical Sciences (Bangkok, Thailand)
AMSA	Army Medical Surveillance Activity
ASD (HA)	Assistant Secretary of Defense for Health Affairs
BAMC	Brooke Army Medical Center
BSL	biosafety level
BSL-3E	biosafety level 3 (enhanced)
CDC	Centers for Disease Control and Prevention
CDHAM	Center for Disaster and Humanitarian Assistance Medicine
CENTCOM	United States Central Command
CHCS	Composite Health Care System
CHPPM	see USACHPPM
CLIP	Clinical Laboratory Improvement Program
COCOM	Combatant Command
CONPLAN	operations plan in concept
CONUS	continental United States
CSH	combat support hospital
DHHS	Department of Health and Human Services
DMDC	Defense Manpower Data Center
DMSS	Defense Medical Surveillance System
DNBI	disease nonbattle injury
DoD	Department of Defense
EAMC	Eisenhower Army Medical Center
ELISA	enzyme-linked immunosorbent assay
epi-chiefs	epidemiology chiefs' biweekly teleconference
Epi-X	Epidemic Information Exchange
ESBL	extended-spectrum beta- lactamase
ESSENCE	Electronic Surveillance System for the Early Notification of Community-Based Epidemics
ETEC	enterotoxigenic *Escherichia* coli
EUCOM	United States European Command
EWORS	Early Warning Outbreak Recognition System
FAO	Food and Agriculture Organization of United Nations
FDA	Food and Drug Administration
FEMA	Federal Emergency Management Agency
FRI	febrile respiratory illness
FY	fiscal year
GAO	United States Government Accountability Office
GARP	Genetic Algorithm for Rule-Set Prediction
GEIS	Global Emerging Infections Surveillance and Response System
HHS	Department of Health and Human Services
HIV	human immunodeficiency virus
HL7	Health Level Seven
HSV	herpes simplex virus
IFA	immunofluorescence assay
Ig	immunoglobulin
KEMRI	Kenya Medical Research Institute
JBAIDS	Joint Biological Agent Identification and Diagnostic System
JHU/APL	Johns Hopkins University Applied Physics Laboratory

LRMC	Landstuhl Regional Medical Center
MAMC	Madigan Army Medical Center
MEDCOM	Medical Command
MHS	military health system
MIDRP	Military Infectious Diseases Research Program
MPH	Master of Public Health
MTF	military treatment facility
NAMRU-2	Naval Medical Research Unit No. 2 (Jakarta, Indonesia)
NAMRU-3	Naval Medical Research Unit No. 3 (Cairo, Egypt)
NASA	National Aeronautics and Space Administration
NATO	North Atlantic Treaty Organization
NEHC	Navy Environmental HealthCenter (renamed Navy and Marine Corps Public Health Center in November 2007)
NEPMU	Navy Environmental and Preventive Medicine Unit
NHRC	Naval Health Research Center
NIH	National Institutes of Health
NMC	Naval Medical Center
NMRC	Naval Medical Research Center
NMRCD	Naval Medical Research Center Detachment (Lima, Peru)
NNMC	National Naval Medical Center
NORAD	North American Aerospace Defense Command
NORTHCOM	United States Northern Command
NSTC	National Science and Technology Council
OCONUS	outside the continental United States
PACAF	Pacific Air Forces
PACOM	United States Pacific Command
PCR	polymerase chain reaction
PHEO	Public Health Emergency Officer
PIPM	pandemic influenza policy model
POPM	Program Office for Preventive Medicine
RSV	respiratory syncytial virus
RT-PCR	reverse transcriptase-polymerase chain reaction
SARS	severe acute respiratory syndrome
SOUTHCOM	United States Southern Command
TAMC	Tripler Army Medical Center
TIGER	Triangulation Identification for Genetic Evaluation of Risks
TSN	The Surveillance Network®
USACHPPM	United States Army Center for Health Promotion and Preventive Medicine
USAID	United States Agency for International Development
USAMRIID	United States Army Medical Research Institute of Infectious Diseases
USAMRMC	United States Army Medical Research and Materiel Command
USAMRU-K	United States Army Medical Research Unit-Kenya
USDA	United States Department of Agriculture
USFK	United States Forces Korea
USMI	United States Medicine Institute for Health Studies
USUHS	Uniformed Services University of the Health Sciences
WARN	Worldwide Antimalarial Resistance Network
WARUN	Walter Reed/AFRIMS Research Unit-Nepal
WB	Western blot
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research
WRAMC	Walter Reed Army Medical Center
WRBU	Walter Reed Biosytematics Unit

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