ANNEX B (DISEASE INTELLIGENCE)

1. SITUATION

a. Influenza Pandemic Threat: Refer to Appendix 1 (Influenza Pandemic Threat).

b. Mission and Intent of Higher and Supporting Organizations: Refer to Base OPLAN.

c. Environment: Refer to Appendix 2 (Global Environment).

2. MISSION.

a. Actively conduct all-source disease intelligence activities (monitoring, requesting information, tasking, analysis, product development, distribution) using all available information sources internal to CDC and the USG, from SLTT partners, international non-governmental organizations (NGOs), foreign governments, and international health agencies. Provide a regular flow of disease intelligence to the CDC Director, subordinate elements of CDC, supporting Federal authorities and departments, SLTT partners, and international cooperating agencies to enable informed decision making and implementation of appropriate actions in the event of an influenza pandemic.

3. EXECUTION

a. Concept of Intelligence Operations.

1) CDC will aggressively establish tasking, requesting, and coordination channels to receive all timely and useful health, laboratory, and other information that can enable the earliest possible domestic detection of human and animal infection, provide daily situational awareness of an influenza pandemic's national and international spread and impact, and fulfill key items of the Director's Critical Information Requirements. Refer to Base OPLAN 3.d.2.

2) Infection with a novel influenza virus can be diagnosed and the earliest U. S. cases of pandemic influenza can be identified. Laboratories will play a pivotal role in disease surveillance, monitoring the pandemic's geographic spread, and the continued efficacy of medical countermeasures. Laboratory services will facilitate clinical treatment by

distinguishing patients with influenza from those with other respiratory illnesses. They will monitor circulating viruses for the emergence of genetic and antigenic variants, and support development and testing of antiviral drugs and vaccines.

3) As disease spreads and sequential stages/phases are declared, CDC will increase its monitoring and analytical capabilities to provide support and presence in the DEOC. Tasks and priorities will be established to ensure all critical disease intelligence is obtained through domestic and international surveillance and monitoring structures and sources. Available CDC surveillance and monitoring assets will be deployed and will respond directly to the DEOC.

4) Coordination will be implemented with USG agencies and SLTT governmental authorities to activate information and reporting channels. International agency and non-governmental organization coordination will be affected to provide a channel for a two way flow of disease intelligence that will facilitate efficient and effective deployment and utilization of countermeasures. CDC DEOC will provide periodic disease intelligence spot reports; disease intelligence daily summaries and status reports; and future projections of disease spread, progression, and severity. Refer to Annex N (Reports and Products).

5) Tasks to Subordinate Organizations: Refer to Appendix 3 (Collection Plan).

6) Recommendations and Requests for SLTT Organizations: Refer to Appendix 3 (Collection Plan).

7) Coordinating Instructions: Refer to Base OPLAN.

b. Critical Disease Intelligence Requirements

1) Inter-Pandemic Period: (Who Phases 1-2; U. S. Stage 0):

a) Where and when was infection confirmed in migratory birds, what is the current status of disease in migratory birds, and what are the implications for human health?

b) Where and when was infection confirmed in domestic or commercial animals, what is current status of disease in domestic and commercial animals, and what are the implications for human health?

c) Where is CDC staff investigating animal infections; what are the epidemiological, clinical, and laboratory statuses of the investigation?

d) What evidence exists for emergence of mutations in the virus that have implications for human health?

2) Pandemic Alert Period: (WHO Phase 3-5; U. S. Stage 0-1)

a) In what countries and locations are there confirmed cases of human infection?

b) In what countries and locations are CDC staff members working on human case/cluster investigations or containment efforts; what is the status of the investigation/effort; and what has been discovered about sources of infection, modes (contact/droplet/airborne) of transmission, risk groups, response to treatment, mortality rate/attack rate and other complications, and local capacity to contain or slow transmission?

c) What evidence suggests disparate disease effects or emerging stigmatization around any special, vulnerable, or at-risk population groups, including racial/ethnic minorities?

d) In what countries and locations are there confirmed episodes of infected wild, domestic, or commercial animals; when did each episode begin; is the spread of infection in animals continuing or has it ceased?

e) Is the sensitivity of surveillance adequate to accurately assess and assure the absence of documented and reported disease?

f) What evidence shows that genetic mutations in the virus have rendered them resistant to antiviral therapy or have genetic mutations affected viral antigenicity making it resistant to vaccine induced immunity?

3) Pandemic Period: (WHO Phase 6; U. S. Stages 2-6)

a) Where in the U. S. are SLTT partners working on human case/cluster investigations, quarantine events, or containment efforts and what is the status of the investigation/event/effort?

b) Where in the U. S. are CDC staff members working on human case/cluster investigations, quarantine events, or containment efforts; what is the status of the investigation/event/effort; and what has been discovered about sources of infection, modes (contact/droplet /airborne) of transmission, risk groups, response to treatment, mortality rate/attack rate and other complications, and local capacity to contain or slow transmission?

c) Where and in what populations are the first or subsequent pandemic waves increasing, stabilizing, or decreasing, and what are the implications for pandemic response?

d) Where and in what key sector (i.e., socio-economic, racial/ethnic, age group, geographic) is the first or subsequent pandemic wave increasing, stabilizing, or decreasing and what are the implications for pandemic response?

e) What are the characteristics of adverse events related to antiviral use; what actions have been taken to eliminate them; and what are the results of these actions?

f) What are the characteristics of adverse events related to vaccine use; what actions have been taken to eliminate them; and what are the results of these actions?

g) What are the influenza attack and absentee rates in CDC's work force and how is continuity of operations affected?

h) Are there confirmed reports of emergence of genetic variants of the virus in the population; if yes, what is its impact on the efficacy of antiviral drugs?

i) Are there confirmed reports of emergence of antigenic variants of the virus in the population; if yes, what is its impact on the efficacy of the vaccine?

j) Has a distinct antigenic variant arisen and can CDC provide the required seed material for vaccine production?

c. REPORTS AND PRODUCTS THAT CONTAIN DISEASE INTELLIGENCE INFORMATION.

In the pandemic alert and pandemic periods, it will be critical for CDC decision-makers to have immediate access to all available scientifically analyzed information about developing

events including relevant peer reviewed scientific publications. Presenting timely and sound analysis will require utilization of a number of different intelligence products. Refer to Table 7 to Appendix 3 (Disease Intelligence Collection Plan).

1) Incident Action Plan (IAP):

The IAP is the primary incident management document and will normally cover a 24-hour operational period, usually 1700-1700. The IAP will include all appropriate maps, epidemiological graphs, synopses of media stories, etc. The IAP is intended to focus the incident management staff on tasks/objectives to be accomplished during the upcoming 24-hour period. Refer to Annex N (Reports and Products).

2) Director's Morning Summary:

This daily briefing will draw from the Incident Action Plan covering a 24-hour period. The briefing will be focused on updating the CDC Director and CC Directors regarding the current situation, objectives, planning assumptions, activities that have occurred and the most up-to-date information possible. Refer to Annex N (Reports and Products).

3) Afternoon Update Summary:

This briefing essentially mirrors the Director's Morning Summary in format and purpose, but will be concise and include only those developments that have occurred since the Director's Morning Summary briefing of which the Director and senior CDC policy makers need to be aware and that require analysis. Refer to Annex N (Reports and Products).

4) Situation Reports:

Situation Reports will normally be prepared on a daily basis, at the end of the work day, or at the same time each day, summarizing significant developments for quick reference of all CDC personnel responding to a pandemic event. Normally these will not include detailed analysis, but will be quick snapshots of key happenings. Refer to Annex N (Reports and Products).

5) Spot Reports:

Spot reports will be submitted to the IM for approval before dissemination. Spot reports are alerts to decision-makers regarding fast-breaking developments and would be issued on an urgent basis during a pandemic crisis. Refer to Annex N (Reports and Products).

6) Executive Decision Support Briefs:

In substance, these briefs will be similar to individual items in the Director's Morning Summary, i.e., a description of a development in the event, accompanied by brief analysis. These will be issued on an as-needed basis. Refer to Annex N (Reports and Products).

7) Executive Decision Support Memoranda:

These memoranda and products will serve the same general function as the Executive Decision Support Brief, i.e., responding to an inquiry from a decision-maker or providing a vehicle for an analyst to target information toward a specific executive audience. Refer to Annex N (Reports and Products).

8) Long Term Analyses:

While these reports will also address breaking events in a pandemic, they will focus on broader or longer term implications of the event. Their primary purpose will be to provide a wider perspective to policy makers on fast-moving events. Refer to Annex N (Reports and Products).

9) Travel Briefings:

OSEP will provide reports and briefings that will be comprehensive, all-source medical, public health, and security assessments on specific countries for the purpose of informing CDC staff being deployed abroad of the health and security situations they are likely to encounter on arrival. OSEP will provide the personal security information, site situational awareness, and respond to other requests for information, both classified and unclassified. Refer to Annex N (Reports and Products).

10) Media Updates:

These public health updates are designed to keep the general public apprised of the overall health information situation. This public health information will be provided to media outlets, including the internet. Refer to Annex N (Reports and Products).

11) Surveillance Data Reporting:

The Technical Specialty Unit within the IMS Planning Section will aggregate surveillance data from State epidemiologists and will report to the SA Section and other interested parties. The SA Section will provide the latest epidemiological information for inclusion in the IAP. Refer to Annex N (Reports and Products).

12) Field Reports:

Field Reports provide information to the IM and CDC Staff concerning field operations where CDC personnel have been deployed. Refer to Annex N (Reports and Products).

4. SUPPORT SERVICES

Refer to Base OPLAN and Annex I (Support Services).

5. MANAGEMENT AND COMMUNICATIONS

a. A Sensitive Compartmented Information Facility (SCIF) is available as a repository for Special Intelligence documents. Secret Internet Protocol Router Network (SIPRNET) World-Wide and Joint Worldwide Intelligence Communications System (JWICS) capabilities are also available within the same facility.

b. Liaison with governmental intelligence agencies must be coordinated through the Office of Security and Emergency Preparedness (OSEP).

c. Secure video teleconferencing (VTC) and telecommunications are available within the SCIF.

d. Executive Intelligence Briefings will be collected, analyzed, produced, and briefed by OSEP personnel.

APPENDIXES:

1. Influenza Pandemic Threat Estimate.
2. The Global Environment.
3. Disease Intelligence Collection Plan.
4. Laboratory Services.

APPENDIX 1 (INFLUENZA PANDEMIC THREAT ESTIMATE)

1. INFLUENZA PANDEMIC THREAT ESTIMATE

e. Influenza viruses have threatened the health of animal and human populations for centuries. Their genetic and antigenic diversities and their ability to change rapidly due to genetic re-assortment and mutations make it very difficult to develop a universal vaccine and highly effective antiviral drugs. Each year an estimated 36,000 deaths and 226,000 hospitalizations occur in the United States, notwithstanding the wide-scale availability of effective seasonal influenza vaccines and antiviral drugs.

f. A pandemic can occur when a novel strain of influenza virus emerges with the ability to infect humans, cause illness, and readily spread from person to person. Because of lack of prior immunity to the novel virus and its ability to spread to all parts of the world rapidly, such a virus can result in a pandemic. Each of the three pandemics in the last century resulted in infection of approximately 30 percent of the world population and death in 0. 2 percent to 2 percent of those infected. Based on this information and current models of disease transmission, a current influenza pandemic could result in deaths of 200,000 to two million U. S. citizens.

6. PANDEMICS OF THE 20TH CENTURY

When a highly contagious virus is introduced into populations that have little if any immunity, universal susceptibility to infection results in widespread transmission and, if virulence is high, a severe pandemic results. The disease spreads to all parts of the world very quickly, usually within less than a year, and causes illness in more than a quarter of the total population. It is this abrupt upsurge in illness, outstripping the capacity to respond, that makes pandemics so disruptive, in addition to the excess mortality they invariably cause. Avian viruses were involved in the last three pandemics.

a. The Pandemic of 1918-1919.

The 1918-1919 influenza pandemic is generally regarded as the deadliest disease event in human history. In less than one year, influenza killed 40 million people worldwide. Many of the deaths

were from pneumonia caused by secondary bacterial infections. The virus H1N1 also caused primary viral pneumonia, with extensive hemorrhage in the lungs, which was an underlying cause of death in healthy individuals. This form of viral pneumonia often killed healthy individuals in less than 48 hours. Ninety-nine percent of deaths occurred in people younger than 65 years.

With no antibiotics or vaccine available, control efforts worldwide were limited to isolation, quarantine, good personal hygiene, use of disinfectants, and the prevention of public gatherings. Many people wore gauze masks in public. Public institutions, including schools, were often closed and public gatherings banned. Quarantine and isolation, while widely imposed, did little to stop the spread between or within countries.

Throughout the world, the rate of spread and excess mortality outstripped response capacity at all levels. Although public health interventions delayed the onset of the pandemic, they could not stop it. Over 10 million deaths were reported in densely populated India. Even in sparsely populated sub-Saharan African countries, the epidemic moved easily from port cities to the remote villages, killing 1.5 to 2 million people within weeks. Globally, the human toll was enormous; in many areas, life expectancy dropped by 10 years or more.

New observations of U.S. “escape communities” that experienced very little morbidity or mortality during the second wave of the 1918 pandemic suggest that a policy of protective sequestration, if implemented early enough and long enough, was an effective non-pharmaceutical community mitigation strategy. This was effective mainly in small, somewhat isolated, areas.

Historical analyses of the U.S. pandemic experience have also shown that the timing of community non-pharmaceutical intervention mitigation strategies is a key predictor of effectiveness. Cities that imposed multiple social distancing measures within a few days of discovering the first local cases cut weekly death rates in half compared with cities that waited several weeks to initiate these remedies.

b. The Pandemic of 1957-1958.

The pandemic that began in 1957 was caused by H2N2, a less virulent virus than the one responsible for the 1918 pandemic. Vaccines for seasonal epidemics had been developed and were the most effective method for prevention. When used, they reduced the incidence of seasonal influenza by two thirds or more. Antibiotics were available to treat complications, including bacterial pneumonia. In May 1957, WHO received news of extensive influenza epidemics in Hong Kong and Singapore. The epidemics began at the end of February in a single province of China and spread throughout the country in March. Within weeks, laboratories in the WHO network analyzed the virus and identified it as a completely new virus subtype. WHO alerted the world to the onset of a pandemic. Samples of the virus were immediately distributed to vaccine manufacturers throughout the world. This time, pathways of international spread were tracked by the network of laboratories, and the event was accompanied by extensive epidemiological, clinical, and virological studies.

The speed of international spread was swift. Less than six months after the disease reached Hong Kong, every part of the world had documented cases. In tropical countries and Japan, introduction of the virus was followed almost immediately by a succession of outbreaks, quickly resulting in a general community-wide epidemic. In contrast, both Europe and the United States experienced a grace period of at least six weeks before epidemics occurred following the introduction of cases. Epidemiologists believe that an almost silent “seeding” of the population occurred during these weeks. The reasons for the delayed epidemics remain obscure but are thought to be associated with climate and the timing of school holidays. In Europe and the U. S., for example, the epidemics exploded coincident with the opening of schools in September and peaked rapidly. By December, the worst was over, at least for the first wave. Once epidemics began, patterns of morbidity were remarkably similar throughout the world. As with the initial wave in 1918, large numbers of cases occurred and the outbreaks were frequently explosive, but fatalities were much lower. Mortality showed a pattern more characteristic of that seen in seasonal epidemics, with most excess deaths confined to infants and the elderly. During the first wave, cases of illness were concentrated

in school-aged children; this was attributed to their close contact in crowded settings, and not to a particular age-related vulnerability. In most countries, a second wave followed within a month to three months after the disappearance of the first one. This caused very high rates of illness and increased fatalities. The second wave was concentrated in the elderly. Total excess global mortality was estimated at more than two million. In 1918, many countries observed a subset, though smaller, of fatal cases of viral pneumonia with no evidence of bacterial infection. In 1957, however, most such fatalities occurred in persons with underlying disease, and not in the previously healthy.

Vaccines were available in August 1957 in the U. S., in October 1957 in the United Kingdom, and in November 1957 in Japan. The quantities, however, were too small for wide scale use. Moreover, as the disease was so much milder than in 1918, health authorities decided against an expansion of vaccine production to the scale needed for population-wide vaccination.

No country had sufficient vaccine production capacity to cover its entire population, much less to export vaccines elsewhere. Quarantine measures were applied in several countries, managing at best to postpone the onset of an epidemic by a few weeks to two months. The banning of public gatherings and the closing of schools were considered the only measures that could dampen the spread of the pandemic. Even the most extreme option – severe restrictions on international travel and trade – was thought to bring nothing more than a few weeks of freedom from a disease whose international spread might be forestalled, but never stopped. For health authorities, the biggest challenge presented by the 1957 pandemic was the provision of adequate medical and hospital services. Measures to delay the speed of spread and thus flatten the peak occurrence of cases were considered justified if they allowed the maintenance of medical and other essential services.

c. The Pandemic of 1968-1969.

The pandemic that began in 1968 was caused by H3N2 and was even milder than that in 1957. It brought its own set of special epidemiological surprises. The first hint of a pandemic came from a newspaper story, published in the United Kingdom in mid-July 1968, describing

a widespread outbreak of acute respiratory disease in southeastern China. That same month the disease spread to Hong Kong, where it reached maximum intensity within two weeks, causing half a million cases. The virus was rapidly identified as a novel subtype and WHO issued a warning of possible worldwide spread. Initial international spread did resemble that seen during 1957, but there the resemblance ended. Nearly everywhere, clinical symptoms were mild and mortality low. In most countries, the disease spread slowly rather than in the highly visible pattern of explosive outbreaks seen in previous pandemics. In some countries, the impact on absenteeism and on death rates was slight or absent altogether.

The U. S. was the notable exception. The epidemic in the U. S. began in September 1968 in California, carried there by troops returning from Vietnam, and spread eastward to affect the whole country by late December. A significant increase in deaths from influenza-related pneumonia occurred during the first two weeks of January 1969, with deaths concentrated in the elderly. Altogether, around 34,000 pandemic-related deaths, mostly in the elderly, occurred in the United States. Too little vaccine arrived too late. Though vaccine manufacturing began within two months of virus isolation, only 20 million doses were ready when the epidemic peaked in the United States.

In striking contrast, Canada experienced a relatively slight increase in disease incidence and practically no pandemic-related mortality. A similar picture was seen in most parts of Europe, where symptoms were mild and excess deaths negligible. Although accurate mortality estimates are not available, global excess mortality was probably around one million. As the virus was genetically similar to viruses from previous pandemics, including the one as recent as 1957, at least some segments of the world population probably had partial protection either against infection or from severe disease. The occurrence of major epidemics at different times in different parts of the world was another unfortunate but curious feature. Several tropical countries experienced epidemics only at the beginning of 1969. For unknown reasons, Japan experienced numerous imported cases at the start of the pandemic, but was spared a major epidemic until mid-January 1969.

d. Implications for the Next Pandemic.

The past three pandemics appeared suddenly and took the world by surprise. It is reasonable to expect that another novel influenza virus will emerge in the future and cause an influenza pandemic. Influenza A viruses persist in many different animals. Influenza A viruses normally seen in one species can sometimes cross over and cause illness in another species. This creates the possibility that a new virus will develop, either through mutation or mixing of different viruses, in turn creating the possibility for new viral strains that can be highly infective, readily transmissible, and highly lethal in humans.

The full impact of a potential influenza pandemic is difficult to quantify. How the virus will evolve cannot be predicted accurately. During earlier pandemics, significant variations were seen in mortality, severity of illness, and patterns of spread. However, each instance was characterized by a rapid surge and exponential increase in the number of cases within a very brief period of time.

New classes of effective, safe, anti-influenza drugs that were not available during the last pandemic are now available. Newer drugs are used widely for seasonal influenza. It is assumed that these drugs will work against a novel influenza virus subtype and these drugs will be a first line of defense during the first wave of a pandemic. However, if a pandemic arrives sooner rather than later, there may not be adequate stockpiled supplies of these drugs. It is also assumed that U.S. industry can produce adequate supplies of an effective pandemic vaccine, but there will be an inevitable delay of between four and six months between the emergence of a pandemic strain and the availability of a vaccine matched to the pandemic virus. Non-pharmaceutical interventions, such as school closure and other forms of social distancing, may play a significant role in slowing viral transmission especially if implemented broadly at the community level early in the pandemic. (Refer to Annex F – Community Intervention).

HHS estimates of morbidity, mortality, and healthcare utilization requirements for pandemics of different severity are noted below. Refer to Table 5.

Table 4: Aggregate Number of Episodes of Illness, Health Care Utilization, and Death During Moderate and Severe Influenza Pandemic Scenarios*		
Characteristic	**Moderate (1958/68-like)**	**Severe (1918-like)**
Illness	90 million (30%)	90 million (30%)
Outpatient medical care	45 million (50%)	45 million (50%)
Hospitalization	865,000	9, 900,000
Intensive Care Unit (ICU) care	128,750	1,485,000
Mechanical ventilation	64,875	745,500
Deaths	209,000	1,903,000
*Estimates based on extrapolation from past pandemics in the United States. Note that these estimates do not include the potential impact of modern interventions.		

While a pandemic will lead to a significant toll that is measured in human illness and death, its impact will extend far beyond hospitals, clinics, and doctors' offices. The impact of a pandemic will be pervasive, removing essential personnel from the workplace for weeks. Absenteeism across multiple sectors will threaten the functioning of critical infrastructure providers, the movement of goods and services, and operation of anchor institutions such as schools and universities. This has significant ramifications for the economy, national security, and the basic functioning of society.

The economic repercussions of a pandemic could be significant. The Congressional Budget Office has estimated that a pandemic on the scale of the 1918 outbreak could result in a loss of five percent of Gross Domestic Product, or a loss of national output of about $600 billion. A pandemic will affect the economy directly through illness and mortality caused by the disease and the associated lost output. It will also result in indirect costs, from actions taken to prevent and control the spread of the virus.

Refer to Avian Influenza: Assessing the Pandemic Threat (WHO, January 2005).

APPENDIX 2 (THE GLOBAL ENVIRONMENT)

1. INTERNATIONAL

The world may be on the brink of another influenza pandemic. Health experts have been monitoring a new and extremely severe influenza virus – the H5N1 strain. The H5N1 strain first infected humans in Hong Kong in 1997, causing 18 cases, including six deaths. Since mid-2003, this virus has caused the largest and most severe outbreaks in poultry on record. In December 2003, infections in people exposed to sick birds were identified.

As of 11 January 2008, 349 human cases have been laboratory confirmed in 14 countries in Asia, the Middle East, and Africa, and 216 (61.9%) of these people have died. Most cases have occurred in previously healthy children and young adults. To date, this virus has not spread easily from birds to humans, nor is there evidence of sustained human-to-human transmission. However, if H5N1 evolves to a form as contagious as seasonal influenza, a pandemic could begin.

a. The Disease in Birds.

Avian influenza is an infectious disease of birds caused by type A strains of the influenza virus. The disease occurs worldwide. While all birds are thought to be susceptible to infection with avian influenza viruses, many wild bird species carry these viruses with no apparent signs of harm. Other bird species, including domestic poultry, develop disease when infected with avian influenza viruses. In birds, the viruses cause two distinctly different forms of disease – one common and mild, the other rare and highly lethal. In the mild form, outbreaks can escape detection unless regular testing for viruses is in place. The second and far less common highly pathogenic form is difficult to miss. Highly pathogenic avian influenza (HPAI) is characterized by sudden onset of severe disease, rapid contagion, and a mortality rate that can approach 100% within 48 hours. In this form of the disease, the virus not only affects the respiratory tract, as in the mild form, but also invades multiple organs and tissues. All 16 HA (hemagluttinin) and nine NA (neuraminidase) subtypes of influenza viruses are known to infect wild waterfowl, thus providing an extensive reservoir of influenza viruses perpetually circulating in bird populations. In wild birds, routine testing

will nearly always find some influenza viruses. The vast majority of these viruses cause no harm.

To date, all outbreaks of HPAI in birds have been caused by viruses of the H5 and H7 subtypes. Highly pathogenic viruses possess a tell-tale genetic signature – a distinctive set of basic amino acids in the cleavage site of the HA – that distinguishes them from all other avian influenza viruses and is associated with their exceptional virulence. Not all virus strains of the H5 and H7 subtypes are highly pathogenic, but most are thought to have the potential to become so. Recent research has shown that H5 and H7 viruses of low pathogenicity can, after circulation for sometimes short periods in a poultry population, mutate into HPAI.

Considerable circumstantial evidence has long suggested that wild waterfowl introduce avian influenza viruses, in their low pathogenic form, to poultry flocks, but do not carry or directly spread highly pathogenic viruses. This role may, however, have changed very recently: at least some species of migratory waterfowl are now thought to be carrying the H5N1 virus in its highly pathogenic form and are introducing it to new geographical areas located along their migration routes.

Avian influenza viruses are readily transmitted from farm to farm by the movement of live birds, people (especially when shoes and clothing are contaminated), and contaminated vehicles, equipment, feed, and cages. Highly pathogenic viruses can survive for long periods in the environment, especially when temperatures are low.

For disease caused by HPAI, the most important control measures are rapid culling of all infected or exposed birds, proper disposal of carcasses, the quarantining and rigorous disinfection of farms, and the implementation of strict biosecurity measures. Restrictions on the movement of live poultry are another important control measure. The logistics of recommended control measures are most straightforward when applied to large commercial farms. Control is far more difficult under poultry production systems in which most birds are raised in small backyard flocks scattered throughout rural or around urban areas.

Culling is the first line of defense for containing outbreaks. If culling fails or proves impractical, vaccination of poultry in a high-risk area can be used as a supplementary

emergency measure, provided quality-assured vaccines are used. The use of poor quality vaccines or vaccines that poorly match the circulating virus strain may accelerate mutation of the virus. Poor quality animal vaccines may also pose a risk for human health, as they may allow infected birds to shed the virus while still appearing to be disease-free.

Outbreaks in backyard flocks are associated with a heightened risk of human exposure and infection. Poverty exacerbates the problem because households frequently prepare and consume poultry when deaths or signs of illness appear in flocks, which carries a high risk of exposure to the virus. Moreover, as deaths of birds in backyard flocks are common, for a variety of reasons owners may not interpret deaths or signs of illness in a flock as a signal of avian influenza and a reason to alert the authorities. This tendency may help explain why outbreaks in many rural areas have gone undetected for months. The frequent absence of compensation to farmers for destroyed birds further works against the spontaneous reporting of outbreaks and may encourage owners to hide their birds during culling operations.

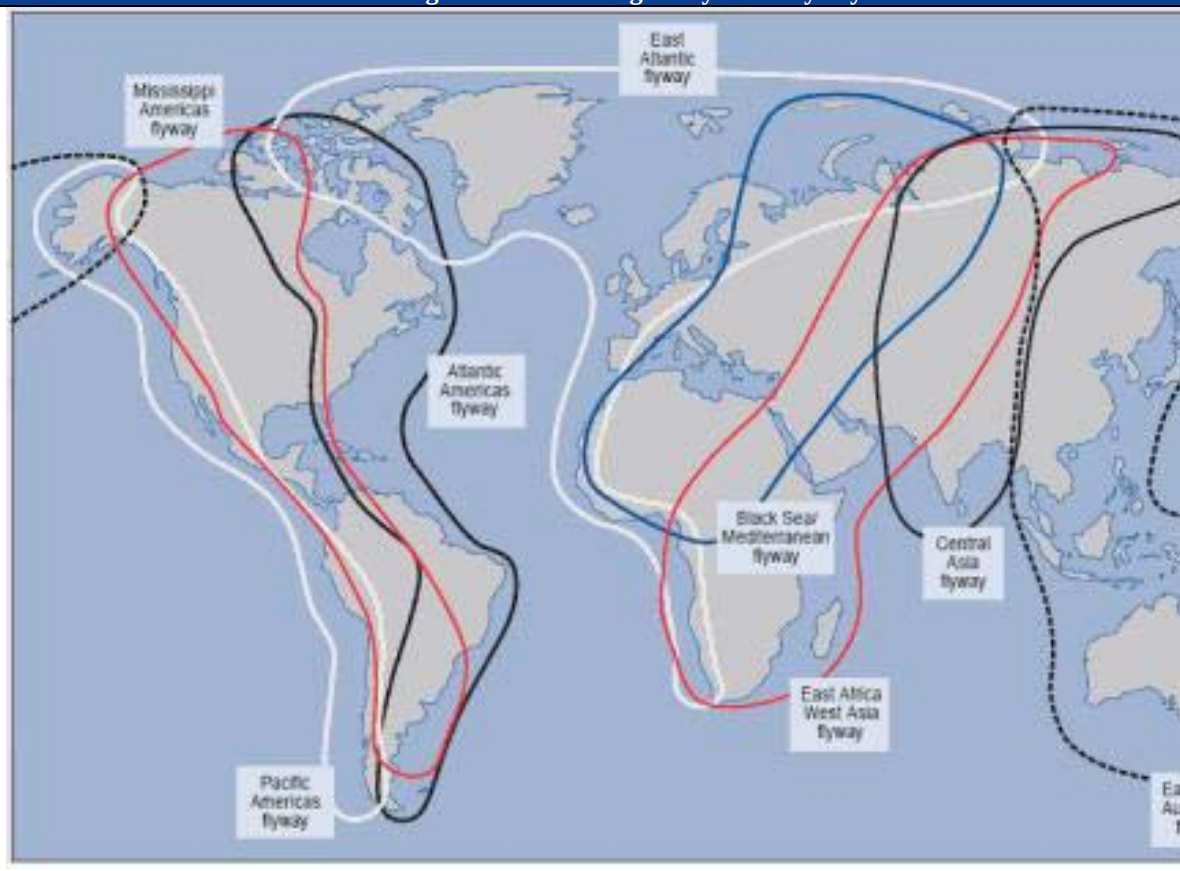
Extensive culling and vaccination of poultry have been effective, although temporary, strategies for halting avian and human H5N1 disease in some countries. Vietnam is an example of a country that aggressively culled and vaccinated domestic poultry in 2004-2005 after 90 human H5N1 cases were reported. No human case occurred in 2006, but new outbreaks in poultry were rediscovered in late 2006 (and have persisted into 2007) followed by new reports of human illness and death.

b. The Role of Migratory Birds.

Scientists are increasingly convinced that at least some migratory waterfowl are now carrying the H5N1 virus in its highly pathogenic form, sometimes over long distances, and introducing the virus to poultry flocks in areas that lie along their migratory routes (Figure 1). If this new role of migratory birds is scientifically confirmed, it will mark a change in a long-standing stable relationship between the H5N1 virus and its natural wild-bird reservoir. Evidence supporting this altered role began to emerge in mid-2005 and has since been strengthened. The death of more than 6,000 migratory birds, infected with the highly pathogenic H5N1 virus that began at the Qinghai Lake nature reserve in central China in late

April 2005, was highly unusual and probably unprecedented. Prior to that event, wild bird deaths from HPAI viruses were rare, usually occurring as isolated cases found within the flight distance of a poultry outbreak. Scientific studies comparing viruses from different outbreaks in birds have found that viruses from the most recently affected countries, all of which lie along migratory routes, are almost identical to viruses recovered from dead migratory birds at Qinghai Lake. Viruses from Turkey's first two human cases, which were fatal, were also virtually identical to viruses from Qinghai Lake. While migratory birds have played a significant role in global spread there is accumulating evidence in Southeast Asia that commercial poultry operations also play a significant role in inter-country spread. There is also the possibility that smuggling of infected poultry could contribute to the spread of avian influenza in commercial flocks.

Figure 1: Global Migratory Bird Flyways

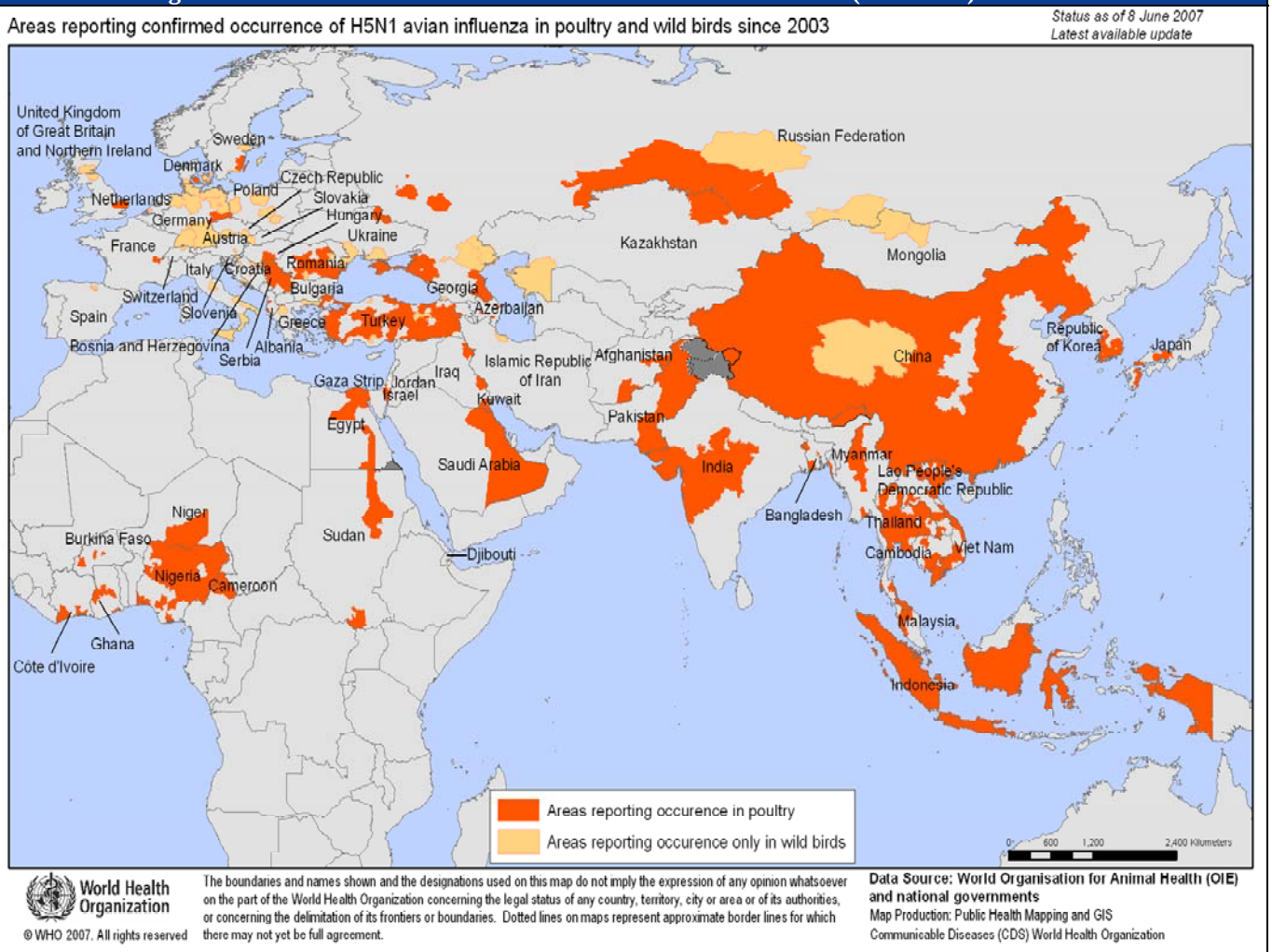


Source: United Nations Food and Agriculture Organization

c. COUNTRIES AFFECTED BY OUTBREAKS IN BIRDS.

As of 15 September 2007 Avian H5N1 has been confirmed in 66 countries throughout Asia, the Middle East, Europe, and Africa.

Figure 2: Nations with Confirmed Cases of H5N1 Avian Influenza (June 2007)



a.

Source: http://www.pandemicflu.gov

d. Countries with Human Cases in the Current Outbreak.

As of 11 January 2008, 349 human cases have been reported in 14 countries in Asia, the Middle East, and Africa. The first patients in the current outbreak, which were reported from Vietnam, developed symptoms in December 2003 but were not confirmed as H5N1 infection until 11 January 2004. Thailand reported its first cases on 23 January 2004. The first case in Cambodia was reported on 2 February 2005. The next country to report cases was Indonesia, which confirmed its first infection on 21 July 2005. China's first two cases were reported on 17 November 2005; subsequently China reported that additional study revealed a case in November 2003. Confirmation of the first cases in Turkey came on 5 January 2006, followed by the first reported case in Iraq on 30 January 2006. Indonesia experienced 33 confirmed cases and 25 deaths prior to 12 May 2006. Since then, the number of confirmed cases has increased to 116 with 94 deaths reported as of 3 January 2008. Azerbaijan confirmed its first human case on 14 March 2006.The first confirmed case in Africa occurred on 20 March 2006 in Egypt. A second African country (Djibouti) confirmed its first case on 12 May 2006. Nigeria experienced its first death from H5N1 on 31 January 2007. The Peoples Democratic Republic of Laos reported its first human case on 26 February 2007. WHO confirmed the first Myanmar human case on 14 December 2007. Most human cases have coincided with outbreaks of highly pathogenic H5N1 avian influenza in poultry. Although, ~60% of the laboratory-confirmed cases have been fatal, Influenza A H5N1 avian influenza in humans is still a rare disease. Refer to Figure 2 and Table 6.

b.

Table 5: Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO;3 January 2008												
Country	2003		2004		2005		2006		2007		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	8	5
Cambodia	0	0	0	0	4	4	2	2	1	1	7	7
China	1	1	0	0	8	5	13	8	5	3	27	17
Djibouti	0	0	0	0	0	0	1	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	25	9	43	19
Indonesia	0	0	0	0	20	13	55	45	42	34	117	94
Iraq	0	0	0	0	0	0	3	2	0	0	3	2
Laos PDR	0	0	0	0	0	0	0	0	2	2	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	1	1
Pakistan	0	0	0	0	0	0	0	0	1	1	1	1
Thailand	0	0	17	12	5	2	3	3	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	2	0	101	47
Total	4	4	46	32	98	43	115	79	86	58	349	216
WHO reports only laboratory-confirmed cases.												

e. The Disease in Humans.

Of all influenza viruses that circulate in birds, the Influenza A H5N1 virus is the greatest present threat to human health for two main reasons. First, the H5N1 virus has caused by far the greatest number of human cases of very severe disease and the greatest number of deaths. It has crossed the species barrier to infect humans on at least three occasions in recent years: in Hong Kong in 1997 (18 cases with six deaths), in Hong Kong in 2003 (two cases and one death) and in the current outbreaks that began in December 2003 and were first recognized in January 2004.

A second implication for human health, of far greater concern, is the risk that the H5N1 virus, if given enough opportunities, will develop the characteristics required to start another influenza pandemic. The virus has met all prerequisites for the start of a pandemic except

one: an ability to spread efficiently and in a sustained manner among humans. While H5N1 is presently the virus of greatest concern, the possibility that other avian influenza viruses known to infect humans might cause a pandemic cannot be ruled out.

During the first documented outbreak of human infections with H5N1, in Hong Kong, the 18 human cases coincided with an outbreak of HPAI, caused by a virtually identical virus in poultry farms and live markets. Extensive studies of the human cases determined that direct contact with diseased poultry was the source of infection. Human infections ceased following the rapid destruction of Hong Kong's entire poultry population, estimated at around 1.5 million birds. Some experts believe that the drastic action may have averted the beginning of an influenza pandemic at that time.

All evidence to date indicates that close contact with dead or sick birds is the principal source of human infection with the H5N1 virus. Especially risky behaviors identified include the slaughtering, de-feathering, butchering, and preparation for consumption of infected birds. In a few cases, exposure to chicken feces when children played in an area frequented by free-ranging poultry is thought to have been the source of infection. Swimming in water where the carcasses of dead infected birds have been discarded or which may have been contaminated by feces from infected ducks or other birds might be another source of exposure.

f. Clinical Features in Initial Human Cases.

In many patients, the disease caused by the H5N1 virus follows an unusually aggressive clinical course, with rapid deterioration and high fatality. Clinical data from cases in 1997 and the current outbreak are beginning to provide a picture of the clinical features of the disease, but much remains to be learned. The incubation period for H5N1 avian influenza may be longer than that for seasonal influenza, which is generally two to three days. Current data for H5N1 infection indicate an incubation period ranging from two to eight days and possibly as long as 17 days. However, the possibility of multiple exposures to the virus makes it difficult to define the incubation period precisely.

Initial symptoms include a high fever, usually with a temperature higher than 38°C (100.4°F), and influenza-like symptoms. Diarrhea, vomiting, abdominal pain, chest pain, and

bleeding from the nose and gums have also been reported as early symptoms in some patients. Watery diarrhea without blood appears to be more common in H5N1 avian influenza than in normal seasonal influenza. In two patients from southern Vietnam, the clinical diagnosis was acute encephalitis; neither patient had respiratory symptoms at presentation. In another case, from Thailand, the patient presented with fever and diarrhea, but no respiratory symptoms. All three patients had a recent history of direct exposure to infected poultry.

Many patients have symptoms in the lower respiratory tract when they first seek treatment. Difficulty in breathing develops around five days following the first symptoms. Respiratory distress, a hoarse voice, and a crackling sound when inhaling are commonly seen. Sputum production is variable and sometimes bloody. Most recently, blood-tainted respiratory secretions were observed in a patient in Turkey. Limited data on patients indicates the presence of a primary viral pneumonia in H5N1, usually without microbiological evidence of bacterial supra-infection at presentation. Turkish clinicians also reported pneumonia as a consistent feature in severe cases; as elsewhere, these patients did not respond to treatment with antibiotics.

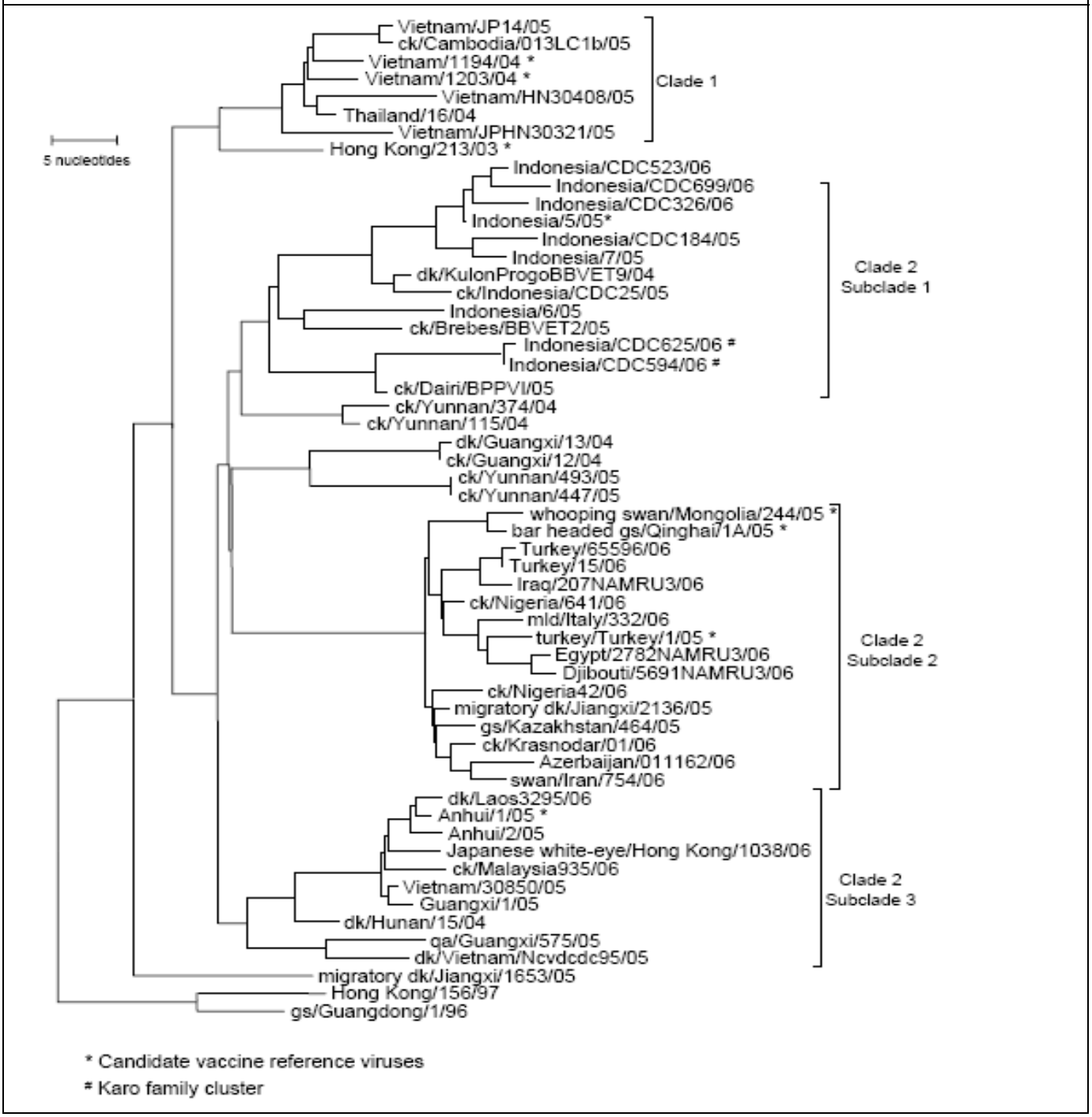
For treatment of seasonal human influenza, antiviral drugs, i.e., oseltamivir and zanamivir can reduce the duration of viral replication and speed the resolution of symptoms provided they are administered within 48 hours following symptom onset. Limited evidence suggests that these drugs can improve prospects of survival of humans infected with avian influenza virus. However, prior to the outbreak in Turkey, most patients were detected and treated late in the course of the illness. For this reason, clinical data on the effectiveness of oseltamivir are limited. Assembling the evidence on whether antiviral drugs would be more effective in treating human infection with H5N1 viruses, if given at higher doses and for longer periods of time than is recommended for seasonal human influenza, is an urgent priority and this is being undertaken by WHO. Refer to Avian Influenza Fact Sheet (WHO, February 2006) and http://www.who.int/mediacentre.

g. Genetic Characteristics of Recent H5N1 Viruses

The hemagglutinin (HA) sequences of the majority of H5N1 viruses circulating in avian species during the past 3 years separated into two distinct phylogenetic clades (genetic groups). Clade 1 viruses circulating in Cambodia, Thailand and Viet Nam were responsible for human infections in those countries during 2004 and 2005. Clade 2 viruses circulated in birds in China and Indonesia during 2003 – 2004 and subsequently during 2005 – 2006 spread westwards to the Middle East, Europe and Africa. This latter genetic group of viruses has been principally responsible for human infections during the later part of 2005 and 2006. Six sub-clades of clade 2 have been distinguished, three of which (subclades 1, 2, and 3) also differ in geographical distribution and have been largely responsible for human cases in Indonesia, in countries in the Middle East, Europe and Africa, and in China, respectively (Figure 3: Evolution of the H5N1 hemagglutinin gene (Clade Diagram)).

These avian viruses lack the ability to spread easily from person-to-person (and in some cases did not produce a severe human infection) and therefore have not precipitated larger outbreaks or a pandemic. Pandemic viruses can also arise due to genetic re-assortment between human and animal influenza viruses. This can occur when a single animal or person is co-infected by both a human influenza virus and an avian influenza virus. Re-assorted viruses have been frequently identified and are thought to have been responsible for the 1957 and 1968 pandemic viruses.

Figure 3: Evolution of the H5N1 Hemagglutinin Gene (Clade Diagram)



2. NATIONAL

a. HPAI Influenza A H5N1 has not been detected either in wild, domestic, or commercial animals, or humans in the United States. Based upon the historical experience, computer modeling, and given the ease, speed, and frequency of international travel, a pandemic influenza virus is very likely to spread rapidly to the United States with the onset of the next pandemic.

b. It is clear that an influenza pandemic has the potential to pose disease control challenges unmatched by any other natural or intentional infectious disease event. Without adequate planning and preparations, an influenza pandemic in the 21st Century has the potential to cause enough illnesses to overwhelm current public health and medical care capacities at all levels.

c. Several factors are critical to understanding the potential impact of a pandemic in the United States. First, the United States' population is large and increasingly urbanized and concentrated, allowing viruses to be transmitted easily within populations. Second, levels of international travel are much greater than in the past, allowing viruses to quickly spread globally. Third, the U.S. population is comprised of increasing numbers of immunocompromised persons, elderly persons, and persons with chronic medical conditions, thus increasing the potential for more complicated illnesses and deaths to occur. This combination of factors suggests that the next pandemic may lead to more illnesses occurring quicker than in the past, overwhelming the country and its health systems if it is not adequately prepared.

APPENDIX 3 (DISEASE INTELLIGENCE COLLECTION PLAN)

THIS DISEASE INTELLIGENCE COLLECTION PLAN IS MADE UP OF FOUR DISTINCT PARTS:

1) A description of international disease surveillance and monitoring activity.
2) A description of domestic disease surveillance and monitoring activity.
3) A comprehensive list of sources of disease intelligence including internal CDC sources, other USG sources, international sources, SLTT, and non-government organization sources.
4) A collection plan tasking/requesting matrix that captures the collection requirement, the agencies capable of responding to the requirements, and the status of the tasking or request for such information.

1. INTERNATIONAL DISEASE SURVEILLANCE AND MONITORING

Reference: Implementation Plan for the National Strategy for Pandemic Influenza, Chapter 4

a. SITUATION

1) Avian Influenza A (H5N1) is currently the major pandemic threat and the current focus of global surveillance and containment efforts.
2) Rapid containment of avian Influenza A (H5N1) outbreaks in poultry is likely to be the most effective method for preventing spread to other countries, reducing opportunities for avian-to-human infection, and developing of sustained human-to-human transmission.
3) Efficient and sustained human-to-human transmission of a novel Influenza A virus such as H5N1 may signal an imminent pandemic.

b. AGREED EPIDEMIOLOGICAL "TRIGGER" FOR INTERNATIONAL RESPONSE AND CONTAINMENT

WHO stated that containment will be strongly considered in the following circumstances:

1) Moderate to severe respiratory illness (or deaths) in three or more health care workers who have no known exposure other than contact with ill patients, and laboratory confirmation of infection (novel influenza virus) in at least one of these workers.

2) Moderate-to-severe respiratory illness (or deaths) in 5 to 10 persons with evidence of human-to-human transmission in at least some, and laboratory confirmation of infection (novel influenza virus) in more than two of these persons.
3) Compelling evidence that more than one generation of human-to-human transmission of the virus has occurred.
4) Isolation of a novel (influenza) virus combining avian and human genetic material or a virus with an increased number of mutations not seen in avian isolates from one or more persons with moderate-to-severe respiratory illness (acute onset) supported by epidemiological evidence that transmission patterns have changed.
5) Community outbreaks of human H5N1 infection (e.g., >5 cases not involving members of the same household).
6) One or more instances of sustained human-to-human transmission.

c. SURVEILLANCE FOR AND CONTAINMENT OF A POTENTIALLY PANDEMIC INFLUENZA A SUBTYPE IS DEPENDENT ON:

1) The rapidity of initial discovery of avian infections/deaths due to HPAI.
2) The rapidity of initial discovery of human infections/deaths suspected of being related to HPAI.
3) The rapidity of confirmation of a novel influenza subtype as the etiologic agent of these human infections/deaths.
4) The rapidity of effective human containment efforts.
5) Determining the etiology of these human infections; i.e., avian (or other mammalian species)-to-human transmission vs. human-to-human transmission.
6) Containment of H5N1 outbreaks (animal and human) in the country or region of origin is of primary importance. When a case or cluster of human H5N1 infection is detected, ongoing local disease surveillance efforts must be sufficiently robust to evaluate the effectiveness of community containment efforts. If local efforts are insufficient, public health authorities must be prepared to support ongoing surveillance efforts in the affected country or region. Country laboratories are key assets for detecting and confirming novel

influenza strains. If sustained human-to-human spread of H5N1 is detected, the international public health community must be prepared to assist the affected country by mounting a major effort to contain or slow the spread of disease.

c. MISSION. Limit spread of pandemic influenza virus in animals, prevent animal-to-human and human-to-human spread outside the United States, and delay or prevent introduction of the virus into the United States.

e. CONCEPT OF OPERATIONS

1) It is anticipated that WHO will coordinate global efforts to detect and report suspected cases using standardized case definitions and reporting protocols.

2) Obtain reports on potential cases of pandemic influenza from public health and veterinary authorities, poultry workers, and the public.

3) Engage non-traditional groups such as nature societies, the media, and civic organizations in avian influenza surveillance activities.

4) Ensure that cases and clusters of human infection with H5N1 are promptly detected, reported, and investigated.

5) Identify patients with risk factors for disease caused by pandemic influenza.

6) Detect each and every case and cluster (family, healthcare, or institutional) especially during the Pandemic Alert Period (WHO Phases 3, 4, 5).

7) Coordinate village-based human influenza surveillance systems in affected regions.

8) Use enhanced laboratory capacity to confirm suspected cases and clusters of human infection with avian influenza.

9) Sequence the genomes of avian influenza isolates from humans to detect changes that might affect human-to-human transmissibility (e.g., re-assortment or changes in receptor binding sites).

10) Investigate suspected avian Influenza A (H5N1) outbreaks in poultry.

2. DOMESTIC DISEASE SURVEILLANCE AND MONITORING

References: Implementation Plan for the National Strategy for Pandemic Influenza – Chapters 5 & 6.

a. SITUATION

1) All persons living in the U. S. will be susceptible to infection and illness caused by a pandemic influenza virus. Surveillance systems will identify initial cases, facilitate the collection of clinical specimens for virus sub-typing and isolation, and assist in monitoring the disease burden throughout the country and in all age, socioeconomic, racial, and ethnic groups.

2) During a pandemic (WHO Phase 6), the clinical attack rate will be 30%. Fifty percent of the individuals who become ill will seek medical advice and/or treatment. Surveillance should focus on healthcare settings to make surveillance feasible and sustainable.

3) Risk groups for severe disease and deaths cannot be predicted before a pandemic begins. Surveillance systems are critical to creating ongoing situational awareness and should be comprehensive to allow monitoring of the disease and its complications, including deaths among all age, socioeconomic, racial, and ethnic groups. It should be flexible to allow modifications to focus on specific subgroups, if necessary.

4) In an affected community, an initial pandemic wave will last for approximately six to eight weeks. The surveillance needs or focus in each community may change during the course of a pandemic from ensuring rapid detection of first cases and collection of clinical samples for typing to monitoring spread and disease burden, to recognizing the end of the pandemic period.

5) The seasonality cannot be predicted. Sensitive, timely surveillance established in advance of the introduction of a novel influenza virus subtype in the United States will be critical to detect the introduction of the virus. Therefore, pre-pandemic surveillance and classified exchange of surveillance data with the cooperation of USG partners should operate year-round. However, it will be more difficult to detect and evaluate the impact of the virus responsible for the pandemic if it occurs concurrently with seasonal influenza.

6) An influenza pandemic occurring in the next few years will likely be caused by Influenza A (H5N1) and will originate outside of the United States. However, the ability to detect any novel influenza subtype will be available.

7) Surveillance-related activities will vary under different situations and appropriate adjustments will be made to meet those needs.

b. MISSION.

Provide timely and accurate information on the introduction, spread, and impact of a pandemic virus in animals and humans in the United States; characterize its epidemiologic, clinical, and virologic characteristics; and determine the evolution of genetic and antigenic variants of the virus.

c. CONCEPT OF OPERATIONS

1) Establish, enhance, or utilize sensitive, timely, and comprehensive laboratory, epidemiologic, and clinical information systems and sources required to reliably detect and monitor the occurrence of pandemic influenza among initial human cases as well as widely affected communities.

2) Ensure that testing by real time reverse transcriptase – polymerase chain reaction (RT-PCR) for H5N1 and other influenza viruses with pandemic potential is available at state public health laboratories, LRN laboratories, and CDC.

3) Provide guidance to ensure that Federal, SLTT, and private sector medical facilities have protocols in place for transporting influenza specimens to appropriate LRN reference laboratories.

4) Mitigate sustained transmission of pandemic influenza in the general population.

5) Assess effectiveness of treatment guidelines, vaccines, antiviral drugs, and public health interventions.

6) Determine antigenic and genetic changes in circulating influenza viruses over time, particularly for possible antiviral and vaccine resistance patterns.

7) Monitor and report all adverse events related to use of antiviral drugs or vaccine.

8) Provide ongoing information from the national influenza surveillance system on a pandemic's impact on health and the healthcare system.

3. LIST AND DESCRIPTION OF EACH POTENTIAL REPORTING AGENCY THE U.S. INFLUENZA SURVEILLANCE SYSTEM

a. Allows CDC to:

1) Find out when and where influenza activity is occurring.
2) Determine what type and subtype of influenza viruses are circulating.
3) Detect changes in the influenza viruses.
4) Track influenza-related illness.
5) Measure the impact influenza is having on severe complications and deaths in the United States.
6) Monitor antiviral resistance of circulating strains.

b. CDC, STATE, LOCAL, TERRITORIAL, AND TRIBAL SOURCES

1) CDC Seasonal Influenza Surveillance System.

This system collects and reports virus, morbidity, and mortality information on influenza activity in the United States each week from October through May. CCID (NCIRD and NCPCCID) is responsible for this system. Sources of information include:

a) Laboratory Surveillance.

About 75 WHO and 50 NREVSS collaborating laboratories located throughout the United States report the total number of respiratory specimens tested and the number of positive for influenza types A and B each week. Some laboratories also report the Influenza A subtype of the viruses they have isolated and the ages of the persons from whom the specimens were collected. Some of the influenza viruses collected by laboratories are sent to the CDC for more testing.

b) Pneumonia and Influenza Mortality Surveillance.

Each week, the vital statistics offices of 122 cities report the total number of death certificates filed and the number of those for which pneumonia or influenza was listed as the underlying or as a contributing cause of death. The percentage of all

deaths due to pneumonia and influenza are compared with a baseline and epidemic threshold value calculated for each week.

c) Influenza – Associated Pediatric Mortality.

Influenza-associated pediatric mortality is a newly added nationally notifiable condition. Laboratory confirmed influenza-associated deaths in children less than 18 years old are reported through the Nationally Notifiable Disease Surveillance System (NNDSS).

d) Influenza-Associated Pediatric Hospitalization.

The New Vaccine Surveillance Network (NVSN) provides population based estimates of laboratory confirmed influenza hospitalization rates for children less than five years old residing in three counties: Hamilton County, OH; Davidson County, TN; Monroe County, NY. Children admitted to NVSN hospitals with fever or respiratory symptoms are prospectively enrolled and respiratory samples are collected and tested by viral culture and RT-PCR. NVSN estimated rates are reported every two weeks.

e) Influenza-Like Illness Surveillance.

Each week approximately 1,000 health care providers around the country report the total number of patients seen and the number of those patients with influenza-like illness (ILI) by age group. For this system, ILI is defined as fever (temperature of >100 degrees F) plus either a cough and/or a sore throat.

f) Emerging Infections Program (EIP).

The EIP Influenza Project conducts surveillance for laboratory-confirmed influenza related hospitalizations in persons less than 18 years of age in 57 counties covering 11 metropolitan areas of 10 states. Cases are identified by reviewing hospital laboratory and admission databases and infection control logs for children with a documented positive influenza test conducted as part of routine patient care.

g) State Influenza Activity Reports.

State epidemiologists report levels of influenza activity in their jurisdictions each week. Influenza activity is reported as no activity, sporadic, local, regional, or widespread.

2) Laboratory Response Network (LRN).

CDC works with LRN to develop protocols for sub-typing of influenza and to provide diagnostic reagents to national, state, and local public health laboratories required for timely and accurate diagnosis of pandemic influenza virus. (NCPDCID)

3) Reports of Influenza-like Illnesses on Arriving Conveyances.

Investigates reports of influenza-like illness among passengers arriving at U.S. ports of entry. (CCID)

4) BioSense.

Provides data on influenza activity primarily through collection of close to real time electronic data from sentinel hospital emergency departments and in-patient and out-patient departments. (CCHIS-NCPHI)

5) COGH-Global Disease Detection (GDD)

Serves as the CDC centralized clearinghouse for global pandemic-related influenza outbreak data.

6) OSEP.

Provides classified medical, public health, political, and infrastructure documents as appropriate.

c. UNITED STATES GOVERNMENT AGENCIES

1) U.S. Department of the Interior.

Monitors influenza in wild animals including migratory birds. DOI will also conduct investigations on dead animals and birds to detect whether the cause of death was due to influenza virus infection.

2) **U.S. Department of Agriculture.**

Conducts surveillance in poultry and other commercial farm animals. It will investigate suspected avian influenza outbreaks in poultry and recommend containment measures.

3) **U.S. Department of State.**

Will provide relevant information on an influenza pandemic from around the world through its extensive network of information gathering resources.

4) **U.S. Department of Defense.**

Provides disease intelligence and monitoring through several key medical service hubs and overseas laboratories. DOD has established strong working relationships with the CDC and international health agencies.

a) **U.S. Department of Defense Global Emerging Infections Surveillance and Response System. (DOD-GEIS)**

Operates a central hub system that leverages the surveillance and response assets of a network of DOD service hubs and overseas medical research units (NAMRU-2 Jakarta, NAMRU-3 Cairo, AFRIMS Bangkok, USAMRU Kenya, and NMRCD Lima).

b) **U.S. Army Center for Health Promotion and Preventive Medicine.**

Provides worldwide technical support for implementing military preventive medicine, public health, and health promotion/wellness services.

c) **U.S. Army Medical Research Institute of Infectious Diseases.**

Participates in support of emerging disease investigations, to protect military personnel and civilians from the threat of infectious diseases.

d) **Naval Medical Research Center.**

Participates in support of emerging disease investigations to protect military personnel and civilians from the threat of infectious diseases.

e) Naval Environmental Health Center.

Ensures Navy and Marine Corps readiness through leadership in prevention of disease and promotion of health to include updated preventive medicine and vector-borne disease profiles of countries of military importance.

f) U.S. Air Force General Surveillance Office.

Operates the DOD Influenza Surveillance Program to: (1) detect local respiratory outbreaks; (2) provide isolates to the World Health Organization; (3) detect emerging strains.

g) U.S. Armed Forces Medical Intelligence Center.

Analyzes and disseminates finished intelligence on foreign disease and environmental conditions through the Defense Intelligence Agency (DIA) and the National Biosurveillance Integration Center (NBIC) in coordination with HHS and CDC. The exchange of classified data will take place via the secure communications and networks within the CDC SCIF.

d. INTERNATIONAL SOURCES

1) WHO-Global Influenza Surveillance Network (GISN).

Laboratories located throughout the world report the total number of respiratory specimens tested and the number positive for influenza types A and B each week. Some laboratories also report the Influenza A subtype (H1N1 or H3N2) of the viruses they have isolated and the ages of the persons from whom the specimens were collected. Some of the influenza viruses collected by laboratories are sent to CDC for more testing.

2) Field Epidemiology Training Program (FETP).

Will assist and work with GDD to provide timely and accurate surveillance of an influenza pandemic.

3) International Emerging Infections Programs (IEIPs).

Will assist and work with GDD to provide timely and accurate detection and reporting on pandemic influenza.

4) **Regional Emerging Disease Intervention (REDI) Center in Singapore.**

Will obtain, analyze, and report influenza surveillance data and conduct outbreak investigations to determine the extent and cause of outbreak.

5) **US-China Collaborative Program on Emerging and Re-Emerging Infectious Diseases (US-CCPERID).**

Will obtain, analyze, and report influenza surveillance data and conduct outbreak investigations to determine the extent and cause of outbreak.

6) **Food and Agriculture Organization (FAO).**

Will provide ongoing surveillance in poultry and other commercial farm animals. Will investigate suspected avian influenza outbreaks in poultry and advise on containment measures around the world.

7) **World Organization for Animal Health (OIE).**

Will carry out ongoing surveillance in poultry and other commercial farm animals. Will investigate suspected avian influenza outbreaks in poultry and advise on containment measures around the world.

e. NON-GOVERNMENTAL ORGANIZATIONS (NGO)

1) **International Red Cross (IRC).**

Will provide information on any unusual disease activity to WHO for further monitoring and investigation.

2) **American Red Cross (ARC).**

Will encourage reporting and provide information on any unusual disease activity to WHO for further monitoring and investigation.

3) **Doctors without Borders (MSF).**

Will provide information on any unusual disease activity to WHO for further monitoring and investigation.

4) **Village Volunteers.**

Will provide information on any unusual disease activity to WHO for further monitoring and investigation.

4. DISEASE INTELLIGENCE COLLECTION PLAN MATRIX. (SEE TABLE 6, NEXT PAGE)

Table 6: Disease Intelligence Collection Plan Matrix (Fold Out)

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APPENDIX 4 (LABORATORY SERVICES)

1. SITUATION

a. Laboratory services are required to develop appropriate and specific diagnostic tests and make them available to various laboratories involved in monitoring and diagnosis of pandemic influenza infection. These services are critical for effective disease surveillance. When combined with other disease related information, they can provide essential and accurate situational awareness.

b. Pre-pandemic planning is essential to ensure the timeliness of diagnostic testing and the availability of diagnostic supplies and reagents, address staffing issues, and disseminate protocols for safe handling and shipping of specimens. Once a pandemic is underway, the need for laboratory confirmation of clinical diagnoses may decrease as the virus becomes widespread.

2. MISSION.

Through diagnostic testing, identify the earliest U. S. cases of an influenza pandemic, support disease surveillance to monitor the pandemic's geographic spread and impact of interventions, facilitate clinical treatment by distinguishing patients with influenza from those with other respiratory illnesses, and monitor circulating viruses for antiviral and vaccine resistance.

3. EXECUTION

a. Concept of Operations.

Laboratory services within CCID will monitor preparedness and laboratory capacity for seasonal influenza and assess surge capacity. Additionally, CCID laboratories will provide technical support to the WHO Influenza Network and international ministries of health and agriculture in analyzing novel avian and human influenza virus isolates with pandemic potential for their antigenicity, Ribonucleic Acid (RNA) sequence, and drug sensitivities, work with SLTT laboratories to ensure that diagnostics for identifying "pandemic alert" strains are available and are used safely and effectively, and provide guidance on biosafety

and safe handling of clinical specimens from potential influenza pandemic related cases. Further, it will interact with FDA to expedite the approval process or seek exemptions for new diagnostics, and other licensure and IDE related issues. This approach will be continuously monitored through all phases/stages of a pandemic and reassessed/changed as required.

b. Tasks to be Performed by CCID During the Inter-Pandemic and Pandemic Alert Periods (WHO Phases 4-6; U. S. Stages 1-6).

1) Provide Support for Laboratories for Seasonal Influenza Surveillance:

CCID will assist SLTT public health laboratories and clinical laboratories to participate in laboratory-based surveillance for new subtypes of influenza through the U. S. -based laboratories in the World Health Organization Global Influenza Surveillance network (WHO-GISN), the National Respiratory and Enteric Virus Surveillance System (NREVSS) and others.

2) Facilitate Laboratory Testing for Novel Influenza Subtypes:

CCID will facilitate proper use of diagnostic testing for a pandemic influenza virus involving a range of laboratory assays, including rapid antigen tests, reverse-transcriptase polymerase chain reaction (RT-PCR), virus isolation, and immunofluorescence antibody (IFA) assays.

a) CCID will provide guidance to SLTT partners, hospitals, and clinicians to enhance their surveillance to identify patients who may present with possible cases of novel influenza, and help prepare to process and test specimens from suspected cases of infection with:

(1) Avian Influenza A (H5N1) and other avian influenza viruses.

(2) Other animal influenza viruses (e.g., swine influenza viruses).

(3) New or re-emergent human influenza viruses (e.g., H2) with pandemic potential.

(4) CCID should provide appropriate assistance when contacted by SLTT health departments after receiving reports of suspected human infection with novel

Influenza A virus from clinicians. CCID will be contacted via the CDC Emergency Response Hotline: 770-488-7100.

3) Assist in Testing for Human Cases of Avian Influenza:

Recommendations on laboratory testing for human cases of avian influenza are as follows:

a) CCID should provide guidance on transport of specimens from suspected cases of human infection with novel influenza viruses for testing to public health laboratories with proper biocontainment facilities.

b) CCID will receive specimens from suspected human cases of avian influenza to identify and subtype Influenza A viruses (e.g., H1, H3, H5, and H7) from public health laboratories that lack appropriate bio-containment facilities.

4) Assist in Testing for Human Influenza Strains with Pandemic Potential:

During the Pandemic Alert Period, diagnostic laboratories will be on the alert for new human subtypes of influenza with pandemic potential and CCID should coordinate either directly, or through the SLTT laboratories, the following activities:

a) SLTT public health laboratories that can detect human and avian influenza subtypes by RT-PCR should report all unusual subtypes to CCID.

b) Public health laboratories that can detect human (but not avian) influenza subtypes by Immunofluorescence antibody (IFA) staining or Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) should send Influenza A isolates that cannot be sub-typed to CCID.

c) Public health laboratories should send specimens to CCID if a patient meets the clinical and epidemiological criteria for infection with a novel influenza virus.

d) If new or re-emergent human influenza strains with pandemic potential are suspected, laboratories should conduct RT-PCR only under BioSafety Laboratory (BSL-2) containment conditions and viral culture only under BSL-3 conditions. Handing certain isolates, such HPAI, will require working in BSL-3 with enhancements; otherwise specimens must be sent to CCID.

5) Laboratory Reporting:

SLTT health departments that report laboratory-confirmed seasonal influenza cases to CCID use a variety of reporting mechanisms, including faxes, the Public Health Information System (PHLIS), and a web-based NREVSS data-entry system. Cases of novel influenza should be reported to CCID by the same mechanisms.

6) Distribution of Diagnostic Reagents and Test Information:

CCID will continue to work with USDA and FDA to address any regulatory barriers to emergency distribution and use of diagnostic tests and reagents during a pandemic. CCID will provide updated preparedness information regarding diagnostic tests and reagents to SLTT public health partners via the Laboratory Response Network (LRN), Association of Public Health Laboratories (APHL), and Health Alert Network (HAN).

7) Laboratory Planning to Support the Response to an Influenza Pandemic:

CCID should assess projected needs for scaled-up diagnostic activity during the early stages of a pandemic, in terms of its laboratory staffing, training, reporting, and supplies, and should develop strategies to address them. CCID should also provide guidance to SLTTs for their planning concerning these issues. Some aspects of this planning, such as surge capacity planning, can be coordinated with bioterrorism preparedness planning.

a) Staffing and Training:

CCID should plan for its own laboratories, and assist SLTTs through guidance, for increased staffing needs. Cross-training personnel during the regular influenza season in the use of rapid diagnostic tests and RT-PCR protocols and in reporting results should be considered. They should also consider recruiting and training temporary staff for employment during a pandemic.

b) Supplies and Equipment:

All diagnostic laboratories are likely to require additional diagnostic supplies and equipment to process large numbers of samples during the initial stages of a pandemic. Preparedness strategies include:

(1) Establish the current level of diagnostic supplies, including PPE for laboratory personnel (e.g., gloves, masks).

(2) Assess anticipated equipment and supply needs, and determine a trigger point for ordering extra resources. Laboratories should also consider the need for back-up sources of supplies if most laboratories in a State or large city rely on the same manufacturer for particular supplies or equipment.

(3) Determine how consumption of supplies will be tracked during a pandemic.

c) Specimen Management:

Laboratory staff should anticipate receiving a much larger number of specimens in a very short time.

8) Partnerships with Healthcare Providers and Clinical Laboratories:

CCID should continue to build partnerships with healthcare providers, including physicians who participate in the Sentinel Provider Network (SPN) and public health laboratories during the regular influenza season.

a) Assist Clinical and Hospital Laboratories:

(1) Work with SLTT health departments to address laboratory surge capacity issues and train personnel.

(2) Provide guidance on the shipment of clearly labeled specimens from patients with suspected novel influenza to SLTT health departments. Advise hospital laboratories NOT to attempt to isolate influenza viruses from patients with suspected novel influenza virus infection.

(3) Assist in instituting surveillance for influenza-like illnesses (ILI) among laboratory personnel working with novel influenza viruses.

b) Assist State and Local Public Health Laboratories:

(1) Help enhance laboratory-based monitoring of seasonal influenza virus subtypes.

(2) Help conduct testing for novel subtypes of influenza viruses only if BSL-3 laboratories (with enhancements when appropriate; i.e., while working with HPAI) are available.

(3) Assist in instituting surveillance for ILI among laboratory personnel.

(4) Help conduct preparedness planning to support the response to an influenza pandemic.

c. TASKS TO BE PERFORMED DURING THE PANDEMIC PERIOD.

1) General Responsibilities of CCID:

a) Work with U. S. and global partners to characterize new influenza pandemic viruses in terms of antigenicity, RNA sequence, and drug susceptibility, and to monitor changes over time.

b) Provide guidance to diagnostic and SLTT public health laboratories to ensure the availability, and the safe and effective use of diagnostic tests and reagents.

c) Provide guidance for, and when requested, testing of positive samples, and performing viral isolation, especially at the beginning of a pandemic.

d) Provide laboratory support for the selection of seed strains to be used in a vaccine against the pandemic virus.

e) Provide situational reports on current status of international and domestic laboratory capacities and shortfalls that would prevent labs from conducting testing.

2) Laboratory Support for Disease Surveillance:

a) CCID will develop the required diagnostic tests and make them available. CCID and the LRN will work with SLTT public health departments to make diagnostic testing for the pandemic virus readily available, both at CCID and at SLTT public health laboratories that have implemented RT-PCR protocols.

b) As soon as a pandemic strain has been identified, the CCID Influenza Laboratory will develop, produce, and disseminate RT-PCR and IFA reagents, as needed. As

necessary, CCID and the APHL will also update the RT-PCR protocol currently available to public health laboratories through the APHL website.

c) As the pandemic continues, CCID will advise SLTTs on when confirmatory testing (i.e., sub typing) is required. This would require planning for surge capacity. Although confirmatory testing will be required when the pandemic begins, the level of testing will decrease as the virus becomes widespread.

d) CCID will advise SLTTs on the percentage of isolates per week or month that they should send to CCID as part of efforts to monitor changes in the antigenicity and antiviral susceptibility of the pandemic virus. Throughout the pandemic, CCID will provide updated instructions on the collection of clinical and epidemiological data that should accompany isolates. CCID could ask some SLTT public health laboratories to perform virus isolation or RT-PCR sub typing before sending specimens to CCID.

e) CCID will work with the U. S.-based WHO collaborating laboratories, NREVSS laboratories, and/or Emerging Infectious Program sites to conduct special studies or establish additional laboratory-based surveillance systems.

3) Laboratory Support for Clinicians:

CCID will assist public health laboratories to scale up to manage increased numbers of requests for influenza testing. As part of this effort, CCID will work with SLTT public health laboratories and the LRN to provide clinical laboratories with guidelines for safe handling, processing, and rapid diagnostic testing of clinical specimens from patients who meet the case definition for influenza pandemic. APHL and CDC will work together with the clinical laboratory community to determine effective strategies for clinical laboratory testing and their possible role for providing surge capacity for novel influenza virus testing during a pandemic. If private laboratories perform RT-PCR testing during the early phase of an influenza pandemic, the results should be confirmed in consultation with the state public health laboratory. SLTT health laboratories should provide guidance

to healthcare providers on specimen submission and shipment, laboratory result reporting, and use of commercial tests.

4) Biocontainment Procedures:

a) During an influenza pandemic, laboratory procedures should be conducted under appropriate biosafety conditions.

b) Commercial antigen detection testing for influenza should be conducted using BSL-2 work practices.

c) RT-PCR testing may be conducted using BSL-2 work practices and virus isolation using BSL-3 practices (with enhancements when required; i.e., working with HPAI).

5) Occupational Health Issues Related to Laboratory Workers:

a) To protect the health of laboratory workers during a pandemic, public health, clinical, and hospital laboratories should maintain the safety practices used during the Inter-pandemic and Pandemic Alert Periods.

b) Laboratory procedures should be under appropriate biocontainment conditions.

c) Routine vaccination with seasonal vaccine of all eligible laboratory personnel who are exposed to specimens from patients with respiratory infections should be encouraged.

6) Partnerships with Healthcare Providers and Clinical Laboratories:

CCID should provide continued guidance and assistance to SLTT public health laboratories, and to clinical and health care laboratories through APHL.

a) Clinical and Hospital Laboratories:

(1) Provide guidance and support that will be required to scale up and manage increased numbers of requests for influenza testing.

(2) Provide guidance on shipment of selected specimens from possible influenza pandemic patients to SLTT health departments.

b) SLTT Public Health Laboratories:

(1) Scale up to manage increased numbers of requests for influenza testing.

(2) Provide guidelines on all aspects of specimen management and diagnostic testing to healthcare providers and clinical laboratories.

(3) Monitor the pandemic virus and conduct special studies related to vaccine development, or other aspects of the response