Surveillance and Control of Human Cases of Avian Influenza

Provisional Guidelines for Public Health Services in Ukraine

First Edition, June 2007

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With technical support provided by:
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US Centers for Disease Control and Prevention
World Health Organization
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Abstract

Outbreaks of highly pathogenic avian influenza are occurring in domestic fowl in many countries, posing a considerable human public health risk. The outbreaks are largely caused by a novel H5N1 strain of influenza A, against which people are not immune. The H5N1 viruses have been able to cross the species barrier and infect humans, causing severe disease with high mortality. The ability of these viruses to rapidly mutate and acquire genes from viruses affecting other species raises the concern that they will gain the ability to spread efficiently among humans and cause a global influenza pandemic.

The early detection of cases of H5N1/novel influenza in humans plays a critical role in combating a potential pandemic. The main benefits of having ascertained clear and fast recognition of transmission to human beings include:

- Prompt implementation of public health and medical interventions aimed at preventing, delaying, or containing human-to-human virus transmission.
- More effective medical care of infected individuals, resulting in reduced mortality.
- Reduced economic and social impact of a potential pandemic.

The guidelines outlined in this report provide comprehensive recommendations to help Ukrainian health care workers promptly identify, report, confirm, and classify potential cases of avian influenza in humans; analyze data; investigate and respond to cases and outbreaks; and improve other aspects of an early warning system for humans. They are most appropriate for the current and the next stages of pandemic preparedness (phases 3 and 4 of the World Health Organization [WHO] Pandemic Alert Period) and designed primarily for health care personnel working at rayon and regional sanitary-epidemiological stations. In addition to general recommendations for the human avian influenza surveillance system as a whole, the guidelines include specific sections devoted to communication with the public as well as infection control in health facilities.

Based on the latest WHO standards and recommendations, this edition was developed by a multi-agency task force of experts under the leadership of the Ukrainian Ministry of Health. The guidelines will be piloted in Odesa oblast in 2007. Periodic revisions are expected as more evidence and feedback from users become available.
Contributors

This manual was prepared by the Ministry of Labor, Health, and Social Affairs multi-agency task force headed by Serhiy Berezhnov, the First Deputy Minister of Ukraine, with technical assistance from PATH and the US Centers for Disease Control and Prevention.

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<table>
<thead>
<tr>
<th>Acronyms</th>
<th>Definition</th>
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<tbody>
<tr>
<td>API</td>
<td>Anti-Plague Institute</td>
</tr>
<tr>
<td>ARI</td>
<td>Acute respiratory infection</td>
</tr>
<tr>
<td>BSL</td>
<td>Biosafety level</td>
</tr>
<tr>
<td>CDC</td>
<td>US Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>EDTA</td>
<td>Ethylenediaminetetraacetic acid</td>
</tr>
<tr>
<td>HPAI</td>
<td>Highly pathogenic avian influenza</td>
</tr>
<tr>
<td>ILI</td>
<td>Influenza-like illness</td>
</tr>
<tr>
<td>MoES</td>
<td>Ministry of Emergency Situations</td>
</tr>
<tr>
<td>MoH</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>NIC</td>
<td>National Influenza Center</td>
</tr>
<tr>
<td>PATH</td>
<td>Program for Appropriate Technology in Health</td>
</tr>
<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
</tr>
<tr>
<td>PPE</td>
<td>Personal protective equipment</td>
</tr>
<tr>
<td>RIC</td>
<td>Regional influenza center</td>
</tr>
<tr>
<td>RNA</td>
<td>Ribonucleic acid</td>
</tr>
<tr>
<td>RT-PCR</td>
<td>Reverse transcriptase polymerase chain reaction</td>
</tr>
<tr>
<td>SARI</td>
<td>Severe acute respiratory infection</td>
</tr>
<tr>
<td>SES</td>
<td>Sanitary-epidemiological station</td>
</tr>
<tr>
<td>SST</td>
<td>Serum separator tube</td>
</tr>
<tr>
<td>VTM</td>
<td>Viral transport medium</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
What Is Avian Influenza?

There are three types of influenza viruses: A, B, and C. Influenza type A viruses can infect humans, birds, pigs, horses, and other animals, but wild birds are the natural hosts for these viruses. Influenza B viruses are usually found only in humans and are less frequently associated with severe epidemics than are influenza A viruses. Influenza type C viruses cause mild illness in humans (often in young children) and are not a significant concern for human health. Only influenza type A viruses can cause pandemics.

Avian influenza (“bird flu”) is an infectious disease of birds caused by various subtypes of type A influenza virus.

Sixteen hemagglutinin (H) subtypes and nine neuraminidase (N) subtypes of type A influenza virus are known. To date, all outbreaks of the highly pathogenic form have been caused by subtypes H5 and H7.¹

1. Description of the Disease in Birds

Influenza infections occur naturally among birds worldwide.

Infection causes a spectrum of symptoms in birds, ranging from mild illness to a highly contagious and rapidly fatal disease that can cause severe epidemics. The latter is known as “highly pathogenic avian influenza,” or HPAI. HPAI is characterized by sudden onset, severe illness, and rapid death, with a mortality rate that can approach 100 percent. Some birds, such as ducks, can get and spread the disease without showing signs of illness.

The current outbreaks of HPAI began in mid-2003. The causative agent, the H5N1 virus,² began to circulate widely in poultry in parts of Southeast Asia, spreading within months to affect eight countries in an outbreak that was unprecedented in its geographical extent. Never before have so many countries been simultaneously affected by HPAI; the outbreak has already resulted in the loss of more than 100 million birds. The disease remained confined to Southeast Asia until mid-2005, when the virus spread through parts of Central Asia to Europe, Africa, and the Middle East—affecting more than 60 countries in all.

Migratory waterfowl—most notably wild ducks and geese—are the natural reservoir of avian influenza viruses, and these birds are also the most resistant to infection. Direct or indirect contact of wild migratory waterfowl with domestic flocks (e.g., through droppings from infected wild birds) has been implicated as a frequent cause of bird epidemics.

Complete transmission routes and patterns of avian influenza viruses from bird to bird remain unclear and are a focus of study. Some species are more resistant to infection than others. Domestic poultry, including chickens and turkeys, are particularly susceptible to epidemics of rapidly fatal influenza.

¹The subtypes differ based on proteins on the surface of the virus: the hemagglutinin (H) protein governs entry of virus into cells; immunity to the H subtype prevents infection. The neuraminidase (N) protein governs release of new virus into the body; immunity to the N subtype reduces severity of the disease.

²The H5N1 virus is also of particular concern for human health, as explained on page 8.
2. The Risk and Significance of Transmission to Humans

The current outbreaks of HPAI are closely monitored by experts around the globe because one of the subtypes, H5N1, has crossed the species barrier on a number of occasions and caused severe illness with high case fatality in humans (Table 1). This poses a theoretical risk of a new influenza pandemic—that is, a global epidemic affecting a large proportion of the population.

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>TOTAL CASES</th>
<th>TOTAL DEATHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azerbaijan</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Cambodia</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>China</td>
<td>25</td>
<td>16</td>
</tr>
<tr>
<td>Djibouti</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Egypt</td>
<td>34</td>
<td>14</td>
</tr>
<tr>
<td>Indonesia</td>
<td>99</td>
<td>79</td>
</tr>
<tr>
<td>Iraq</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Lao PDR</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Nigeria</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Thailand</td>
<td>25</td>
<td>17</td>
</tr>
<tr>
<td>Turkey</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Vietnam</td>
<td>93</td>
<td>42</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>310</strong></td>
<td><strong>189</strong></td>
</tr>
</tbody>
</table>

Influenza pandemics have been documented since the 16th century and have occurred at intervals ranging from 10 to 50 years. Each pandemic was caused by a new virus subtype. During a pandemic, an estimated 25 to 30 percent of the world population may become ill, and up to 1 percent of the population may die.

All previous pandemics have been caused by H1, H2, or H3 viruses. The H5 virus has never circulated among humans, so it meets the requirement of a novel virus.

Three prerequisites are normally required for a pandemic to occur. H5N1 meets the first two criteria.

1. (+) A novel virus A subtype must emerge.
2. (+) The virus must be able to replicate in humans and cause serious disease.
3. (−) The virus must be efficiently transmitted from one human to another.

In addition to H5N1, two avian influenza strains—H9N2 and H7N7—have caused illness in humans, but the outbreaks were not as severe as those caused by the H5N1 strain.
It is thought that there are two mechanisms by which a bird influenza virus can evolve into a pandemic strain. In the 1918 pandemic, it is believed that an avian H1N1 virus mutated sufficiently over time (genetic shift) to acquire the ability to be transmitted easily from person to person. In contrast, the 1957 and 1968 pandemics were caused by reassortments, or mixing of genes, between human and avian viruses.

The spread of infection in birds increases the likelihood of human contact with infected birds. If more humans become infected over time, the likelihood increases that humans, if concurrently infected with human and avian influenza strains, could serve as the “mixing vessel” for a novel strain with sufficient human genes to be easily transmitted from person to person. Such an event would mark the start of an influenza pandemic because the human population has little or no immune protection against such virus subtypes. Moreover, existing vaccines, which are developed each year to match currently circulating strains and protect humans during seasonal epidemics, would be ineffective against a new virus.

**The longer the current H5N1 strain circulates, the greater the possibility that people will become infected with H5N1—and the greater the risk of a pandemic.**

To date, human infections have not resulted in sustained human-to-human transmission. Although a certain percentage of confirmed H5N1 cases are from disease clusters involving two or more individuals from a single family, possible human-to-human transmission of the H5N1 virus cannot be conclusively demonstrated in most instances because of family members’ potential concurrent exposure to infected birds. However, these reports do highlight the concern that changes in the circulating avian H5N1 virus might transform it into a virus that can be transmitted efficiently from human to human.

H5N1 is currently considered the most likely virus to ignite the next pandemic. Theoretically, however, any influenza strain may have pandemic potential.

### 3. How Human Infections Might Occur

Avian influenza viruses do not usually infect humans. Nevertheless, as mentioned above, several instances of human infections and outbreaks have been reported since 1997.

To date, most cases of H5N1 infection in humans are the result of direct contact with poultry or with objects or surfaces contaminated with feces from infected poultry (with a few cases of suspected human-to-human transmission among persons with intimate contact). These observations suggest a **respiratory route of transmission from birds to humans.** Exposure risk is considered highest during slaughter, defeathering, butchering, and preparation of poultry for cooking. Infections have not occurred when individuals have used personal protective equipment (PPE) in the culling process.

**Food safety:** There is no evidence that properly cooked poultry or poultry products, such as eggs, can be a source of infection. Normal cooking at temperatures greater than 70°C will inactivate the virus.
4. WHO Phases for Pandemic Influenza

The World Health Organization (WHO) has designed a six-phase system for informing the world of the seriousness of the threat of pandemic influenza and to facilitate pandemic planning (Table 2).

TABLE 2. Summary of WHO Phases of Pandemic Influenza

<table>
<thead>
<tr>
<th>PERIOD</th>
<th>PHASE</th>
<th>DESCRIPTION</th>
<th>PUBLIC HEALTH GOAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inter-</td>
<td>1</td>
<td>No new influenza virus subtypes in humans.</td>
<td>Strengthen influenza pandemic preparedness at all levels.</td>
</tr>
<tr>
<td>pandemic</td>
<td>2</td>
<td>No new influenza virus subtypes in humans. A circulating animal influenza</td>
<td>Minimize the risk of transmission to humans; detect and report such transmission</td>
</tr>
<tr>
<td></td>
<td></td>
<td>virus subtype poses a substantial risk of human disease.</td>
<td>rapidly if it occurs.</td>
</tr>
<tr>
<td>Pandemic</td>
<td>3</td>
<td>Human infection with a new subtype but no human-to-human spread, or at</td>
<td>Ensure rapid characterization of the new virus subtype and early detection,</td>
</tr>
<tr>
<td>Alert</td>
<td></td>
<td>most, rare instances of spread to a close contact.</td>
<td>notification, and response to additional cases.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Small cluster(s) with limited human-to-human transmission, but spread</td>
<td>Contain the virus within limited foci or delay spread to gain time to implement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>is highly localized, suggesting that the virus is not well-adapted to</td>
<td>preparedness measures, including vaccine development.</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Large cluster(s), but human-to-human spread is still localized, suggesting</td>
<td>Maximize efforts to contain or delay spread, to possibly avert a pandemic and to</td>
</tr>
<tr>
<td></td>
<td></td>
<td>the virus is better adapted to humans but may not yet be fully</td>
<td>gain time to implement pandemic response measures.</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Efficient and sustained transmission in the general population.</td>
<td>Minimize the impact of pandemic.</td>
</tr>
</tbody>
</table>


As of June 2007, the world was in phase 3: a new influenza virus subtype causing disease in humans but not yet spreading efficiently and sustainably between humans.
5. Epidemiology of WHO-Confirmed Human Cases of Avian Influenza A (H5N1) Infection

Results from the first analysis of epidemiological data on all 205 laboratory-confirmed H5N1 cases officially reported to WHO (analyzed by onset date from December 2003 through April 2006) have allowed several preliminary conclusions on the epidemiology of this infection:

- Cases have occurred year round. In each of the three years in which cases have occurred, however, the incidence of human cases peaked during the period roughly corresponding to winter and spring in the northern hemisphere.
- Half of the cases occurred in people less than 20 years of age; 90 percent of cases occurred in people less than 40 years of age.
- The overall case-fatality rate was 56 percent. Case fatality was high in all age groups but highest in persons aged 10 to 39 years.
- The case-fatality profile by age group differs from that seen in seasonal influenza, where mortality is highest in the elderly.
- The overall case-fatality rate was highest in 2004 (73 percent), followed by 63 percent to date in 2006 and 43 percent in 2005.
- The median incubation period was 3 to 4 days. The median duration from onset of symptoms until hospitalization was 4 to 5 days across all years studied. The overall median number of days from onset of symptoms until death was 9 days.
- Assessment of mortality rates and the time intervals between symptom onset and hospitalization and between symptom onset and death suggests that the illness pattern did not change substantially during the three years.

Because of several limitations, the extent to which these cases are representative of all human infections with H5N1 cannot be inferred. Multiple selection biases may have occurred because some patients may have died before being tested or diagnosed, mildly symptomatic patients may not have sought medical care, and false-positive or false-negative test results may have occurred.

6. Routine Surveillance of ARI and Seasonal Influenza in Ukraine

Health service organizations and government bodies perform surveillance of acute respiratory infection (ARI) and seasonal influenza to prevent the spread of these infections and reduce their social and economic effects. Their objectives are to reduce morbidity, complications, and case-fatality rates and minimize the impact on the country’s economy.

Routine surveillance is carried out at the national level by the Ministry of Health (MoH) and the National Influenza Center (NIC), at the regional level by oblast and the Crimea Autonomous Republic sanitary-epidemiological stations (SES), and at the local level by rayon and municipal SES with assistance from the nationwide network of health facilities that provide clinical material for laboratory tests and monthly information about registered cases.

National notification, reporting, and case/outbreak investigation requirements are described in Chapter 13. In cooperation with WHO, the NIC and the SES virological laboratories provide laboratory diagnosis and systematically research the etiology and dynamics of influenza virus strain structure during epidemic and inter-epidemic periods to forecast influenza epidemiological processes and determine potential causative agents of future epidemics. In cooperation with the US Centers for Disease Control and Prevention (CDC), the NIC researches antiviral resistance and antigenic and genetic characteristics, and provides recommendations on influenza prophylaxis and treatment.

The following methods and laboratory tests are used to identify influenza viruses in Ukraine:

- Virus culture in chicken embryos and Madin-Darby canine kidney cells culture.
- Serological methods (rise in antibody titers in paired serum specimens).
- Rapid diagnosis methods (e.g., polymerase chain reaction [PCR], immunofluorescence assay, rapid antigen detection tests).

With the support of the MoH and the NIC, the country’s SES carry out retrospective and current epidemiological analysis with the aim of forecasting influenza and ARI epidemiological processes for the near and more distant future in specific areas, regions, and the country as a whole. They also continuously monitor the circulation and ecology of causative agents in specific ecological/geographic regions of Ukraine to forecast morbidity/incidence rates.

Based on the current epidemiological analysis and laboratory test results, prevention and infection-control measures aimed at reducing incidence rates and preventing outbreaks—particularly in organized settings—are planned and implemented. These activities may include restrictive measures, such as temporary postponement of school studies and quarantine. Recommendations on immunization and planning of supplies for pharmacological prophylaxis and treatment are provided as well.

With 8 to 10 million cases annually, influenza and ARI remain the most widespread registered infections in Ukraine. The rate of reported influenza and ARI usually ranges from 15,000 to 17,000 per 100,000 people per year. In 2006, the total ARI incidence rate\(^6\) was 15,764 per 100,000; the influenza incidence was 156 per 100,000, the lowest rate in the past 10 years. The highest rates were 2,921 per 100,000 in 2000 and 2,279 per 100,000 in 2003. At that time, H1N1 epidemics were registered in many regions of Ukraine.

On average, 3 to 16 influenza deaths are reported annually. All such cases are laboratory-confirmed. No assessment of the sensitivity of mortality surveillance has been carried out recently.

\(^6\)There is no standard case definition for influenza or ARI in Ukraine.
Epidemiological analysis indicates that the proportion of ARI and influenza cases among schoolchildren is increasing. Schoolchildren are also the first to be affected during an epidemic. Implementation of non-pharmaceutical interventions (e.g., temporary postponement of school studies, social distancing, and infection control in the community) may reduce the peak incidence of cases during an outbreak, but there is limited scientific evidence available to support this.\footnote{Recent modeling studies regarding similar response measures during the influenza pandemic in 1918 suggest that, while it was crucial to implement such interventions early to decrease the peak incidence, the overall effect on total outbreak incidence and mortality was limited.} Use of appropriate seasonal human influenza vaccine during the pre-epidemic period has been an effective measure in the prevention of the infection among risk groups and at industrial enterprises.

7. **Rationale for Human Influenza Surveillance in Ukraine**

The highly pathogenic avian influenza A (H5N1) virus has produced outbreaks among wild birds and poultry in Ukraine. Most outbreaks have occurred during the spring and autumn seasons. These have occurred in the Crimea Autonomous Republic, Odesa, Sumy, and Kherson oblasts. These areas coincide with the historical routes of migrating birds. As part of the response to these outbreaks, 70,000 birds were culled; this had a significant impact on these oblasts’ economies. Whereas the risk of avian influenza outbreaks exists throughout the country, the risk is believed to be higher in these regions; in territories that border the Danube, Dniester, Southern Bug, and Dniper river basins; and in northern areas bordering Polissya’s swampy terrains. Poultry trade may play a role in the infection spread as well.

To date, no cases of H5N1 infection in humans have been registered in Ukraine. However, the number of human cases with a high case-fatality rate that have been registered in neighboring countries (such as Turkey) is of concern.

H5N1 surveillance in humans is integrated into a broader respiratory disease/influenza surveillance system. The goals of this broader influenza surveillance in Ukraine are as follows:

1. Describe the epidemiology of influenza and the burden of disease.
2. Provide isolates for identifying influenza viruses.
3. Provide data for program planning and preparedness.
4. Serve as an early warning system for outbreaks of avian or pandemic influenza.

In addition to the benefits of seasonal influenza surveillance, the early detection of H5N1 influenza cases in humans plays a critical role in combating a potential pandemic. The main benefits of having ascertained clear and fast recognition of transmission to human beings will ultimately include:

- Prompt implementation of public health and medical interventions aimed at preventing, delaying, or containing human-to-human virus transmission.
- More effective medical care of the infected persons, resulting in reduced mortality.
- Reduced economic and social impact of a potential pandemic.
8. **Key Components of Influenza Surveillance**

Key components of influenza surveillance include:

1. **Sentinel surveillance for seasonal influenza and severe respiratory infections.**

   This includes institution of surveillance for *severe acute respiratory infection* (SARI) in sentinel hospitals and surveillance for *influenza-like illness* (ILI) in ambulatory patients.

   The objectives of sentinel surveillance are to:
   - Provide data on the burden and epidemiology of seasonal influenza.
   - Obtain specimens for analysis and confirmation of influenza.
   - Provide influenza isolates to WHO’s international influenza surveillance system.
   - Provide additional specimen collection, data analysis, and response infrastructure to support the early warning system for influenza A (H5N1) or other novel influenza viruses.

   Chapter 14 and the section below provide more details.

2. **Development of an early warning system for influenza A (H5N1) outbreaks.**

   An early warning system for human cases aims at detecting unusual or unexplained ARI events that may be the result of influenza A (H5N1) infection, wherever they occur in the country. Any such case should lead to appropriate public health and laboratory investigations and response.

   This H5N1 early warning system includes:
   - Defining and acting on “triggers” (defined in Chapter 13) for investigation, active surveillance, and response.
   - Training health care providers in all oblasts to identify cases according to WHO case definitions and trigger criteria.
   - Fostering coordination with veterinary services and other stakeholders.
   - Nationwide public education and awareness about risk-reduction methods and reportable events.

   Chapters 11 through 13 provide more information on these topics.
9. Description of Proposed Human Seasonal and Avian Influenza Surveillance System Laboratory Support in Ukraine

Seasonal Influenza Surveillance

Sentinel influenza surveillance sites have been chosen to represent the population. These include facilities that capture both adult and child respiratory patients.

If a case defined as ILI or SARI arrives at a sentinel site facility (Chapter 14), the response should unfold as follows:

• For all SARI cases and a random sample of ILI cases presenting to sentinel sites within 72 hours of symptom onset, specimens are sent by the recognizing clinician to the oblast SES laboratory.
• The oblast SES performs virus isolation and initial confirmation.
• The NIC provides final confirmation of positive isolates. The NIC also undertakes periodic quality control assessments of oblast laboratories.
• Influenza isolates confirmed at the NIC are shared with WHO collaborating centers.

Oblasts that are not part of the sentinel surveillance system should operate with traditional routine ARI surveillance as before.

Avian Influenza Surveillance

The response for avian influenza cases should unfold as follows:

• Clinicians identify cases meeting any of the triggers for H5N1 investigation specified in Chapter 13. They observe appropriate PPE and infection-control procedures.
• Two sets of oropharyngeal (most important), nasopharyngeal, and serologic specimens are collected (at a minimum, one smear and one blood sample).
• One set of specimens is sent to the NIC in Kiev (following the procedures outlined in Chapter 19). A second set of specimens is sent to the Odesa Regional Influenza Center (RIC) based at the Odesa Anti-Plague Institute (API) (Figure 1). Or, as additional regional influenza centers receive PCR capacity and biosafety certifications, the second sample may instead be directed to the closest qualifying RIC for reverse transcriptase polymerase chain reaction (RT-PCR) analysis.
• The NIC undertakes RT-PCR analysis for influenza A and B viruses and subtyping for H1, H2, H3, and H5. Confirmed influenza A specimens that are positive for H5 or unsubtypable are immediately sent to WHO collaborating centers.
• Only procedures appropriate for biosafety level (BSL) 2 are performed at the NIC unless or until the NIC receives additional biosecurity upgrades to perform enhanced BSL 3 laboratory testing.
• The Odesa API receives samples and performs confirmatory testing simultaneously, including enhanced BSL 3 analysis and storage of viral isolates. All subsequent results of analysis performed at an RIC are immediately shared with the NIC.
Then the National Influenza and Acute Respiratory Infections Center in Kiev will:

- Receive and analyze monthly/weekly influenza and ARI morbidity reports and samples (isolates) from all regional centers.
- Determine the epidemiological situation and forecast dynamics of the epidemic process based on the information received.
- Confirm and identify seasonal influenza viruses isolated in the country’s other virological laboratories.
- Determine and monitor the etiological structure of influenza and ARI in Ukraine.
- Systematically research the characteristics of influenza virus strain structure, identify and study atypical and new strains of seasonal influenza, and determine the pandemic potential of the circulating strains.
- Identify the etiology of influenza epidemics and alert the MoH about strains with increased pathogenicity and virulence.
- Analyze and systematize information to produce annual etiological forecasts for Ukraine, and advise on the recommended preventive and infection-control measures.
- Provide technical assistance, evaluation, and quality control to virological laboratories and regional centers.
- Communicate and cooperate with WHO and the CDC regarding influenza diagnosis, surveillance issues, and submission of isolates to the WHO international influenza surveillance system.
10. Clinical Description of Human Cases of H5N1 Avian Influenza

The incubation period for influenza A (H5N1) infection in humans usually ranges from 2 to 7 days.

The reported symptoms of avian influenza in humans have ranged from typical influenza-like symptoms (e.g., fever, cough, sore throat, and muscle aches) to viral pneumonia and acute respiratory distress. Gastroenterological symptoms are sometimes reported as well (Table 3). Lower respiratory symptoms develop early in illness, and overall severity of the disease is high. Clinically apparent pneumonia with chest x-ray changes are seen in most patients, although the x-ray changes have been nonspecific.

Common laboratory findings have included lymphopenia (<1 x 10^9/liter), thrombocytopenia, and slightly or moderately raised alanine aminotransferase and aspartate transaminase. In fatal cases, the illness has rapidly progressed to respiratory distress and subsequent respiratory failure within one week of the onset of symptoms, despite ventilator support.

**TABLE 3. Prevalence of Selected Clinical Symptoms and Findings Among 59 Patients with Confirmed Avian Influenza A (H5N1) in Hong Kong, Thailand, Vietnam, and Cambodia (1997–2005)**

<table>
<thead>
<tr>
<th>CLINICAL PRESENTATION</th>
<th>PREVALENCE (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever ≥38°C†</td>
<td>98</td>
</tr>
<tr>
<td>Cough†</td>
<td>88</td>
</tr>
<tr>
<td>Shortness of breath†</td>
<td>62</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>55</td>
</tr>
<tr>
<td>Sore throat†</td>
<td>52</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>39</td>
</tr>
<tr>
<td>Headache</td>
<td>28</td>
</tr>
<tr>
<td>Myalgia</td>
<td>29</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>23</td>
</tr>
<tr>
<td>Vomiting</td>
<td>31</td>
</tr>
<tr>
<td>Pulmonary infiltrates</td>
<td>88</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>64</td>
</tr>
<tr>
<td>Increased aminotransferase levels</td>
<td>67</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>54</td>
</tr>
</tbody>
</table>


†These most-prevalent symptoms have formed a basis for influenza A (H5N1) clinical (probable) case definition to increase its specificity. Chapter 11 provides additional details on this case definition.
11. WHO Case Definitions\(^8\) for Human Infections with Influenza A (H5N1) Virus

Suspected H5N1 Case

**Clinical Presentation**

Unexplained acute lower respiratory illness with fever (≥38ºC) and cough, shortness of breath, or difficulty breathing

**AND**

**Epidemiological Criteria**

One of the following exposures within 7 days prior to symptom onset:

- Close contact (within 1 meter) with a person who is a suspected, probable, or confirmed H5N1 case (e.g., caring for, speaking with, or touching this person).
- Exposure to poultry or wild birds or their remains (e.g., handling, slaughtering, defeathering, butchering, preparing for consumption) or to environments contaminated by their feces in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month.
- Consumption of raw or undercooked poultry products in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month.
- Close contact with a confirmed H5N1-infected animal other than poultry or wild birds (e.g., cat or pig).
- Handling samples (animal or human) suspected of containing the H5N1 virus in a laboratory or other setting.

---

\(^8\)Note 1: The case definitions apply to the current phase of pandemic alert (WHO’s pre-pandemic phase 3) and may change as new information about the disease or its epidemiology becomes available.

**Note 2:** The case definitions are not intended to provide complete descriptions of disease in humans, nor are they to be used as screening criteria to determine who should have specimens collected for H5N1 screening. Rather, they are intended to standardize reporting of cases to WHO and ensure comparability of data.

**Note 3:** In clinical situations requiring decisions concerning treatment, care, or triage of persons who may have H5N1 infection, decisions should be based on clinical judgment and epidemiological reasoning, and not on adherence to the case definitions. While most patients with H5N1 infection present with fever and lower respiratory complaints, the clinical spectrum is broad.
Probable H5N1 Case (Notify WHO)

DEFINITION 1: A person meeting the criteria for a suspected case

AND

one of the following additional criteria:

- Infiltrates or evidence of an acute pneumonia on chest radiograph plus evidence of respiratory failure (e.g., hypoxemia, severe tachypnea) or
- Positive laboratory confirmation of an influenza A infection, but insufficient laboratory evidence for H5N1 infection.

OR

DEFINITION 2: A person dying of unexplained acute respiratory illness who is considered to be epidemiologically linked by time, place, and exposure to a probable or confirmed H5N1 case.

Confirmed H5N1 Case (Notify WHO)

A person meeting the criteria for a suspected or probable case

AND

one of the following positive results in a national, regional, or international laboratory whose H5N1 test results are accepted by WHO as confirmatory:

- Isolation of an H5N1 virus.
- Positive H5 PCR results from tests using two different PCR targets (e.g., primers specific for influenza A and H5 hemagglutinin).
- A fourfold or greater rise in neutralization antibody titer for H5N1 based on testing of an acute serum specimen (collected 7 days or fewer after symptom onset) and a convalescent serum specimen. The convalescent neutralizing antibody titer must also be 1:80 or higher.
- A microneutralization antibody titer for H5N1 of 1:80 or greater in a single serum specimen collected at day 14 or later after symptom onset and a positive result using a different serological assay, for example, a horse red blood cell hemagglutination inhibition titer of 1:160 or greater or an H5-specific western blot positive result.
12. Suspected and Probable Influenza A (H5N1) Case Notification Procedures

Any suspected human case of avian influenza A (H5N1) identified by providers requires immediate notification of the rayon SES without any delay, by any existing means of communication (telephone, fax, email, or in person).

In turn, the rayon SES must notify the following institutions within 1 hour:

• The oblast SES (which must notify the MoH and the NIC within 1 hour).
• The rayon veterinary service and the rayon administration (to coordinate epidemic and epizootic response measures).
• The regional/rayon hospital (to prepare for transportation and admission of the patient(s)).

In accordance with International Health Regulations, 2005, the MoH will immediately notify WHO of all probable or confirmed cases of influenza A (H5N1) in humans.

13. Procedures to Strengthen the Early Warning System for Humans

An early warning system for humans aims at detecting unusual or unexplained events of ARI that should trigger appropriate public health and laboratory investigations.

Routine Seasonal Influenza and ARI Surveillance

All institutions rendering health services are required to strictly adhere to the national notification reporting and investigation requirements summarized in Table 4.

**TABLE 4. National Notification Reporting and Investigation Requirements**

<table>
<thead>
<tr>
<th>DISEASE/CONDITION</th>
<th>REPORTING BY ALL PROVIDERS AND LABORATORIES</th>
<th>REPORTING BY SES</th>
<th>INVESTIGATION BY SES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>URGENT</td>
<td>MONTHLY</td>
<td>URGENT</td>
</tr>
<tr>
<td>Acute respiratory infection (ICD* codes J00–06)</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Influenza (J10–11)</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Fatal case of acute infectious disease</td>
<td>Within 24 hours</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Suspected or probable influenza caused by a new viral subtype (J09)</td>
<td>Within 1 hour</td>
<td>No</td>
<td>Within 1 hour</td>
</tr>
</tbody>
</table>

*ICD (International Statistical Classification of Diseases and Related Health Problems) codes for all respiratory infections are provided in Annex 3.
The institution should follow standard investigation procedures specified in MoH decree 30, “On influenza and ARI prophylactic and control measures in Ukraine” (February 9, 1998), and decree 488, “On avian influenza prophylactic and control measures and pandemic prevention” (July 17, 2006), and check each case for potential exposure to the H5N1 virus within the 7 days prior to symptom onset using the Suspected or Probable Human Case of Avian Influenza A (H5N1) Investigation Card (Figure 2).

Triggers Requiring Public Health Investigation, H5N1 Laboratory Specimen Collection, and Response

Triggers are risk factors or clinical criteria that might elevate suspicion that a human case of respiratory illness (e.g., SARI) is more likely caused by the influenza A (H5N1) virus than by other respiratory pathogens.

Laboratory specimen collection for influenza A (H5N1) testing and public health investigation should occur upon observation of any of the following triggers:

1. Any report about a suspected or probable influenza A (H5N1) case in humans by a health care provider or a laboratory.
2. Any report about a sudden fatal case of ARI by a health care provider.
3. Any severe case of influenza that is type A or unsubtypable.
4. Any febrile person with documented exposure to persons or animals strongly suspected to have influenza A (H5N1).
5. Two or more SARI cases with onset of symptoms within 7 to 14 days of each other in the same geographical area and/or believed to be epidemiologically linked.

The following triggers also require immediate public health investigation:

1. Reports of excessive wild bird or poultry deaths.
2. Rumors from newspapers or other sources.
3. Unusual distribution of ILI or SARI by age or time as seen in reports from ILI and SARI sentinel surveillance sites (see Chapter 14 for ILI and SARI case definitions).

If the public health team verifies that the case is a suspected or probable human case of avian influenza, the institution should follow the investigation and response procedures specified in this manual (Chapters 15 through 18).
FIGURE 2. Suspected or Probable Human Case of Avian Influenza A (H5N1) Investigation Card

<table>
<thead>
<tr>
<th>Case identification</th>
<th>Full name of patient:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Date of birth: Day/ / Month/ / Year/ /</td>
</tr>
<tr>
<td></td>
<td>Address/telephone:</td>
</tr>
<tr>
<td></td>
<td>Occupation/place of study:</td>
</tr>
</tbody>
</table>

| Case detection and notification history | Date and facility at which the patient presented for the first time: Day/ / Month/ / Year/ / |
|                                       | Health facility name: |
|                                       | Date case was reported to SES: Day/ / Month/ / Year/ / |
|                                       | Date case investigation started: Day/ / Month/ / Year/ / |

| Hospitalization | Date and place: Day/ / Month/ / Year/ / |
|                | Hospital 1 name: |
|                | Hospital 2 name: |

<table>
<thead>
<tr>
<th>Current health status</th>
<th>Symptoms (indicate date of onset for each symptom, if known):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fever ≥38°C? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Shortness of breath? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Cough? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Sore throat? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Rhinitis? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>General weakness? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Conjunctivitis? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Muscle/joint aches? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Diarrhea? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Pulmonary infiltrates on a radiogram? ○ Yes ○ No ○ Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current health status</th>
<th>Outcome: ○ Alive ○ Dead ○ Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>If dead, date of death: Day/ / Month/ / Year/ /</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prophylaxis against influenza</th>
<th>Patient vaccinated against seasonal influenza in the last 6 months? ○ Yes ○ No ○ Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Was the patient taking any antiviral influenza medications during the 7 days prior to symptom onset? ○ Yes ○ No ○ Unknown</td>
</tr>
<tr>
<td></td>
<td>If yes, name of antiviral:</td>
</tr>
<tr>
<td></td>
<td>Received at facility:</td>
</tr>
<tr>
<td></td>
<td>Start date: Day/ / Month/ / Year/ /</td>
</tr>
</tbody>
</table>
### Exposure history

**During the 7 days prior to the onset of symptoms, has the patient:**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Been in close contact with a person who is a suspected, probable, or confirmed case of avian influenza A/H5N1?</td>
<td>○ Yes</td>
<td>○ No</td>
<td>○ Unknown</td>
<td>If yes, give dates and other details:</td>
</tr>
<tr>
<td>Been in close contact with a person who died from ARI who is considered to be epidemiologically linked to a probable or confirmed case of avian influenza A/H5N1?</td>
<td>○ Yes</td>
<td>○ No</td>
<td>○ Unknown</td>
<td>If yes, give dates and other details:</td>
</tr>
<tr>
<td>Been handling samples (animal or human) suspected of containing H5N1 virus in a laboratory or other setting?</td>
<td>○ Yes</td>
<td>○ No</td>
<td>○ Unknown</td>
<td>If yes, give details (location, type, frequency, duration of exposure):</td>
</tr>
<tr>
<td>Been exposed to poultry or wild birds or their remains (e.g., handling, slaughtering, defleshing, butchering, preparing for consumption) or to environments contaminated by their feces in an area where H5N1 infections in animals or humans have occurred in the last month?</td>
<td>Domestic poultry?</td>
<td>○ Yes</td>
<td>○ No</td>
<td>○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Wild birds?</td>
<td>○ Yes</td>
<td>○ No</td>
<td>○ Unknown</td>
</tr>
<tr>
<td></td>
<td>Specify type:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consumed raw or undercooked poultry products in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month?</td>
<td>○ Yes</td>
<td>○ No</td>
<td>○ Unknown</td>
<td></td>
</tr>
<tr>
<td>Been in close contact with a confirmed H5N1-infected animal other than poultry or wild birds (e.g., cat or pig)?</td>
<td>○ Yes</td>
<td>○ No</td>
<td>○ Unknown</td>
<td></td>
</tr>
<tr>
<td>If exposed, was he/she wearing PPE?</td>
<td>○ Yes</td>
<td>○ No</td>
<td>○ Unknown</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Specify:</td>
<td>○ Respirator</td>
<td>○ Mask</td>
<td>○ Gloves</td>
</tr>
</tbody>
</table>

### Laboratory testing

<table>
<thead>
<tr>
<th>Question</th>
<th>Date of sample collection:</th>
<th>Shipped to:</th>
<th>Specimen number:</th>
<th>Day/ Month/ Year/</th>
<th>Nasopharyngeal swab</th>
<th>Oropharyngeal swab</th>
<th>Serum</th>
<th>Nasopharyngeal wash/aspirate</th>
<th>Other:</th>
</tr>
</thead>
</table>

### Classification

**Final case classification:**

- ○ Suspected H5N1 case
- ○ Probable H5N1 case
- ○ Confirmed H5N1 case
- ○ Discarded

---

This form should be promptly sent to the regional SES and the NIC.

Responsible person: __________________________ Telephone: __________________________ Signature: __________________________
Monitoring High-Risk Occupational Groups for Early Signs of Influenza-Like Infection

The head of each rayon SES must assume personal responsibility for the development and timely update of a rayon-specific list of persons in occupational groups that are at high risk of contracting influenza A (H5N1) infection. The rayon SES head should also assume control over monitoring the health status of these individuals using the register suggested in Figure 3.

At a minimum, these groups should include:

- People involved in the culling of infected or potentially infected birds.
- Farmers exposed to potentially infected animals.
- Health care workers caring for patients with probable or confirmed influenza A (H5N1) infection.
- Laboratory workers handling clinical specimens from patients with probable or confirmed influenza A (H5N1) infection.
- Mortuary room workers dealing with bodies of probable or confirmed influenza A (H5N1) cases.

Each of the people in the register should be informed about clinical symptoms of ILI and provided with the contact details of a designated health care official or health facility (contactable 24 hours a day, 7 days a week). They should be instructed to:

- Check their temperature and presence of respiratory symptoms twice daily for 7 days following their last contact with potentially infected animals or humans.
- Not self-medicate if a fever develops. Instead, they should limit interactions with others and immediately seek assistance from the designated health care official/health facility.

While self-reporting is encouraged, SES personnel are advised to actively contact identified individuals and/or cooperate with their employers to verify the absence of ILI during the entire monitoring period.

If a probable influenza A (H5N1) infection is suspected, a prompt investigation and response should be initiated as specified in these guidelines.
FIGURE 3. Form for Monitoring Contacts Potentially Exposed to Influenza A (H5N1) Infection (Monitoring Until 7 Days After Last Exposure)

Rayon: _________________________ Patient's name or suspected animal source/place of exposure: _____________________________________________________________

Facility name and telephone (for monitoring of contacts among occupational groups): ___________________________________________________________________________

<table>
<thead>
<tr>
<th>N</th>
<th>First and Last Name</th>
<th>Address and Telephone</th>
<th>Sex</th>
<th>Age</th>
<th>Occupation</th>
<th>Character and Duration of Exposure (e.g., Relationship with Case*)</th>
<th>Last Contact</th>
<th>Fever (≥38°C) After Last Exposure? (Y/N)</th>
<th>Cough?</th>
<th>Sore Throat?</th>
<th>Dyspnea?</th>
<th>If the Contact Falls Ill During the Observation Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 2 3 4 5 6 7 Date Started</td>
<td>Place:</td>
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<td>1 2 3 4 5 6 7 Date Started</td>
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<td>1 2 3 4 5 6 7 Date Started</td>
<td>Place:</td>
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</tr>
</tbody>
</table>

*Household member (H), friend (F), work colleague (W), other (O) (specify).
Active Search for Human Respiratory Infections in Cases of Unexplained or Unusual Mortality or Confirmed Cases of Influenza A (H5N1) in Birds or Animals

Unexplained or unusual mortality in poultry, wild birds, or animals may indicate an outbreak of HPAI A (H5N1).

As shown in Figure 4, the rayon veterinary office will normally be the first to be notified about such an event. They will promptly notify the rayon SES and veterinary department and convene the rayon avian influenza response commission.

**FIGURE 4. Reporting Channels for Suspected Cases of Avian Influenza**

This notification may be followed by testing of deceased birds/animals and, in the case of a positive result, measures to control the animal infection, such as culling.

Active surveillance is initiated following HPAI signals from the veterinary service or upon identification of suspected and probable human cases.

Health services carry out active surveillance to detect and investigate probable human cases as early as possible and implement containment measures to prevent further spread.

This is performed by surveillance teams composed of SES personnel and rayon health facility workers. The teams should be equipped with transportation, PPE, mobile telephones, flashlights, thermometers, and sufficient supplies of case investigation and contact monitoring forms.
The first step is to determine target population groups. Depending on the scope of the problem, these groups may include:

- People living in villages with suspected H5N1 outbreaks in poultry or wild bird die-offs.
- Persons and health care workers involved in H5N1 poultry investigations and response.
- Workers, buyers, and vendors in live animal markets (especially bird markets).
- Poultry cullers.
- Poultry or swine farm workers.
- Veterinarians.
- Hunters.
- Dealers or traders in wild/exotic birds.
- Zoo workers.

Through hospital-based records and ward reviews, interviews with possibly exposed persons and their families, and other active surveillance procedures (e.g., house-to-house visits), the surveillance team should interview the target population to verify the presence of both clinical symptoms and epidemiological contact with a potential source of infection using the standard case definition. For example:

For each case, the team’s actions should be as follows:

<table>
<thead>
<tr>
<th>IF THERE ARE:</th>
<th>THEN:</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO clinical signs or symptoms and NO contact with suspected source of infection</td>
<td>Deliver appropriate health education messages on infection prevention and health care-seeking behavior (see Annex 1).</td>
</tr>
<tr>
<td>ONLY fever or other clinical signs of respiratory infection</td>
<td>Refer patient to health facility. Deliver appropriate health education messages on infection prevention (see Annex 1).</td>
</tr>
<tr>
<td>ONLY contact with sick or dead poultry, wild birds, animals, or a human source of infection</td>
<td>Include patient on the list of contacts for close observation (Figure 3) and begin monitoring for signs of infection for 7 days. Consider voluntary home quarantine. Advise patient not to self-medicate if fever develops but to limit interactions with others and immediately seek assistance from the designated health care official/health facility that can be contacted 24 hours a day, 7 days a week.</td>
</tr>
<tr>
<td>BOTH clinical signs and contact with a potential source within 7 days of symptom onset</td>
<td>Collect throat swabs and other laboratory specimens. Investigate any suspected or probable case of avian influenza on the spot using the case investigation form (Figure 2). Initiate control measures as recommended in Chapters 17 and 18.</td>
</tr>
</tbody>
</table>
14. Sentinel Surveillance for SARI and ILI

Sentinel surveillance is one of the methods used for seasonal influenza surveillance. Oblasts implementing sentinel surveillance for seasonal influenza should also continue to report cases of ARI as they have done historically so that the traditional ARI surveillance system can be compared to the new SARI and ILI sentinel surveillance system.

Sentinel surveillance is instituted for SARI in hospitals and ILI in ambulatory patients (see case definitions below).

The objectives of sentinel surveillance are to:
- Provide data on the burden and epidemiology of seasonal influenza.
- Obtain specimens for analysis.
- Provide a core specimen collection, transport, and public health response infrastructure for the early warning system for H5N1 or other novel influenza viruses.

ILI Case Definition

Acute illness with fever $\geq 38^\circ C$ and cough or sore throat and an absence of other diagnoses.

SARI Case Definition for Persons $> 5$ Years Old

Moderate to severe acute lower respiratory tract illness requiring hospital admission and consisting of:
- Temperature $\geq 38^\circ C$ and
- Cough and/or sore throat and
- Shortness of breath or difficulty breathing.

SARI Case Definition for Persons $\leq 5$ Years Old

Hospitalized child presenting with:
- Fever $\geq 38^\circ C$ and
- Tachypnea (>60 per minute for infant aged 0 to 1 month, >50 per minute for infant aged 2 to 11 months, or >40 per minute for child aged 12 to 59 months).

and at least one of the following symptoms:
- Inability to drink or breastfeed.
- Lethargy or unconsciousness.
- Repeated vomiting.
- Convulsions.
- Chest in-drawing.

Note: Temperature does not have to be documented; subjective history of fever over previous 3 days is sufficient.

9While these symptoms are common to many diseases, large and sudden increases in the number of ILI cases are often due to influenza.
Specimens should be collected and routinely submitted to the oblast SES laboratory for testing to determine etiology of respiratory infections from:

1. **All cases admitted to the sentinel hospitals that meet the above SARI case definition with onset of symptoms within 72 hours.**

2. **A sample of ILI cases representing the served population if onset of symptoms falls within 72 hours.**
   - At least 3 cases from each respiratory disease outbreak reported in an organized setting served by the clinic.
   - The first 3 to 5 cases with ILI symptoms presenting to the facility per week.

**Note:** If the patient is part of a cluster of respiratory illness or has coincided with another trigger for investigation specified in Chapter 13, then specimens must be collected irrespective of when symptom onset occurred or any sampling strategy.

In cases involving ILI, a nasopharyngeal swab should be taken from adults and children. For SARI cases, a nasopharyngeal swab or aspirate is also recommended. If an ILI or SARI case also meets one of the H5N1 trigger criteria specified in Chapter 13, then throat swabs or other lower respiratory specimens should be collected as well. Procedures for specimen collection, storage, and transport are described in more detail in Chapter 19.

All specimens from influenza sentinel sites should be sent to the regional SES laboratory and accompanied by the corresponding form.

Aggregate data with case counts of hospitalized SARI and outpatient ILI cases by age group should be submitted by sentinel facilities to SES on a weekly basis according to the format below:

<table>
<thead>
<tr>
<th>INFLUENZA SENTINEL STATION SARI / ILI MORBIDITY REPORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza sentinel facility:</td>
</tr>
<tr>
<td>Disease/Age Group</td>
</tr>
<tr>
<td>Total no. of ambulatory visits</td>
</tr>
<tr>
<td>No. of ambulatory patients meeting the influenza-like illness (ILI) definition</td>
</tr>
<tr>
<td>No. of ILI cases from whom laboratory specimen(s) has been collected</td>
</tr>
<tr>
<td>Total no. of hospitalizations</td>
</tr>
<tr>
<td>No. of hospitalized cases meeting the severe acute respiratory infection (SARI) case definition</td>
</tr>
<tr>
<td>No. of SARI cases from whom laboratory specimen(s) has been collected</td>
</tr>
</tbody>
</table>
If no ILI or SARI cases have occurred in a particular age group, a “zero” must be reported. No space can be left blank on the form. The head of each of the sentinel facilities should oversee collection and reporting of data and specimens and monitor trends in ILI and SARI over time. Increases in ILI or SARI cases above a baseline may indicate an epidemic. Oblast and rayon epidemiologists should review sentinel site records on a semiannual basis to ensure quality control and completeness of reporting. These epidemiologists are also responsible for providing reporting clinicians with timely feedback of influenza laboratory testing results. Traditional reporting of ARI and physician-suspected influenza should continue.

If infection with a novel influenza virus is confirmed, or if a case is classified as a suspected or probable H5N1 infection, a case investigation and response measures should be initiated promptly as specified in Chapters 15 through 18.

Guidance for Sentinel Hospital Data Collection and Laboratory Records Maintenance

Sentinel ambulatory clinics and hospitals also should, at a minimum, record the following data for all individuals tested for respiratory viruses:

- Hospital/ambulatory clinic data:
  - Patient’s name.
  - Patient’s date of birth.
  - Patient’s sex.
  - Medical record/surveillance number.
  - Date of onset.
  - Date of sampling.
  - Vaccination status during the last 6 months.
  - Travel information.
  - Contact with disease and/or outbreak (community or institutional).
  - Treatment provided.
  - Symptoms.

The oblast laboratory should, at a minimum, record the following data for each respiratory specimen received:

- Medical record/surveillance number.
- Specimen date.
- Patient’s date of birth.
- Patient’s city, state, or province of origin.
- Date of onset.
- Date of sampling.

The national reference laboratory should, at a minimum, record the following data for each respiratory specimen received:

- Laboratory name.
- Medical record/surveillance number.
- Specimen date.
- Patient’s date of birth.
- Patient’s city, state, or province of origin.
- Date of onset.
- Virus type.
Suggested Scope of Influenza Sentinel Surveillance Data Analysis

The following parameters should be used by sentinel stations for a weekly analysis of surveillance data by age category and in aggregate:

- Number of new cases of ILI and SARI.
- Number of new SARI fatalities.
- Number of laboratory specimens submitted for influenza testing.
- Number of influenza cases meeting the H5N1 trigger criteria specified in Chapter 13.
- Proportion of ILI cases per total ambulatory consultations.
- Proportion of SARI cases per total hospitalizations.
- Number of feedback meetings (during which reporting clinicians are informed of influenza testing results) that have been completed with reporting clinicians.

“Zero reporting” procedures must be observed at all times.

The following parameters should be used by the oblast SES for a weekly analysis of surveillance data by age category and in aggregate:

- Number of new cases of ILI and SARI.
- Number of new SARI fatalities.
- Number of new laboratory-confirmed influenza cases and fatalities.
- Number of laboratory isolates submitted to the NIC for influenza confirmation.
- Number of influenza cases meeting the H5N1 trigger criteria specified in Chapter 13.
- Proportion of ILI cases testing positive for influenza.
- Proportion of SARI cases testing positive for influenza.
- Proportion of laboratory-confirmed influenza cases per total number of SARI cases.
- Proportion of laboratory-confirmed influenza deaths per total number of SARI deaths.
- Proportion of ILI cases per total ambulatory consultations.
- Proportion of SARI cases per total hospitalizations.
- Number of feedback meetings (during which reporting clinicians are informed of influenza testing results) that have been completed with reporting clinicians.

Zero reporting procedures must be observed at all times.

In addition to those mentioned above, the following parameters should be used by the oblast SES for a quarterly analysis of surveillance data:

- Estimated incidence and mortality rates for laboratory-confirmed influenza and SARI.
- Weekly trends in counts and incidence of ILI, SARI, and laboratory-confirmed influenza.
- Demographic characteristics of SARI and laboratory-confirmed influenza cases.

Based on information from several years of surveillance, monthly baselines can be calculated for the above analyses.

Sentinel Surveillance Performance Indicators

To evaluate the efficiency and success of the system, a number of indicators have been established. At least once a year, local surveillance reviews by regional SES and/or RIC should be carried out to ensure data
quality, protocol adherence, and standardization across the country. Such reviews may incorporate the following:

- Audits of hospital and clinic records to determine whether cases of ILI and SARI are being accurately recorded.
- Assessment of local staff knowledge of protocols and case definitions.
- Laboratory equipment and staff assessment, including biosafety assessments.
- Laboratory data audits to determine reporting accuracy.
- Continuing education concerning notifiable disease surveillance and sentinel surveillance protocols.
- The opportunity for local staff to give feedback about inefficiencies in the surveillance system.
- Other quality assurance.

The outcome indicators presented in Table 5 will allow for system evaluation in accordance with the specific objectives of the sentinel surveillance system. The goal of the system is to establish and/or improve surveillance to detect seasonal and avian influenza in humans and to improve national capacity to detect any new strain of influenza in Ukraine.

**TABLE 5. Outcome Indicators for Sentinel Surveillance**

<table>
<thead>
<tr>
<th>OBJECTIVE</th>
<th>INDICATOR</th>
<th>TARGETS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Describe the epidemiology of seasonal influenza and burden of disease.</td>
<td>SARI and ILI case data (including number of specimens submitted for influenza testing) from the sentinel sites are analyzed weekly at the oblast and national levels.</td>
<td>&gt;95% of hospitalized SARI cases are captured in the surveillance system.</td>
</tr>
<tr>
<td></td>
<td>Number and proportion of sampled ILI and SARI cases confirmed by laboratory as influenza are reported by oblast weekly.</td>
<td>At least 20 ILI cases and all qualifying SARI cases have samples submitted and tested on a monthly basis during influenza season per sentinel station. Laboratorv-confirmed influenza cases appear in oblast SES weekly reports within 7 days. Sentinel sites report the number of new cases of ILI, SARI, and laboratory specimens submitted for influenza testing, with zero reporting, during 100% of weeks. Oblasts with sentinel sites report the number of new cases of ILI, SARI, and laboratory confirmations of influenza, with zero reporting, during 100% of weeks.</td>
</tr>
<tr>
<td></td>
<td>Estimate of quarterly incidence of laboratory-confirmed influenza in sentinel site catchment area.</td>
<td>Quarterly incidence reports are based on yearly estimates of the populations served by sentinel site hospitals.</td>
</tr>
<tr>
<td></td>
<td>Seasonal trends in influenza and demographic characteristics of cases analyzed regularly.</td>
<td>Analyses of seasonal trends and epidemiological descriptions of laboratory-confirmed influenza, ILI, and SARI are performed quarterly.</td>
</tr>
<tr>
<td>OBJECTIVE</td>
<td>INDICATOR</td>
<td>TARGETS</td>
</tr>
<tr>
<td>-----------</td>
<td>-----------</td>
<td>---------</td>
</tr>
<tr>
<td>Provide isolates for identification of influenza viruses.</td>
<td>The NIC will receive all influenza isolates from oblasts participating in the surveillance system.</td>
<td>Each oblast submits 100% of its influenza isolates to the NIC. Laboratory staff from all oblasts with sentinel sites have been trained and follow standard protocols provided by the NIC.</td>
</tr>
</tbody>
</table>
| Serve as an early warning system for outbreaks of avian or pandemic influenza. | Clinicians in all oblasts use trigger criteria to initiate case investigations of avian influenza. Clinicians, epidemiologists, and laboratory personnel understand laboratory specimen collection and epidemiological reporting procedures. | The following specialists are trained in avian influenza case detection, investigation, and response:  
  • >95% of rayon epidemiologists.  
  • Clinicians from >95% of oblast and rayon health facilities.  
  • All laboratory personnel involved in influenza and respiratory illness surveillance.  
The number of new suspected or probable cases of influenza A (H5N1) is reported by the oblasts during 100% of weeks and includes zero reporting.  
The number of laboratory specimens submitted for laboratory testing for influenza A (H5N1) is reported by the oblasts during 100% of weeks and includes zero reporting. |

*The criteria below apply to all oblasts in Ukraine, not just those participating in the sentinel surveillance system.*
15. Investigation of Human Cases/Outbreaks of Avian Influenza A (H5N1)

Every reported suspected or probable human case of avian influenza A (H5N1) must be investigated\(^{10}\) by a rayon SES epidemiologist (in cooperation with the regional SES and RIC experts) and facility health care workers within 1 day of notification. The investigation and response team should have experience in field epidemiology, clinical assessment, laboratory specimen collection, infection control, and social mobilization. Additional team members should include Ministry of Emergency Situations (MoES) experts, veterinarians, and environmental health specialists. The size and composition of the team should depend on the size and complexity of the anticipated investigation.

Appropriate PPE should be worn when in contact with symptomatic persons or when entering agricultural premises known to be infected.

Investigation of human cases of influenza A (H5N1) is essential to achievement of the following objectives:

- Confirmation of the diagnosis of recent infection with influenza A (H5N1).
- Reduction of morbidity and mortality through rapid identification and isolation of cases.
- Follow-up with contacts and institutions regarding appropriate precautions, treatment, and clinical management.
- Reduction of further spread by identification of potential human, animal, and/or environmental sources of exposure, risk factors for infection, and implementation of appropriate prevention and control measures, including stamping out vulnerable flocks, performing environmental decontamination, and conducting communication and social mobilization activities.
- Determination of whether the risk for pandemic influenza has increased as evidenced by increased efficiency of human-to-human transmission.
- Determination of key epidemiological, clinical, and virological characteristics for cases, including the mode(s) of transmission and disease diagnosis, manifestations, and treatment.
- Timely exchange of information among clinicians, investigators of public and animal health, and government officials to facilitate critical and informed decision-making at all levels.

The following steps are required in an investigation:

1. **Collect data according to the Suspected or Probable Human Case of Avian Influenza A (H5N1) Investigation Card** (Figure 2) by reviewing medical records and interviewing health care personnel and the patient as needed.

   The collected data should be verified against the information found in the health facility’s infectious disease register #60 and SES register #60. All newly identified cases resulting from the investigation should be recorded in these registers as well. Facilities should continue filling out the investigation cards for all clinical (probable) cases identified.

2. **Verify that all cases meet the suspected or probable influenza A (H5N1) case definition.**

   If a case does not meet the definition, the investigation team should discuss the case with the physician(s). However, any case meeting the H5N1 trigger criteria must have a laboratory specimen collected and submitted for influenza A (H5N1) testing. A case that is incompatible with the clinical and epidemiological description and is not confirmed by specific laboratory tests will be eliminated from epidemiological surveillance reporting.

\(^{10}\)Public health investigation may be triggered by other events, too, such as reports of excessive poultry deaths or rumors from newspapers (see Chapter 13).
3. **Identify the potential source of infection** by analyzing exposure history of the case 7 days prior to the onset of symptoms.

Inquire about possible exposure to sick/dead birds, animals, people, or a contaminated environment. Examine the house and its surroundings for evidence of domestic poultry as needed. Use the case investigation form included in Chapter 13.

The scope of response measures will depend on whether animal-to-human or human-to-human transmission is suspected. For example, if the initial investigation suggests a relationship in time and place with unusual deaths in poultry or other animals, the rayon veterinary authorities and rayon epizootic response commission should initiate immediate investigations to search for the possible source and collect appropriate animal samples for laboratory evaluation. If, however, the initial investigation suggests human-to-human transmission, antiviral prophylaxis should be initiated and exceptional control measures—such as social distancing and voluntary home quarantine—should be carefully considered. (Chapter 17 provides additional detail.)

4. **Collect specimens for laboratory investigation.**

Laboratory testing is currently mandated for confirmation of every case meeting influenza A (H5N1) trigger criteria, including suspected or probable cases of influenza A (H5N1) and symptomatic contacts of suspected or probable cases.

Samples should be collected by specially trained professionals—members of a case investigation/rapid response team. All manipulations should be carried out following standard biosafety guidelines—in particular, using full PPE, including a respirator mask, gown, gloves, and eye protection. (Chapter 19 provides instructions for specimen collection, storage, and transport.)

In general, the use of available rapid diagnostic tests for the detection of human influenza A (H5N1) infections is not recommended. The diagnostic accuracy of available rapid tests for human influenza A (H5N1) infections is unknown; if the test result is positive, differentiation between influenza A subtypes is not possible, and confirmatory tests must be done.

5. **Assess potential for transmission and identify contacts.**

The potential for transmission is usually determined by the number of susceptible contacts. At the present time, the risk to humans is believed to generally be low because avian influenza viruses usually do not cross the species barrier and infect humans. If the epidemiological situation progresses unfavorably, sporadic cases and clusters of human-to-human transmission will be registered, indicating that the virus is adapting to humans and signaling the need to intensify pandemic-preparedness measures, including improving the capacity to contain cases.

The investigation team should identify all close contacts of suspected, probable, or confirmed human influenza A (H5N1) cases during their infectious period (1 day before through 14 days after the onset of symptoms) and follow up with them to promptly detect potential human-to-human transmission of influenza viruses in Ukraine. (Chapters 16 and 17 provide additional detail.)

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**Close contact with a human case is defined as:**

- Having intimate contact (within 1 meter).
- Living in the same household.
- Providing care.
- Having direct contact with respiratory secretions, body fluids, or excretions.

Within 7 days of symptom onset.
6. **Search for additional cases.**

An active search should be conducted to determine if additional cases exist. This can be accomplished by identifying areas and populations of likely risk (people exposed to/closely associated in time and place with the same animal or human source of infection) and visiting those places to find out if anyone else near the potential source of infection has developed signs or symptoms that meet the case definition. The focus should be on health facilities and community settings. Chapters 13 and 17 provide additional information on the search for additional cases.

7. **Analyze outbreak data in the case of a cluster of probable or confirmed human cases.**

Following detection of a cluster of probable or confirmed cases, epidemiological data should be analyzed to characterize patients by person, place, and time. More specifically, the analysis should include a description of the illness in terms of clinical presentation, demographic information, and occupational data; the proportion of cases requiring hospitalization; clinical outcomes and case-fatality ratio; estimated incubation period; and a description of disease transmission patterns and mechanisms.

One of the investigation’s most critical objectives is to determine whether there is evidence of an increase in the virus’ ability to cause human disease and spread with improved efficiency. Examples of situations that might indicate a change in the transmission pattern of influenza A (H5N1) include:

- Sharp increase in the number of confirmed/possible influenza A (H5N1) cases despite adequate control measures in the animal population.
- Absence of exposure to birds or animals among confirmed/probable influenza A (H5N1) cases.
- Clustering of cases with evidence of two or more generations or chains of transmission.
- Increase in cluster frequency, size, duration, or spread within a specific area.
- Changes in epidemiological characteristics (e.g., age distribution, severity of disease).

Detection of two or more cases of confirmed, probable, or suspected influenza A (H5N1) infection that have onset of illness within the same two-week period, are in the same geographical area, and/or are epidemiologically linked requires careful and detailed investigation to assess whether transmission was likely due to a common source of exposure or to human-to-human transmission.

8. **Implement control and prevention measures** in partnership with the rayon avian influenza response commission and rayon veterinary authorities. (See Chapters 17 and 18 and Annex 1.)

9. **Write a report and send it to the MoH (NIC).** The report should include:

- The *Suspected or Probable Human Case of Avian influenza A (H5N1) Investigation Card* (Figure 2) completed for each case.
- An analysis of epidemiological data and a description of control and prevention measures taken and their effectiveness.
16. Preparedness and Organization of Response at the Rayon Level

The epidemic response commission undertakes planning and coordination of response activities at the rayon level. The recommended composition of the commission is as follows:

- Head of local administration.
- SES (chief doctor and epidemiologists).
- Health administration.
- Rayon veterinary service and agricultural department.
- Rayon hospital and polyclinic ambulatory unit.
- Nongovernmental organizations and private-sector entities.
- Representatives of the MoES and the militia.
- Representatives of other agencies (for example, managers of industrial and agricultural enterprises, heads of communal services).

Representatives of the commission should meet as needed to do the following:

- Review the latest human and animal avian influenza surveillance data and the latest pandemic-preparedness directives and materials.
- Review the functioning of the early warning system for humans and identify deficiencies and measures to correct them.
- Review and update the inventory of supplies needed for disease response (including antiviral drugs for treatment and chemoprophylaxis, antibiotics, antipyretics and other medicines, PPE, specimen-collection equipment, cold-chain storage, and transport material) based on the burden assessment. Ensure they are ready for use.
- Review other resources (e.g., personnel, transportation, communications) and identify materials and training needs.
- Determine concrete roles and responsibilities of different services/agencies for response actions.
- Assign clear responsibilities to individuals and units for specific response activities.

In the event of a probable or confirmed case(s) of influenza A (H5N1) in humans or animals, the commission representatives should start planning and implementing response measures. Based on the scope of the problem, central- and/or regional-level involvement should be considered. Financial resources at a certain minimum level should be secured at all times to support investigation and control activities as well as to ensure that there is a safe minimum stock of medicines and supplies.
17. Initial Human Case of Avian Influenza A (H5N1) Control/Response Measures

Control measures are aimed at reducing opportunities for further transmission. They should be initiated immediately upon the case investigation and should not await laboratory confirmation of the causative agent.

1. If an animal source is confirmed, quickly and safely control infection in birds.
Veterinary services must ensure immediate destruction of all infected or exposed poultry, including quarantining and rigorously disinfecting farms to limit avian influenza spread and to reduce opportunities for human exposure.

2. Ensure isolation/hospitalization of all suspected, probable, or confirmed human cases in respiratory (negative pressure) rooms or single rooms.

3. Ensure that personnel transporting and providing care to suspected, probable, or confirmed patients as well as people dealing with infected or exposed poultry wear—and are instructed and trained in how to wear—the following PPE:
   • A particulate respirator that fits well. If a sufficient number of particulate respirators is not available, a tightly fitting surgical mask should be used.
     o Wear masks once and then discard them.
     o Change masks when they become moist.
     o Do not leave masks dangling around the neck.
     o Wash hands after touching or discarding a used mask.
   • Clean gloves, if direct contact with the patient or infected poultry is anticipated.
   • A long-sleeved (preferably fluid-resistant) gown, if direct contact with the patient or infected poultry is anticipated. If a water-resistant gown is not available, a waterproof apron should be worn over the gown, particularly if splashing of potentially infectious material is anticipated.
   • Protective eyewear (face shield or goggles), if close contact (less than 1 meter) with the patient or infected poultry is anticipated. Clean and disinfect reusable equipment after each use.
PPE donning procedures

1. Collect all equipment needed.
2. Wash hands with an alcohol-based hand rub (preferably) or soap and water.
3. Put on PPE in the following order:
   - Fluid-resistant gown.
   - Disposable particulate respirator (or mask). Perform user seal-check of particulate respirator.
   - Hair cover (if used, for example, during an aerosol-generating procedure).
   - Face shield or goggles.
   - Gloves. (Make sure gloves cover cuff of gown sleeves.)

PPE removal procedures

1. Remove PPE, preferably in a separate room, making sure that neither the environment nor other persons can become contaminated.
   - Remove protective eyewear and discard in a rubbish bin. If a reusable face shield is used, place the shield in the container for decontamination.
   - If worn, remove hair cover and discard in rubbish bin.
   - Remove gown and discard in rubbish bin.
   - Remove gloves and discard in rubbish bin. (Gloves may be peeled from hands when gown is removed.)
   - Wash hands with an alcohol-based hand rub (preferably) or soap and water.
   - Remove particulate respirator by grasping elastic bands; do not touch front of particulate respirator (front of particulate respirator may be contaminated). Discard in rubbish bin.
2. Single-use items must be discarded in rubbish bin. Reusable items must be placed in a container for decontamination.
3. Wash hands with an alcohol-based hand rub (preferably) or soap and water.

4. Minimize the number of people exposed. Separate people from known or potential sources of avian influenza virus in animals or humans.

First, advise health care professionals dealing with influenza A (H5N1)-infected patients on infection-control measures to minimize the risk of nosocomial transmission. (Chapter 18 provides detailed instructions.)

Next, conduct public-awareness campaigns and deliver appropriate health education messages to the public. (Detailed instructions and examples of messages are included in Annex 1.)

Carry out domestic cleaning and disinfection, using household disinfection products, to reduce transmission from infectious respiratory secretions on surfaces and via objects such as clothing, towels, bed linens, and utensils that possibly harbor the virus and are capable of transmitting it. Clean and disinfect areas where infected poultry are kept. (Chapter 18 and Annex 1 provide more details.)

If influenza A (H5N1) infection is confirmed in humans or animals, it may be prudent to restrict local movement of people in and out of the affected area, both to reduce the number of people exposed and to lower the risk of extending infection among animals.
5. Conduct targeted prophylaxis* of close contacts with antiviral medications according to the risk stratification described in Table 6.

**TABLE 6. Risk Stratification for Targeted Prophylaxis**

<table>
<thead>
<tr>
<th>EXPOSURE GROUP</th>
<th>TAMIFLU (OSELTAMIVIR) OR RELENZA (ZANAMIVIR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk</strong></td>
<td><strong>Should be administered as chemoprophylaxis continuing for 7–10 days after the last known exposure.</strong></td>
</tr>
<tr>
<td>Household or close family contacts of a probable or confirmed H5N1 case.</td>
<td>This recommendation places a high value on preventing an illness with high case fatality and a low value on adverse effects, development of resistance, and cost. Administration of chemoprophylaxis should begin as soon as possible after exposure. The dose should be that used in seasonal influenza. This recommendation also applies to pregnant women in the high-risk exposure group. The bioavailability of zanamivir outside the respiratory tract is lower than that of oseltamivir. Zanamivir may be active against some strains of oseltamivir-resistant H5N1 virus. Consequently, it might be a reasonable choice for health care workers with a high-risk exposure to an oseltamivir-treated H5N1 patient.</td>
</tr>
<tr>
<td><strong>Moderate risk</strong></td>
<td><strong>Might be administered as chemoprophylaxis, continuing for 7–10 days after the last known exposure.</strong></td>
</tr>
<tr>
<td>Personnel involved in handling sick animals or decontaminating affected environments (including animal disposal) if PPE may not have been used properly. Individuals with unprotected and very close direct exposure to sick or dead animals infected with the H5N1 virus or to particular birds that have been directly implicated in human cases. Health care personnel in close contact with probable or confirmed H5N1 patients (for example, while performing intubation or tracheal suctioning, delivering nebulized drugs, or handling inadequately screened/sealed body fluids without sufficient PPE). This group also includes laboratory personnel who might have had unprotected exposure to virus-containing samples.</td>
<td></td>
</tr>
<tr>
<td><strong>Low risk</strong></td>
<td><strong>Should NOT be administered for chemoprophylaxis.</strong></td>
</tr>
<tr>
<td>Health care workers not in close contact (distance greater than 1 meter) with a probable or confirmed H5N1 patient and having no direct contact with infectious material from that patient. Health care workers who used appropriate PPE during exposure to H5N1 patients. Personnel involved in culling non-infected or likely non-infected animal populations as a control measure. Personnel involved in handling sick animals or decontaminating affected environments (including animal disposal) who used proper PPE.</td>
<td>This recommendation places a high value on avoiding adverse effects, potential development of resistance, and cost. It places a lower value on preventing the low risk of H5N1 disease.</td>
</tr>
</tbody>
</table>

*Possible funding sources: local budgets, funds of companies and individuals, other sources permitted by law.
<table>
<thead>
<tr>
<th>EXPOSURE GROUP</th>
<th>M2 INHIBITORS (AMANTADINE OR RIMANTADINE)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk</strong></td>
<td>Household or close family contacts of a probable or confirmed H5N1 patient.</td>
</tr>
<tr>
<td><strong>Moderate risk</strong></td>
<td>Personnel involved in handling sick animals or decontaminating affected environments (including animal disposal) if PPE may not have been used properly. Individuals with unprotected and very close direct exposure to sick or dead animals infected with the H5N1 virus or to particular birds that have been directly implicated in human cases. Health care personnel in close contact with probable or confirmed H5N1 patients (for example, while performing intubation or tracheal suctioning, delivering nebulized drugs, or handling inadequately screened/sealed body fluids without sufficient PPE). This group also includes laboratory personnel who might have had unprotected exposure to virus-containing samples.</td>
</tr>
</tbody>
</table>
6. **Initiate enhanced surveillance:** Actively search for and establish monitoring of symptom onset in people potentially exposed to influenza A (H5N1) infection for 7 days after the last contact (Figure 3). These people include:

- Persons who have had close contact with a suspected, probable, or confirmed case.
- Persons who could potentially have been exposed to the same source of infection as the patient (e.g., infected poultry or their droppings).

If the number of contacts/potentially exposed people is large, mobile brigades consisting of two or three health care workers should be mobilized as needed. Follow-up should be prioritized based on:

- Increased probability of infection, such as contact with a laboratory-confirmed case.
- Duration and closeness of contact.
- A high-risk (e.g., unprotected) exposure.

Enhanced surveillance should consider the health care-seeking behavior of the population and may include such measures as:

- Active surveillance in hospitals, particularly targeting in-patient and emergency departments.
- Active surveillance of groups that may be at higher occupational risk of exposure (e.g., health care workers or persons in contact with live or dead birds/animals). (See Chapter 13.)
- Active surveillance among family members and close contacts of suspected cases.
- Active surveillance in the general community in affected areas (e.g., door-to-door or use of public service announcements).

If possible, other resources such private practitioners, private laboratories, or medical students should be engaged. Sensitization of practitioners is a cornerstone of a population-based early warning system.

The duration of enhanced surveillance activities will need to be assessed for each investigation, but typically, it would be expected to be undertaken for a minimum of 2 weeks (i.e., 2 incubation periods) after the last human case is identified. However, it will be necessary to maintain enhanced surveillance in areas where human cases have occurred until influenza A (H5N1) outbreaks are controlled in poultry.

**Symptomatic contacts** (fever and respiratory illness) should be referred for collection of specimens for laboratory testing and appropriate medical care, including antiviral therapy. Depending on the severity of illness and the availability of hospital beds, contacts that are ill may be isolated at a health facility or at home while awaiting test results.

**Asymptomatic contacts**/potentially exposed people should be informed of the signs and symptoms of the illness and the need to immediately report the onset of fever and other symptoms to the health facility. The chief of the health facility should ensure medical supervision of potentially exposed people daily (for 7 days after the last exposure) to ascertain their clinical status and appropriately refer contacts who show symptoms. Voluntary quarantine of exposed persons may be necessary if exposure to influenza A (H5N1) is strongly suspected. In such a situation, the quarantine would last for 7 days after the last exposure. Persons in home quarantine may need to be provided with food, access to communications, psychological support, and supplies of their usual medications, especially for any acute or chronic conditions.

Antiviral chemoprophylaxis should be initiated as specified above.
7. **Recommend targeted vaccination with normal seasonal influenza vaccine to selected population groups.**

Targeted vaccination with the current seasonal influenza vaccine is now recommended as one of several measures for reducing opportunities for the simultaneous infection of humans with avian and human influenza viruses.

Minimizing the opportunities for dual infections reduces the chance for viral reassortment and for the emergence of a novel influenza virus with pandemic potential.\(^1\)

In addition to the main target groups, the following populations should be considered for current seasonal influenza vaccination:\(^2\)

1. All persons who could have been in contact with poultry or work on poultry farms potentially affected by HPAI and personnel of the poultry handling/processing industry.
2. Hunters, zoo workers, or vendors in live animal markets.
3. Health care workers involved in the daily care of human cases of HPAI.
4. Health care workers in emergency care facilities in areas where there is confirmed occurrence of HPAI in birds.

See Annex 2 for detailed recommendations on seasonal influenza immunization.

**Additional Exceptional Response Measures if Sustained Human-to-Human Transmission is Highly Probable or Confirmed**

8. **Implement “social distancing” measures as needed.**

- Close schools and workplaces.
- Cancel mass gatherings and public transportation.
- If the MoH decides to establish a “containment zone” around the index cluster, clearly mark the perimeter of the zone with signs and discourage all non-essential movement of persons in and out of the containment zone to the extent possible. Establish clear entry and exit points, and communicate them to the local population. Put screening procedures in place at these points to reduce the spread of pandemic influenza outside the containment zone.

These measures are socially disruptive and may cause considerable discomfort in the affected population.

9. **Follow MoH instructions regarding the need for mass antiviral prophylaxis.**

If a containment zone is established, the global WHO antiviral stockpile as well as regional and national stockpiles of antiviral drugs will be accessed, and all persons in the zone considered unlikely to be infected will be given 20 days of antiviral prophylaxis.

If vaccine is available against the newly identified pandemic virus, as is possible if the pandemic virus is identified as H5N1, and if that stockpile is available to the country through WHO for this purpose, then such vaccine may be used to supplement antiviral prophylaxis within the zone.

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\(^1\)This vaccination does not protect against infection with bird flu. This fact must be understood by those exposed so that they are still aware of the need for general protective measures.

\(^2\)Vaccination should be done in advance of any outbreak. Vaccine will not produce immunogenicity in recipients quickly enough to be effective during an outbreak.
10. Intensify active surveillance in the containment zone and laboratory testing of all possible cases. This is critical for:

- Allowing such cases to be laboratory-confirmed or excluded as cases of pandemic influenza.
- Monitoring the evolution of the outbreak.
- Evaluating the effectiveness of the containment operation.
- Helping guide decisions to modify, continue, or end the containment operation.

Household and any other close contacts should be traced and placed in voluntary home quarantine while laboratory testing is pending for the possible case.

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18. Influenza A (H5N1) Infection-Control Recommendations for Health Facilities

The recommended infection-control precautions should be implemented during the time the patient is infectious—that is, **for 14 days after the onset of symptoms**.

**Standard Precautions**

- Wash hands with soap and water (using a single-use towel for drying hands) or an alcohol-based hand rub before and after patient contact, after removing PPE, and after using the restroom.
- Use PPE based on risk assessment. Avoid contact with blood, body fluids, excretions, and secretions.
- Prevent needlestick/sharps injuries.

**Respiratory Etiquette**

Persons with respiratory illness should be educated to:

- Cover the mouth and nose with a tissue when coughing and dispose of used tissues in waste containers.
- Use a mask when coughing (when a mask can be tolerated).
- Wash hands with soap and water after contact with respiratory secretions.
- Stand or sit at least 1 meter from other persons, if possible.

**Isolation Precautions**

**Barrier precautions**

All individuals providing care for patients with probable or confirmed avian influenza infection should use PPE as specified in Chapter 17.

**Patient placement**

- Place the patient in a negative-pressure room (if available) or a single room and keep doors closed when not being used for entry/exit. Isolation rooms should have their own hand-washing sink, toilet, and bath facilities when possible.
- If single rooms are not available, patients known to be infected with the same organism can share rooms. However, laboratory-confirmed cases should not be mixed with suspected or probable cases.
Room preparation

• Ensure appropriate signage on the door.
• Place a recording sheet at the entrance. All health care workers and visitors should provide their names so that follow-up/contact tracing is possible if necessary.
• Use only essential furniture that is easy to clean.
• Stock linens as needed outside the isolation room.
• Place appropriate waste bags in a foot-operated bin.
• Place a puncture-proof container for sharps inside the isolation room.
• Dedicate non-critical patient equipment (e.g., stethoscope, thermometer, sphygmomanometer) to the patient. Any patient care equipment that is required for use by other patients should be thoroughly cleaned and disinfected prior to use.
• Set up a trolley outside the door to hold PPE.
• Place an appropriate container with a lid outside the door for equipment that requires disinfection and sterilization.
• Keep adequate equipment required for cleaning and disinfection inside the patient’s room and ensure scrupulous daily cleaning of the isolation room.
• Recommend setting up a telephone (e.g., mobile telephone) in the patient’s room to enable the patient or family member/visitor to communicate with health care workers to minimize the necessity for health care workers to enter the room.

Family Member/Visitor Recommendations

• Visitors should be strictly limited to those needed for the patient’s well-being and care. They should be advised about the possible risk of avian influenza transmission.
• Visitors should be provided PPE and instructed in their use and hand-washing practices prior to entering the patient’s room.

Patient Transport Within the Health Facility

• Limit the patient’s movement from the isolation room for essential purposes only and notify the receiving area as soon as possible prior to the patient’s arrival, informing them of the diagnosis and precautions.
• Ensure that the patient wears a surgical mask (if tolerated) during transport.
• If there is patient contact with surfaces, clean and disinfect these surfaces afterward.

Pre-Hospital Care and Transport Outside Health Facilities

• Place a surgical mask on the patient (if tolerated). If not available, have the patient cover his or her mouth and nose with a tissue when coughing.
• Health care workers should use full barrier precautions as indicated above.
• When possible, use vehicles that have separate driver and patient compartments. Optimize the vehicle’s ventilation to increase the volume of air exchange during transport.
• Notify the receiving facility as soon as possible prior to arrival, informing them of the suspected diagnosis and precautions.
• Follow recommended procedures for disposing of waste and disinfecting the vehicle and reusable patient care equipment.
Waste Disposal

Use standard precautions when working with solid waste outside of the isolation room that may be contaminated with avian influenza virus.

Clinical (infectious) waste includes waste directly associated with blood, body fluids, secretions, and excretions; laboratory waste that is directly associated with specimen processing, human tissue, blood, animal tissue, or carcasses; and discarded sharps.

- All generated waste should be removed from the isolation room in bags or containers that do not allow for spillage or leakage of contents. Later, the waste should be treated as infectious waste.
- When transporting waste, use gloves followed by hand washing.
- Liquid waste—such as urine or feces—can be flushed into the sewage system if there is an adequate sewage system in place. Close toilet cover when flushing feces.

Dishes and Eating Utensils

- Recommend the use of disposable dishes and eating utensils.
- Wash reusable items in a dishwasher with detergent at the recommended water temperature.
  If a dishwasher is not available, detergent and hot water should be used. Rubber gloves should be used when washing items by hand.
- If family members are caring for the patient, they should designate dishes and eating utensils for the patient’s use only.
- Disposable items should be discarded with other general waste.

Linens and Laundry

- Place soiled linens directly in a plastic laundry bag in the isolation room. Heavily soiled linens should be folded to contain the heaviest soil in the center of the bundle.
- Mattresses must have protective covers.
- Linens contaminated with biological fluids should be collected in a separate plastic bag for subsequent disinfection and washing.
- Large amounts of solid material (e.g., feces) should be removed from the linens with a gloved hand and toilet tissue and then placed in the toilet for disposal before the linens are placed in the laundry bag.
- When transporting soiled linens, use gloves followed by hand washing.
- Wash and dry linens according to routine facility standards and procedures.

Environmental Cleaning and Disinfection

- Cleaning must precede disinfection.
- The avian influenza virus is inactivated by phenolic disinfectants, household bleach, alcohol, and other registered/licensed disinfectants. Follow the manufacturer’s recommendations for use, contact time, and handling.
- Patient rooms should be cleaned at least daily and terminally cleaned upon discharge.
**Patient Care Equipment**

- If possible, place contaminated patient care equipment in suitable bags before removing it from the isolation room.
- When transporting contaminated equipment, use gloves followed by hand washing. Equipment should be disinfected in specially designated premises.

**Patient Discharge**

- Perform terminal cleaning of the patient’s room.

**Care of the Deceased**

- Use recommended PPE and standard precautions for routine care of the body and hygienic preparation of the deceased.
- The body should be fully sealed in an impregnable body bag prior to removal from the isolation room. No leaking should occur, and the outside of the bag should be kept clean.
- If required, transfer of the body to pathology or the mortuary should occur as soon as possible after death. If an autopsy is considered, the body should be held under refrigeration in the mortuary.
- The body can be safely removed from the body bag for storage in the mortuary or placed in a coffin for burial.
- If the patient’s family wishes to touch the body, they may be allowed to do so. If the patient died during the infectious period, the family should wear gloves and gowns and follow contact with hand washing.
- If family members want to kiss the dead body (e.g., the hands or face), these body parts should be disinfected using a common antiseptic (e.g., 70 percent alcohol). If the family wants only to view the body, there is no need to wear any PPE.
- Traditional ceremonies should be avoided, if possible, during a confirmed outbreak or for a suspected human H5N1 case. Cremation is the safest method.
- Traditional and religious issues must be addressed and discussed with religious authorities as appropriate.
19. Guidelines for Collecting, Storing, and Transporting Specimens for Influenza Diagnostics

Safety

The use of PPE is mandatory if direct or close contact with a patient is anticipated. It is also required when entering a room where aerosol-producing procedures are being performed on infected patients. The level of PPE needed will be determined by the exposure risk.

In general, PPE should include:

- A suitable form of respiratory protection.
- Non-sterile latex gloves (or equivalent if allergic).
- Goggles or a face shield.
- Gown.
- Head covering.

It may also be necessary to include:

- An impermeable apron.
- Suitable rubber boots.

High-risk activities—such as post-mortem examination of a confirmed or strongly suspected human case—should only be conducted in a full-body coverall with easily cleaned waterproof boots, heavy rubber gloves, and eye protection.

PPE is essential for preventing infection during sampling, but it does not alleviate all safety concerns. Individuals taking specimens should comply with all recommended infection-control precautions, including specific personal hygiene measures and the correct use of disinfectants.

Hand-washing techniques

When hands are visibly dirty or contaminated with biological materials, disinfect hands and wash them with soap and water. If hands are not visibly dirty, use an alcohol-based cleanser.

Soap and water. Liquid or bar forms of plain soap are acceptable when washing hands with a non-antimicrobial soap and water. Wet hands with water and apply the amount of product necessary to cover all surfaces. Vigorously perform rotational hand-rubbing on both palms, and interlace fingers to cover all surfaces. Rinse hands with water and dry thoroughly with a single-use towel. Use the towel to turn off the tap/faucet. Make sure the hands are dry. Ensure that towels are not used multiple times or by multiple people. Use running, clean water for hand hygiene whenever possible. Avoid using hot water, as repeated exposure to hot water may increase the risk of dermatitis. When bar soap is used, small bars of soap in racks that facilitate drainage should be used.

Hand cleansers. When using an alcohol-based formulation (or another disinfectant-based hand cleanser), apply a palmful of the product and cover all surfaces of the hands. Rub hands until they are dry.

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13 A significant portion of this section is based on materials taken from WHO’s Collecting, Preserving and Shipping Specimens for the Diagnosis of Avian Influenza A (H5N1) Virus Infection: Guide for Field Operations (2006).
Respiratory protection

The level of respiratory protection required when sampling will depend on a number of factors, including the type of sample to be taken (e.g., sampling for blood is less risky than taking a throat swab, which may cause the patient to cough) and the type of respiratory risk (e.g., droplets and aerosols require different types of protection).

Many types of respirators and masks are available, and the different types offer different levels of respiratory protection. It must be accepted that in some situations, high-efficiency respirators will not be available, and basic gauze masks may be all that can be used. Such masks should be changed every 4 hours.

- Individuals should select a particulate respirator that fits well. A user-seal check (fit check) should be performed each time a disposable particulate respirator is worn.
- Disposable particulate respirators, although similar in appearance to surgical masks, differ significantly from surgical masks because they are specifically designed to protect the wearer from exposure to airborne contaminants by sealing tightly to the face and filtering infectious particles from the air.
- If a particulate respirator is not available, a tightly fitting surgical or procedure mask should be used.
- Surgical and procedure masks do not provide protection against small-particle aerosols (such as droplet nuclei). Aerosol-generating procedures should not be performed if a particulate respirator is not available.

Particulate respirators (see photographs below) are lightweight and fairly comfortable to wear. Models with exhalation valves cannot be used when working in sterile areas (such as operating rooms) because the exhalation valve allows droplets and particles exhaled by the user to escape. Since air must be actively drawn into the mask, the mask will increase the work of breathing when used properly. In addition, it is almost impossible to prevent occasional leaks of contaminated air into the mask.

Disinfectants

Chlorine is one of the disinfectants used against influenza A (H5N1) contamination. Other disinfectants registered in Ukraine may also be used in accordance with the manufacturers’ instructions.

Household bleach is the best compound for preparing chlorine solutions for disinfection. Household bleach is a solution of sodium hypochlorite, which generally contains 5 percent (50 g/liter or 50,000 ppm) available chlorine.
Note that:

- Different products may contain different concentrations of available chlorine. The concentration should be checked before use.
- Household bleach preparations can lose some of their chlorine over time. Use newly manufactured bleach if possible. If the bleach does not smell strongly of chlorine, it may not be sufficient and should not be used.
- Thick bleach solutions should never be used for disinfection purposes (other than cleaning toilet bowls), as they contain potentially poisonous additives.

When preparing chlorine solutions for use, note that:

- Chlorine solutions gradually lose strength. Freshly diluted solutions must be prepared daily.
- Clear water should be used because organic matter destroys chlorine.
- 1:10 bleach solution is caustic. Avoid direct contact with skin and eyes.
- Bleach solutions give off chlorine. Prepare them in a well-ventilated area.
- Use plastic containers for mixing and storing bleach solutions, as metal containers corrode rapidly.

Two different dilutions of bleach are used for disinfection:

- **1:10 bleach solution** (which contains 0.5 percent chlorine concentration) is a strong disinfectant that is used to disinfect:
  - Excreta.
  - Bodies.
  - Spills of blood/body fluids.
  - Vehicles and tires.

  It is also used to prepare 1:100 bleach solution.

- **1:100 bleach solution** (which contains 0.05 percent chlorine concentration) is used to disinfect:
  - Surfaces.
  - Medical equipment.
  - Bedding.
  - Reusable protective clothing before it is laundered.

  It is also recommended for:
  - Rinsing gloves between contacts with different patients (if new gloves are not available).
  - Rinsing gloves, aprons, and boots before leaving a patient’s room.
  - Disinfecting contaminated waste before disposal.

To prepare 1:10 bleach solution, add 1 volume (e.g., 1 liter) of household bleach to 9 volumes of clean water (e.g., 9 liters).

To prepare 1:100 bleach solution, add 1 volume (e.g., 1 liter) of 1:10 bleach solution to 9 volumes of clean water (e.g., 9 liters).

**Note:** 1:100 bleach solution can also be prepared directly from household bleach by adding 1 volume of household bleach to 99 volumes of clean water (e.g., 100 ml of bleach to 9.9 liters of clean water). Preparing it from 1:10 bleach solution is much easier.
Disinfection

All objects that have come in contact with potentially infectious materials should be decontaminated.

Decontamination of surfaces. Wear an apron, heavy-duty gloves, and other barrier protection if needed. Disinfect surfaces by wiping clean with 1:100 chlorine solution, then incinerate all absorbent material in heavy-duty garbage bags. The surfaces must be rinsed with clean water after disinfection.

Disinfection of surfaces in laboratories where PCR work is undertaken. Disinfection is carried out by special disinfectants that do not affect the course of laboratory reaction and do not damage the equipment.

Decontamination of blood or body fluid spills. For spills, use 1:10 chlorine solution to inactivate pathogens before soaking up the fluid with absorbent materials. These absorbent materials must then be incinerated.

Disinfection of hands. The principal means for disinfecting hands is by washing with soap and water. If available, a commercial hand disinfectant containing alcohol, chlorhexidine, or polyvidone iodine can be used. The use of strong chlorine solutions (such as 1:100 chlorine solution) should be avoided, as they are dangerous.

Sterilization and reuse of instruments and materials. In field outbreaks, sterilization and reuse of any instruments or materials are not generally advisable. However, if it is necessary to reuse instruments, these should first be disinfected and cleaned, then sterilized.

Vehicles. Vehicles driven into potentially infected poultry farms should be rigorously disinfected because influenza viruses may survive for weeks in cool, moist, dark conditions and can easily be spread via mud or fecal contamination on vehicle tires or subframes. All gross contamination must be removed from vehicles with a power washer, and then all surfaces that may have been splashed by mud or feces on the farm must be sprayed down with 1:10 chlorine solution. Use of a tire bath with 1:10 chlorine for disinfection of tires is ideal. (The chlorine solution should be replaced after every two or three vehicles, as it will rapidly become exhausted.) Operators of power washers must be very well-protected due to the high risk of their being sprayed with contaminated material.

Monitoring Medical or Veterinary Personnel

If an incident that could lead to infection occurs during a sampling procedure (such as a breakdown of protective procedures), the staff members involved should be monitored for signs of illness (including daily temperature) for the following week. Post-exposure chemoprophylaxis with a neuraminidase inhibitor should be considered.

All staff working with human or animal cases of avian influenza should monitor their own health, and any evidence of ILI within 7 days of exposure to a confirmed or suspected human case or to a potential avian source should be viewed as suspected avian influenza and treated appropriately by a medical doctor.

Taking Specimens

For each type of specimen, two specimens should be taken in separate specimen tubes on each occasion. One can be used for immediate analysis and the other retained for reference purposes, such as retesting.

Each patient sample should be accompanied by an appropriate laboratory notification form containing a unique identifier (such as the patient’s first and last names and age). Specimen tubes should also be marked with information about the type of specimen in the tube and the date on which the specimen was taken.
Specimens to Collect from Suspected Cases

Preferred samples

- **Upper respiratory tract.** Take both types of specimens to allow detection of influenza A (H5N1) and other influenza viruses:
  - Posterior-pharyngeal (throat) swabs are currently the highest-yield upper respiratory tract specimen for detecting influenza A (H5N1) (unlike human influenza). Nasopharyngeal swabs may be collected, too (see below).
  - Nasal swabs with nasal secretions (from the anterior turbinate area) or nasopharyngeal aspirates or swabs are appropriate specimens for detecting human influenza A and B.

- **Lower respiratory tract.** If the patient is intubated, take a tracheal aspirate or collect a sample during bronchoalveolar lavage.

- **Blood.** For serum, obtain acute and convalescent specimens, if possible.

- **Secondary specimens.** These are not essential but can be useful if materials are available.
  - Plasma in ethylenediaminetetraacetic acid (EDTA) for detection of viral ribonucleic acid (RNA).
  - Rectal swab—especially if the patient has diarrhea.
  - Spinal fluid, if meningitis is suspected and a spinal tap is to be performed for diagnostic/therapeutic purposes.

When to Collect the Specimens from Suspected Cases

- **A throat swab should be taken (if possible) within 3 days of symptom onset.** Note that the virus is generally detectable in throat swabs from most patients from the onset of symptoms (or even just before) until the end of the second week and, infrequently, the beginning of the third week. Cases whose initial specimens are negative for influenza A (H5N1) but continue to show symptoms suggestive of this type of infection (or who have a history of exposure that supports the diagnosis) should be sampled again, at least once, as soon as possible.

- Virus may be detectable in **tracheal aspirates** from the onset of lower respiratory complaints (e.g., dyspnea, difficulty breathing, marked cough) or pneumonia **until the second or third week of illness.**

- **An acute-phase serum sample** should be taken **7 or fewer days after symptom onset.** This will usually be done when the patient presents and begins treatment. A convalescent sample should be taken after 3 to 4 weeks. Note that the limited available data on antibody kinetics indicate a development of positivity (initially ELISA [enzyme-linked immunosorbent assay] and not necessarily neutralizing antibody) from day 10 onward.

- **Single serum samples** should be collected at **day 14 or later** after symptom onset, since the likelihood of detecting neutralizing antibodies increases over time, certainly during the first 3 to 4 weeks after onset of symptoms.

- **Blood serum or plasma** for the detection of viral RNA should be taken **during the first 7 to 9 days** after the development of symptoms because the patient is most likely to be RNAemic (having detectable RNA in the bloodstream) at that time.

- Ideally, initial specimens (respiratory and blood) should be collected from suspected patients before antiviral therapy is begun—but treatment must not be delayed in order to take specimens. (Note that standard treatment may render throat swabs negative for virus after 3 or more days of treatment but probably has no effect on the development of neutralizing antibody).

- Specimens should be collected from deceased patients as soon as possible after death.
Sampling Human Contacts

Taking single respiratory tract or blood specimens from contacts of human cases who remain healthy in the days immediately after potential contact with influenza A (H5N1) is unlikely to yield useful results. Individuals who have had contact with human cases or exposure to sick animals should be observed (including their daily temperature) for 7 days after the last contact. If they become ill with an ILI, they should be sampled as outlined above. Blood specimens for serological studies can be taken from contacts for several reasons:

- As a tool for searching for asymptomatic/subclinical cases.
- For studies of the prevalence of influenza A (H5N1) infection.
- To assess possible susceptibility to influenza A (H5N1) infection.

Obtaining Specimens from the Respiratory Tract

Sampling from the respiratory tract is hazardous, as the operator is very close to the patient and the procedure can generate aerosols and droplets. Full PPE is therefore essential.

Choose a sitting position for adults and a supine position for infants and young children. Children may need to be restrained during the sampling process (see photo). It is generally best to avoid having the parent(s) in the room during the sampling procedure, since the sampling procedure can generate aerosols that could present a risk to others in the immediate vicinity.

When taking throat (or nasal) swabs, the swabs must be held correctly. They should be held between the thumb and the first and second fingers, with the shaft protruding beyond the web of the thumb (like a pencil), which ensures greater control (see photo). The swab should not be held between the thumb and forefinger with the base in the palm of the hand.

- Use only sterile dacron swabs with plastic shafts. Calcium alginate or cotton swabs or swabs with wooden sticks may contain substances that inactivate some viruses and inhibit PCR testing. They should only be used if dacron swabs are not available.
- Prepare two vials containing at least 2 to 3 ml of a suitable transport/preservative medium (e.g., viral transport medium [VTM]) for each specimen. These should be marked with:
  - The unique identifier.
  - The specimen date.
  - The type of specimen in the tube (e.g., blood serum, throat swab).

Note: Always mark the tube itself—not the cap, which can get switched during handling—with identifying details. Use an indelible and alcohol-resistant marker. Be aware that stick-on labels can easily come off, especially when the specimen is chilled to very low temperatures. Relevant field data sheets should be filled in.

- Take two specimens and put one into each vial.
- If VTM is not available, or if specimens cannot be stored at appropriate temperatures (e.g., no freezers are available), swabs can be stored and shipped in absolute (100 percent) ethanol. If pure ethanol cannot be used, 99 percent industrial methylated spirit—without additives other than methanol—may be substituted. Put 1 to 2 ml ethanol into a vial, and place the swab tip in the tube. Note that such specimens are suitable only for PCR.
- After a specimen is taken, the tip of the swab should be placed in the vial, and its shaft should be broken or cut off sufficiently short for the lid to be closed. Plastic swab handles usually have a weak point in them to
allow them to be broken off in this manner. Others have a handle made of a brittle plastic that will snap easily.

If the shaft cannot easily be broken off short enough to be put into a small tube such as a cryovial, it will have to be cut. To do this:

- Cut the shaft with scissors, taking care not to touch the tip.
- Allow the tip to slide into the VTM and then cap the tube. Do not let cut portions of the bag or wrap fall into the tube.

Sterilize the cutting edge of the scissors by using a flame (e.g., by using a spirit burner, a Bunsen burner, or another suitable heat source). Allow the scissors to cool before reuse. If this procedure cannot be followed, agitate the swab tip in the medium for 30 seconds and squeeze it against the side of the tube before removing it from the medium and disposing of it in a safe manner (not suitable for ethanol storage).

**Posterior Pharyngeal and Nasopharyngeal Swabs**

Posterior pharyngeal swabs are the best upper respiratory tract specimens to take; evidence to date suggests that they are more likely to be positive than anterior nasal swabs in sporadic influenza A (H5N1) infection. However, if it is difficult to obtain the former (e.g., from babies and young children), nasopharyngeal swabs should be obtained instead.

**Posterior pharyngeal swab (throat swab)**
- Hold the tongue out of the way with a tongue depressor.
- Use a sweeping motion to swab the posterior pharyngeal wall and tonsillar pillars. Have the subject say “aahh” to elevate the uvula. Avoid swabbing the soft palate, and do not touch the tongue with the swab tip. (Note: This procedure can induce the gag reflex.)
- Put the swab into VTM.

**Nasopharyngeal swab**
- Insert a flexible, fine-shafted polyester swab into the nostril and back to the nasopharynx. The swab should be slid straight into the nostril, with the patient’s head held slightly back. The insertion technique should follow the base of the nostril toward the auditory pit. In adults, the swab will need to be inserted at least 5 or 6 cm to ensure that it reaches the posterior pharynx. (Do not use rigid shafted swabs for this sampling method—a flexible shafted swab is essential.)
- Leave the swab in place for a few seconds.
- Withdraw slowly with a rotating motion.
- Put the swab into VTM.
- A second swab should be used for the other nostril and put into a second tube. This can serve as the second sample from the patient.

**Note:** Nasopharyngeal sampling is an invasive process that can cause considerable distress to the patient.

**Nasopharyngeal Aspirate**

The nasopharyngeal aspirate is easier and safer than swabbing in infants and young children.
- Use an aspiration trap.
- Insert a silicon catheter into the nostril toward the auditory pit and aspirate secretion gently by suction.
Blood Specimens

- Standard precautions should always be observed when taking and handling blood specimens because the patient may be infected with a blood-borne pathogen (for example, HIV or hepatitis B).
- Use PPE—at least gloves, plus face shields, masks, and gowns if splashing is anticipated.
- Remove and discard PPE items immediately after completion of task.
- Wash hands every time gloves are removed.

Serum is the best “all around” specimen to collect. Acute and convalescent sera are useful for detecting changes in antibody titer, and serum can be used for detecting viral RNA. An acute-phase serum specimen should be taken soon after onset of clinical symptoms and not later than 7 days after onset.

EDTA-anticoagulated plasma is also valuable for detecting viral RNA in blood and may be better than serum for this particular purpose, since EDTA inactivates RNAses present in the specimen. Heparin is not suitable as an anticoagulant for this type of specimen because of potential inhibition of PCR reactions.

Note that specimens for the detection of viral RNA in the blood should be collected during the first week after the development of symptoms. At least 1 ml of whole blood is needed to obtain a sufficient amount of serum or plasma for tests. This is the maximum that should be taken from infants. However, larger specimens of 3 to 5 ml should be taken from older children and adults, as this will allow a greater range of tests or repeat tests if necessary.

A convalescent-phase serum specimen should be collected 3 to 4 weeks after the onset of symptoms. When a patient is critically ill, a second antemortem specimen should be collected. Blood should be collected either by use of a vacuum venipuncture system or syringes and needles. The specimens should be collected either in a serum separator tube (SST) or a clotting tube (for serum) or an EDTA tube (for plasma).

1. Label the tubes, including the unique patient identification number, using an indelible marker. Always check to ensure that the correct tubes are used for each patient.
2. Place a tourniquet above the venipuncture site. Palpate and locate the vein.
3. Disinfect the venipuncture site meticulously with 70 percent isopropyl alcohol (an alcohol swab) or 10 percent polyvidone iodine by swabbing the skin concentrically from the center of the venipuncture site outward. Let the disinfectant evaporate. Do not re-palpate the vein.
4. Perform venipuncture.
5. If withdrawing blood with conventional disposable syringes, withdraw 3 to 5 ml of whole blood from adults and older children and 1 ml from infants. Under asepsis, transfer the specimen to appropriate transport tubes. Secure caps tightly.
6. If withdrawing blood with a vacuum system (e.g., Vacutainer®), withdraw the desired amount of blood directly into each transport tube.
7. Remove the tourniquet. Use a cotton swab to apply pressure to the venipuncture site until bleeding stops, and apply a bandage.
8. Never recap used sharps. Discard directly into a suitable container (a proper sharps-disposal container if available, or a container such as a coffee or other metal can that was appropriately labeled before use).
9. Recheck that the tubes used for sampling have been correctly labeled.
10. After taking all the samples, complete the appropriate field-data sheets or case investigation forms and the required laboratory request forms using the same identification numbers used on the tubes.
Separation of serum and plasma

Blood samples need to be centrifuged for at least five minutes at 1,500 g (3,000 rpm). This requires an electric centrifuge (ideally with a swing-out head rather than an angle head rotor). Hand centrifuges are not adequate for the separation of serum or plasma from red cells.

Serum separator tubes

The instructions for using these tubes must be followed carefully if the tubes are to work properly.

The tubes contain a gel with an intermediate density between blood cells and blood plasma and, usually, a coagulation (clot) activator.

- Put the blood sample into the tube and then follow the instructions for mixing the contents.
- Allow the clot to form. (Follow the instructions with the tube; do not cut the clotting process short.)
- Centrifuge the tube according to the relevant instructions.

When a filled SST has been properly centrifuged, the sample will separate into a top layer of serum separated by a gel barrier from the cell/clot layer and the clot activator.

Clotting tubes

If a basic sampling tube without any additives is used, the clot can be allowed to form overnight and the serum can be pipetted off the next day. Serum should not be left in contact with the clot for more than 12 hours, as lysis of the red cells can occur.

Whichever type of tube is used, once the serum has been separated, it should be pipetted off without disturbing the gel barrier or the clot. Put the serum into a vial such as a cryovial (without VTM). Ideally, vials for transport of serum should have external caps and internal o-ring seals. If there is no internal o-ring seal, ensure that the cap is closed tightly and then sealed with an inert sealing film, such as Parafilm®.

EDTA tubes

Centrifuge the tubes at high speed (approximately 10,000 g) to compact the cellular fraction. Then pipette off the plasma taking care not to draw blood cells off at the same time.

Filter paper

Blood or serum specimens can also be shipped in air-dried form on filter paper discs or special filter paper strips (e.g., Nobuto strips). Volumes of 0.1 ml of whole blood or serum are put onto the strip, which is then air dried. Strips of this sort can be stored for months at room temperature.

Transport

Blood specimen bottles and tubes should be transported upright and secured in a screw-cap container or in a rack in a transport box. They should have enough absorbent paper around them to soak up all the liquid in case of spillage (see more details below).

Specimens from Patients Who Have Died

If the corpse has an endotracheal tube in place, collect a deep endotracheal aspirate. If the circumstances allow, perform tissue sampling by incision or by needle from the affected lung(s). The operator may use chest radiograph results to guide the sampling, aiming for areas at the margins of interstitial infiltrates, which are most likely the sites of active virus replication for the best diagnostic yield. The lung tissue sample will provide excellent material for various laboratory tests, including RT-PCR, virus isolation, histopathology, bacterial
cultures, direct antigen detection or immunohistochemistry, and cytokine-chemokine analyses. The needle aspiration or the core needle sampling may give sufficient sample for microbiologic studies.

To perform this aspirate, clean a small area on the lateral chest wall between two ribs and make a small incision between the ribs, overlying the lungs with a sterile scalpel. Cut wedge sample(s) from the lung (1 to 2 cm³ minimum), or insert a large-bore needle (e.g., 18G) into the lung tissue and aspirate or cut available material into the needle/syringe. Put the specimen into VTM. The needle sampling should be performed as soon as possible after death.

Throat swabs, nasopharyngeal aspirates, or stool samples may be collected if time, sampling materials, and safety considerations permit, but this should not supersede or delay the collection of the deep endotracheal or lung material.

**Storing Specimens**

Table 7 below indicates the different storage and shipment conditions that can be used and which methods are recommended (based on the likelihood of obtaining a positive influenza A [H5N1] result on laboratory analysis).

**TABLE 7. Suitability of Various Storage/Shipment Conditions for Different Specimen Types**

<table>
<thead>
<tr>
<th>STORAGE/SHIPMENT CONDITIONS</th>
<th>SWABS OR OTHER SPECIMENS IN VTM FOR ISOLATION OF VIRUS</th>
<th>SWABS OR OTHER SPECIMENS IN VTM FOR PCR</th>
<th>SWABS IN ETHANOL FOR PCR*</th>
<th>BLOOD SERUM FOR VIRUS ISOLATION</th>
<th>BLOOD SERUM FOR PCR</th>
<th>BLOOD SERUM FOR ANTIBODIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>-70°C or dry ice or liquid nitrogen</td>
<td>Strongly recommended</td>
<td>n/a</td>
<td>Strongly recommended</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-20°C</td>
<td>Not recommended</td>
<td>Adequate</td>
<td>n/a</td>
<td>Not recommended</td>
<td>Adequate</td>
<td>Strongly recommended</td>
</tr>
<tr>
<td>+4°C</td>
<td>Adequate for up to 4 days storage</td>
<td>Adequate</td>
<td>Adequate for up to 4 days storage</td>
<td>Adequate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Room temperature</td>
<td>Not recommended</td>
<td>Adequate</td>
<td>Not recommended</td>
<td>Adequate for up to 4 days storage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dried blood spot on filter paper</td>
<td>n/a</td>
<td></td>
<td>Adequate</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Where refrigeration is not available.

- Aliquots of specimens should be taken before the specimens are frozen.
- Repeated freezing and thawing of specimens must be avoided.
- If specimens in VTM (or blood sera/plasma) for viral isolation can be taken to the laboratory within 4 days, they may be kept at +4°C and frozen at -70°C on arrival if they are to be stored. Otherwise, they should be frozen at or below -70°C until they can be transported to the laboratory. Freezing at -20°C is not recommended, because the virus does not survive well at this temperature, particularly in frost-free freezers.
- In the absence of freezers (or of VTM), ethanol-preserved swabs are a possible alternative. Storage of such specimens at +4°C (in a standard refrigerator) is better than at room temperature.
- Blood serum samples should be frozen at -70°C for PCR and at -20°C or lower for antibody determination, but they can be stored at +4°C for approximately 4 days.
Specimen Transport

Specimens should be collected and transported in a suitable transport medium on ice or in liquid nitrogen. Specimens for influenza should not be stored or shipped in dry ice (solid carbon dioxide) unless they are sealed in glass or sealed, taped, and double plastic-bagged. Carbon dioxide can rapidly inactivate influenza viruses if it gains access to the specimens through shrinkage of tubes during freezing. The receiving laboratory should be notified before the specimens are shipped.

All specimens to be transported must be packaged in packaging consisting of three layers. Packaging should be strong enough to withstand the shocks and loads normally encountered during transport. Packaging should be constructed and closed so as to prevent any loss of contents that might be caused under normal conditions of transport (e.g., by vibration or by changes in temperature, humidity, or pressure).

Primary receptacles should be packed in secondary packaging in such a way that, under normal conditions of transport, they cannot break, be punctured, or leak their contents into the secondary packaging. Secondary packaging should be placed in a final outer package with suitable cushioning material. Any leakage of the contents should not substantially impair the protective properties of the cushioning material or of the outer packaging.

The primary receptacle(s) should be leak-proof. Absorbent material should be placed between the primary receptacle and the secondary packaging; if several fragile primary receptacles are placed in a single secondary packaging, they should be either individually wrapped or separated so as to prevent contact between them. There should be enough absorbent material to absorb the entire contents of the primary receptacle(s), and there should be a secondary packaging that is leak-proof.
Annex 1

Social Mobilization: Delivering Community Education Messages

Social mobilization involves planned actions and processes to reach, influence, and involve all relevant segments of society across all sectors, particularly at the community level.

This section presents community education messages that should be delivered by public health care workers and medical professionals to help the population know:

1. How to recognize avian influenza in animals and humans.
2. How to prevent its transmission.
3. When to seek treatment.

It should also help the population prevent a panic in the case of a confirmed animal or human infection in the area in which they live.

These messages should be delivered by appropriate communication methods, such as:

- Newspapers.
- Television, radio.
- Presentations at schools.
- Meetings with health care personnel and trusted and respected religious and political leaders.
- Individual consultation of residents seeking advice or recommendation.

Relevant printed education materials (such as leaflets and brochures) should be disseminated during meetings and presentations for future reference.

Several sample questions and answers are presented below. Public health care workers and medical professionals should be prepared to adapt these materials to address beliefs about the disease and the needs of specific populations.

Q: What is bird flu? Will it cause the next influenza pandemic?

A: Avian influenza (“bird flu”) is a disease of wild and farm birds caused by avian influenza viruses. Bird flu viruses do not usually infect humans, but since 1997, there have been a number of confirmed cases of human infection from bird flu viruses. Most of these resulted from direct or close contact with infected birds. The spread of bird flu viruses from an infected person to another person has been very rarely reported; it has not been reported to continue beyond one person. A worldwide pandemic could occur if a bird flu virus were to change so that it could be easily passed from person to person. Experts around the world are watching for changes in bird flu viruses that could lead to an influenza pandemic.

Q: What types of birds can be infected with bird viruses?

A: Avian influenza viruses can infect chickens, turkeys, pheasants, quail, ducks, and geese, as well as a wide variety of other birds, including migratory waterfowl.
Each year, there is a flu season for birds just as there is for humans, and as with people, some forms of the flu are worse than others, depending on how strong the virus is. A weak virus may cause only mild illness in infected poultry and birds, but a strong virus could cause severe and extremely contagious illness—and even death—among infected poultry and birds.

Q: **What are the signs and symptoms of bird flu in birds?**
A: Infection causes a wide spectrum of symptoms in birds, ranging from mild illness to a highly contagious and rapidly fatal disease resulting in severe epidemics. Specific symptoms include:

- Decrease in activity.
- Drastic decline in egg production.
- Facial swelling with swollen and bluish-violet colored combs and wattles.
- Hemorrhages on internal membrane surfaces.
- Gasping for breath.
- Muscle weakness/paralysis.
- Diarrhea.
- Sudden death.

Virus isolation is needed for definitive diagnosis.

Q: **Is it safe to eat poultry?**
A: Yes, it is safe to eat properly cooked poultry. Cooking destroys germs, including bird flu viruses. Be sure to:

- Cook thoroughly: Ensure that poultry meat reaches 70°C or that the meat is not pink; egg yolks should not be runny.
- Separate raw meat from cooked or ready-to-eat foods; do not use the same knife or the same chopping board; do not use raw or soft-boiled eggs in food preparations that will not be heat-treated/cooked.
- Keep clean and wash your hands after handling frozen or soft raw chicken or eggs; thoroughly wash surfaces and utensils that have been in contact with raw meat.

Q: **What else can I do to reduce my risk of becoming ill?**
A: 1. **Avoid contact with chickens, ducks, and other poultry unless absolutely necessary,** particularly on any farm where animals have been ill, slaughtered, or are thought to harbor avian influenza. Do not let poultry into your house. Discourage children from playing with birds or keeping them as pets.

   Note that birds that are infected can spread the disease before they show signs of illness. Some birds, such as ducks, can get and spread the disease and never show signs of illness.

   **If there is contact with poultry:** Do not rub your eyes or eat, drink, or smoke before washing your hands with soap and water.

   2. **Avoid close contact with people who are sick.** When you are sick, stay home and/or keep your distance from others; cover your nose and mouth with a tissue when you cough or sneeze to protect others from catching a virus.
3. **Wash hands with soap and water often**, especially:
   - After going to the toilet.
   - After changing a child’s diaper.
   - Before preparing or eating food or feeding a child/infant.
   - After handling raw foods.
   - After blowing your nose, coughing, or sneezing.
   - After handling garbage.
   - Before and after treating a cut or wound.
   - After handling animals or animal waste.
   - After visiting markets.

4. **Regularly clean the areas where poultry are kept.** Clean or sweep feces and unconsumed feed from the yard every day. Burn or bury feathers and other waste away from the farm. Bury the waste deep and with lime so that scavengers do not dig it up.

5. **Take precautions in preparing and consuming poultry meat or eggs as specified above.**

6. **Take precautions if you are visiting a farm or other area where poultry are kept.** After leaving the area, wash your hands with soap and water, brush and disinfect your clothing, shoes, and the wheels of bicycles, motorcycles, or other vehicles.

**Home slaughtering**
- Sick birds (or birds from flocks in which one or more birds are sick) should never be slaughtered for consumption. Eggs for human or animal consumption should never be marketed.
- The slaughter should take place in a confined area away from birds. Children and animals should be kept away.
- The person performing the slaughter should wear personal protective equipment and observe strict hygiene. After slaughter, the area should be cleaned and disinfected and feathers and animal remains safely disposed of.

**Buying poultry or eggs**
- Purchase only poultry and poultry products from shops with evident high food-hygiene standards.
- Avoid buying live poultry, as bird flu can spread through close contact with infected live poultry.
- Select fresh poultry with no signs of illness (such as unusually dark color, hemorrhage, etc.).
- Select fresh eggs without feces stains on the shells. Avoid buying eggs with cracked shells.
- Remember that canned poultry products can be safely consumed, as all processed foods undergo a heat treatment process that effectively destroys viruses.

**Q:** What additional measures should I take if there is avian influenza in poultry in the area?

**A:**
1. **Do not bring in contamination from other farms or markets.**
   - Brush or wash off your shoes and the wheels of your bicycle/motorcycle or other vehicle and change clothing immediately after returning from farms or live-bird markets (so you do not carry the virus home on your clothing, shoes, or equipment).
• Clean or disinfect anything coming into the farm that may have contacted poultry or poultry droppings outside the farm. This includes clothing, tools, and equipment such as cages and bicycle or vehicle tires.
• Do not borrow equipment or vehicles from other farms.
• Do not transport live or dead chickens, ducks, or other poultry from one place to another—even if you think your birds are healthy.
• Do not bring other animals, such as chicks, ducklings, or piglets, from another farm.
• Do not buy or accept animals, eggs, or manure from other farms.

2. **Separate your poultry from wild birds and any domestic birds that roam free.**
   • Keep poultry brought to the farm/homestead from another location separate from your flock for at least 14 days.
   • Keep all your poultry fenced or caged away from other animals and wild birds and any source of water that could have been contaminated by wild birds.

3. **If recommended by authorities, bring your birds to be vaccinated.**

4. **Remember that hunting is prohibited** in the 10-km zone surrounding any place where H5N1 virus has been found.

*If you have had contact with* the carcass of any chicken that has died from avian influenza, the feces of the chicken, or an environment that has had sick or dead chickens in it:

• Wash your hands thoroughly.
• Report any sick or dead bird(s) to the rayon veterinary office immediately.
• Monitor your temperature for 7 days. If you develop a high fever (≥38°C), respiratory complaints, or an eye infection, immediately consult your doctor.

*If poultry have died in your back yard,* decontaminate the yard and immediately report the case to the rayon veterinary office.

• Wear personal protective equipment. At a minimum, cover your face and wear gloves or plastic bags over your hands.
• If authorities cannot come promptly, bury the dead poultry at a depth of at least 2.5 meters. This must be away from water supplies.
• Clean the area of all chicken droppings. Scrape or use a rake and bury the chicken droppings.
• Clean the chicken shed or area where the droppings have been with soap (or bleach) and water.

**Note:** Avian flu looks like other poultry diseases, especially Newcastle disease. Even if you think you know what is making your birds sick or die, still tell authorities, just to be safe.

**Note:** If your poultry or your neighbor’s poultry are sick or have died from avian influenza, it is important to protect your community by culling any surviving birds and disinfecting your farm. Do not kill birds yourself—wait for the people sent by the government, who will do it properly. After your birds have been culled, follow the government authority’s instructions about obtaining compensation and about disinfecting your farm.
Q: What should I do if I think someone else has avian influenza?

A: • Take the person to a health care provider immediately.
  • Until you bring the person to the health care provider, take specific protective actions: wash your hands frequently, wear a mask or cover your mouth and nose with a cloth, have the person who is ill wear a mask or cover their mouth and nose with a cloth, and limit the number of people who come within a meter of the sick person.
  • Contact the nearest rayon hospital or ambulatory facility for additional guidance.

Q: Will the seasonal flu shot protect me against pandemic influenza?

A: No, it will not. But flu shots can help you avoid seasonal flu.

Q: Is there a special vaccine to protect me against pandemic influenza?

A: No, currently there is no vaccine to protect humans against avian viruses. Even though vaccine-development efforts are under way, there are a number of constraints to development and mass production. Because viruses change over time, a specific pandemic influenza vaccine cannot be produced until a pandemic influenza virus emerges and is identified. If a pandemic influenza virus is identified, it will likely take an additional 4 to 6 months to develop, test, and begin producing a vaccine.
Seasonal Influenza Vaccination Recommendations

The Justification for Vaccine Use

Influenza virus types A and B are common causes of acute respiratory illnesses, although influenza A viruses are the principal cause of large epidemics as well as pandemics. Influenza viruses undergo frequent changes in their surface antigens. Immunity resulting from infection by one influenza virus does not protect fully against antigenic variants of the same subtype (influenza A viruses) or type (influenza B viruses). As a consequence, influenza outbreaks occur every year.

Influenza poses a considerable economic burden both on society and the individual in terms of consumption of health care resources and lost productivity.

During influenza epidemics, attack rates of 5 to 10 percent are commonly observed, and they may reach 20 to 30 percent in children. While attack rates are highest among children, rates of serious complications, such as pneumonia, are highest among persons aged 65 or older, children younger than 2 years, and persons of any age who have medical conditions that place them at increased risk for complications from influenza. In the United States, the majority of influenza-related deaths occur in persons older than 70 years. The average annual excess mortality among all age groups during influenza epidemics is estimated to be 7 to 23 per 100,000.

Economic considerations cannot be ignored, either. Indirect costs of influenza epidemics can include those associated with lost days of work and education, the need to increase the number of hospital beds for those needing supportive care, the increased use of antibiotics for actual or suspected cases of secondary bacterial infection (which may accelerate the development of resistance), and general social disruption. Recent estimates from France, Germany, and the United States indicate that the total annual cost of influenza outbreaks vary from US$1 to $6 million per 100,000 inhabitants.

Influenza vaccination is the primary and single most cost-effective method of preventing influenza and its severe complications. Antiviral agents used for chemoprophylaxis or treatment of influenza are adjuncts to vaccine, but they are not substitutes for annual vaccination. Most of the widely licensed influenza vaccines are manufactured according to the quality requirements defined by the World Health Organization (WHO) and have proven to be efficacious and safe. New influenza vaccines must be designed annually to match the circulating viruses that are expected to cause the next epidemic. Current influenza vaccines contain antigens from two influenza A virus strains (an H3N2 and an H1N1 strain) and one B strain, according to the annual recommendation of the WHO. This recommendation is based on intensive surveillance of new influenza strains around the globe to ensure optimal antigenic match between the virus strains in the vaccine and the viruses circulating in the subsequent influenza season.

The effectiveness of influenza vaccine depends primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the viruses in the vaccine and those in circulation. Vaccines containing strains that match the predominant circulating strains have been reported to be 70 to 90 percent efficacious for preventing (laboratory-confirmed) illness in healthy adults. Retrospective studies of people with predisposing medical conditions have found reductions of up to 50 percent in the rates of severe respiratory illness and death. In such persons, the main benefit of vaccination may be to prevent severe consequences of infection rather than preventing uncomplicated illness.
**Types of Influenza Vaccine**

Inactivated and live attenuated influenza vaccines are available and can be used to reduce the risk of influenza virus infection and its complications. Although both types of vaccines are effective, they differ in several aspects.

Inactivated influenza vaccine contains killed viruses, and thus cannot produce signs or symptoms of influenza virus infection. In contrast, live attenuated influenza vaccine contains live, attenuated viruses, and therefore, has a potential to produce mild signs or symptoms related to influenza virus infection.

*Only inactivated vaccine is currently registered and available in Ukraine.*

There are three types of inactivated influenza vaccine that show comparable efficacy but differ in terms of reactogenicity.

- *Whole-virus vaccines* often cause local reactions in children lasting for 1 to 2 days. Transient systemic reactions such as fever, malaise, and myalgias may occur in a minority of vaccine recipients within 6 to 12 hours of vaccination.

- *Split vaccines* are vaccine formulations consisting of disrupted viral particles.

- *Subunit vaccines*, specifically the ones containing hemagglutinin and neuraminidase surface glycoproteins purified from other viral components, show reduced systemic reactogenicity both in children and adults as compared to whole-virus preparations. Consequently, they are more attractive, particularly for use in children.

Whole-virus vaccines are being replaced by less reactogenic split virus and subunit vaccines.

**Recommendations for Using Inactivated Influenza Vaccines**

**Objective:** The primary objective for the prevention of influenza is to reduce the incidence of severe illness and premature death in groups at increased risk of severe disease, and as a consequence, to reduce the need for specialized health care services and pharmacological supplies, in particular antibiotics.

The inactivated vaccine is approved for persons 6 months of age and older, including those with high-risk conditions. Annual influenza vaccination is recommended for the following groups:

<table>
<thead>
<tr>
<th>TARGET GROUPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residents of institutions for the elderly or disabled</td>
</tr>
<tr>
<td>All individuals ≥6 months of age with one or more of the following chronic conditions: chronic cardiovascular, pulmonary, metabolic (such as diabetes mellitus or renal dysfunction), or immunodeficiency (caused by medications or HIV)</td>
</tr>
<tr>
<td>Persons &gt;60 years of age</td>
</tr>
<tr>
<td>Children aged 6–23 months</td>
</tr>
<tr>
<td>Women who will be pregnant during the influenza season</td>
</tr>
<tr>
<td>Individuals who are receiving long-term aspirin therapy and therefore might be at risk of experiencing Reye’s syndrome after influenza virus infection</td>
</tr>
</tbody>
</table>

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14Hypertension is not considered a high-risk condition.
### TARGET GROUPS

<table>
<thead>
<tr>
<th>Persons at increased risk for influenza-associated clinic or hospital visits</th>
<th>Children aged 24–59 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons aged 50–59 years</td>
<td></td>
</tr>
<tr>
<td>Persons who live with or care for persons at high risk for influenza-related complications</td>
<td>Health care workers</td>
</tr>
<tr>
<td>Healthy household contacts and caregivers of children aged 0–59 months and persons at high risk for severe complications from influenza</td>
<td></td>
</tr>
</tbody>
</table>

The Ministry of Health of Ukraine and WHO recommend increasing vaccination of high-risk individuals and aiming at vaccination coverage of elderly people of at least 50 percent by 2007 and 75 percent by 2010.

**Notes**

**General population:** In addition to the groups for which annual influenza vaccination is recommended, vaccination providers should administer influenza vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza or retransmitting influenza to others should they become infected. In this case, the cost of vaccination can be covered by local budgets or other sources permitted by law (funds of companies, organizations, or individuals).

Persons who provide essential community services should be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Students and other persons in institutional settings (e.g., those who reside in dormitories) should be encouraged to receive vaccine to minimize the disruption of routine activities during epidemics.

**Breastfeeding mothers:** Inactivated influenza vaccine is safe for mothers who are breastfeeding and their infants.

**Use of Seasonal Influenza Vaccines in Humans at Risk of H5N1 Infection**

Targeted vaccination with the current seasonal influenza vaccine is now recommended as one of several measures for reducing opportunities for the simultaneous infection of humans with avian and human influenza viruses. Minimizing the opportunities for dual infections reduces the chance for viral reassortment and for the eventual emergence of a novel influenza virus with pandemic potential.15

In addition to the above target groups, the following populations should be considered for current seasonal influenza vaccination:

1. All persons who are expected to be in contact with poultry or poultry farms potentially being affected by highly pathogenic avian influenza (HPAI), especially cullers involved in destruction of poultry; people living and working on poultry farms where HPAI has been reported or is suspected or where culling takes place; and hunters, zoo workers, vendors in live animal markets, and others having direct contact with animals.

2. Health care workers involved in the daily care of strongly suspected or confirmed human cases of HPAI, collection of specimens for laboratory investigation, and personnel of laboratories investigating H5N1 virus or material from suspected cases.

3. Health care workers in emergency care facilities in areas where there is confirmed occurrence of HPAI in birds.

4. Close contacts of HPAI human cases.

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15This vaccination does not protect against infection with bird flu. This fact must be understood by those exposed so that they are still aware of the need for general protective measures.
Other Aspects of Influenza Vaccine Use

<table>
<thead>
<tr>
<th>STORAGE</th>
<th>IN A REFRIGERATOR AT +2–8°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage</td>
<td>Usually 1 dose (consult the manufacturer’s package insert). Two doses administered at least 1 month apart are recommended for children aged 6 months to 9 years who are receiving influenza vaccine for the first time.</td>
</tr>
<tr>
<td>Route</td>
<td>Intramuscular. Adults and older children should be vaccinated in the deltoid muscle; infants and young children should be vaccinated in the anterolateral aspect of the thigh.</td>
</tr>
</tbody>
</table>
| Contraindications | 1. Persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine.  
2. Persons with moderate to severe acute febrile illness. |
| Timing        | The optimal time for vaccination efforts is usually during November–December, but can often be extended into January. Providers should routinely offer influenza vaccine throughout the influenza season, even after influenza activity has been documented in the community. People have peak antibody protection against influenza virus infection 2 weeks after vaccination. |

Role of Physicians in Increasing Vaccination Levels

Vaccination rates among target populations in Ukraine are not in line with WHO recommendations despite the well-established efficacy and effectiveness of current inactivated influenza vaccines. Clearly, influenza vaccines are still seriously underutilized, which is often due to perceptions related to influenza and influenza vaccinations that are based on insufficient or inappropriate information among the general population. Too often, influenza is viewed as a comparatively mild disease that does not pose a serious threat. At the same time, influenza vaccination is frequently considered ineffective or even a cause of the flu. In addition, the current mode of the vaccine administration by injection represents a barrier for individuals with a fear of needles.

Health care professionals are in a key position to spread the information regarding influenza vaccine effectiveness, cost-effectiveness, and safety and explain the favorable risk-benefit ratio of influenza vaccination to people in target groups, and thus, to motivate them to take the vaccine. *The single most important factor influencing the use of influenza vaccine is a trust in the doctor’s recommendation.*

Current inactivated influenza vaccines have an excellent safety record. About 300 million vaccine doses are being administered annually around the globe, and the overall rate of adverse reactions is extremely low. The most frequently occurring side effects are local reactions at the site of vaccination, which usually do not last more than 1 to 2 days. Generally, the reactions are mild and of a transient nature. When educating patients regarding potential side effects, clinicians should emphasize that inactivated influenza vaccine contains non-infectious killed viruses or their fragments and cannot cause influenza.

Possible actions by primary-care physicians to encourage vaccine uptake in target populations may include:

- Making/updating the records of people recommended for vaccination.
- Sending invitation letters together with information leaflets to people recommended for vaccination.
- Organizing polyclinics to administer vaccine to as many target subjects as possible in a time-efficient way.
- Promoting vaccination of family members of at-risk patients and health care personnel.
- Displaying appropriate information in patient waiting rooms and in offices.

Increased use of influenza vaccines is expected to significantly reduce epidemics and to improve our preparedness for potential new pandemic outbreaks.
Use of Vaccines in the Private Sector

Beyond government programs, physicians may prescribe influenza vaccine to any person wishing to reduce the risk of influenza, except where it is medically contraindicated. Private practitioners should ensure that their use of vaccines is consistent with national guidelines.

Some Aspects of Developing a Human Vaccine Against Pandemic Influenza

H5N1 is presently considered the most likely virus to ignite the next pandemic. The increasing spread and evolution of H5N1 viruses in Asia have brought the world closer to another pandemic than at any time since 1968, when the last of the previous century’s three pandemics began.

Data from initial clinical trials of a vaccine being developed to protect humans against infection with H5N1 avian influenza indicate that the experimental vaccine evoked an immune response in a small group of healthy adults. Although more trials are needed, the findings reconfirm the feasibility of developing an H5N1-specific vaccine.

Vaccines are the principal medical intervention for protecting individuals against pandemic influenza. If available rapidly and in sufficient quantities, they can reduce the morbidity and mortality that have traditionally made pandemics so socially disruptive as well as deadly.

However, many problems need to be resolved before vaccines can assume such a role in mitigating the effects of the next pandemic. Pandemic vaccine production faces two major challenges: first, two doses would almost certainly be required to compensate for the lack of existing immunity within the world population and, second, at least based on current trials of pandemic vaccines, much higher concentrations of antigen\(^\text{16}\) might be needed to achieve an immune response, further limiting the number of people who can be vaccinated.

Strategies for stretching limited antigen supplies—by adding an adjuvant to the vaccine formulation or by injecting the vaccine into the skin rather than into muscle—have been proposed. Adjuvants are chemicals that can be added to the vaccine formulation to boost the immune response, theoretically allowing the use of smaller doses of antigen to achieve an immune response. Such antigen-sparing strategies using adjuvants are currently being tested by several manufacturers.

At present, 90 percent of production capacity for all influenza vaccines is concentrated in Europe and North America, in countries that account for only 10 percent of the world’s population. Current global manufacturing capacity (estimated at 300 million doses of regular trivalent influenza vaccine per year) is inadequate to meet the expected global needs during a pandemic and cannot be rapidly augmented.

Because the present total global manufacturing capacity for influenza vaccine is limited, any decision to manufacture a pandemic vaccine in large quantities prior to the start of a pandemic would, if necessary, compromise the capacity to produce vaccines for seasonal influenza. Seasonal epidemics of influenza predictably cause an estimated 250,000 to 500,000 deaths each year. In the current situation, the capacity to respond to seasonal influenza must be balanced against preparations for pandemic influenza. However, once a pandemic has been declared, all manufacturers would stop production of seasonal vaccines and produce only the pandemic vaccine.

Even with the use of an adjuvant, however, it is important to remember that current production technologies can take up to six months to produce the seasonal vaccine supply. Therefore, it is doubtful at this time that enough H5N1 vaccine can be produced to meet global needs during the first wave of a pandemic.

\(^{16}\text{Antigen is the component of the vaccine that elicits an immune response.}\)
Preparedness Planning for Vaccination Against a Pandemic Influenza Virus

The primary goal of a pandemic response is to decrease health impacts, including severe morbidity and death, and minimize societal and economic impacts.

The Ministry of Health of Ukraine has submitted a request to WHO to take into account the need of Ukraine’s high-risk populations in a pandemic in the case of a threat of pandemic influenza virus spread or if other complications of avian influenza arose.

Initial pandemic vaccine stocks will be used to vaccinate designated priority groups. After vaccination of these priority groups, vaccination of all those who desire it will be phased in depending on available supplies.

Vaccination of priority groups

A provisional list of priority groups for receiving vaccination and rationale for prioritization is provided in the table on the following pages. To prepare for vaccination of priority groups, the Ministry of Health and regional sanitary-epidemiological stations (SES) and health administrations should:

• Identify a process for finalizing national recommendations for pandemic influenza vaccination and develop region-specific modifications for priority groups, depending on local circumstances.
• Develop specific priority groups and their definitions, identifying occupational categories as needed.
• Estimate the size of relevant priority groups.
• Develop a plan for how persons in priority groups will be identified at polyclinics and how vaccine would be most efficiently provided to these groups.
• Educate medical professionals and other stakeholders about the need for priority groups and the rationale for selecting them.

The recommendations summarized in the following table are based on the following assumptions:

• The greatest risk of hospitalization and deaths will be in infants, the elderly, and those with underlying health conditions.
• The health care system may be overwhelmed due to the large number of illnesses and complications from influenza requiring hospitalization and critical care. (The demand may increase by 25 percent or more.)
• During a pandemic, 25 to 30 percent of people will become ill during a 6- to 8-week wave. At the peak of pandemic disease, 10 percent of the workforce will be absent due to illness or caring for an ill family member.
• The amount of pandemic vaccine needed will be updated, taking into consideration regional needs based on the above recommended priority groups.
Vaccine priority group recommendations

The recommendations are based on the 2005 HHS [US Department of Health and Human Services] Pandemic Influenza Plan. They are currently being debated in the United States and other countries because of numerous ethical implications. They may be revised in the near future.

<table>
<thead>
<tr>
<th>TIER</th>
<th>VACCINE PRIORITY GROUP RECOMMENDATIONS</th>
<th>RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Manufacturers/suppliers of antiviral medications and vaccine</td>
<td>The health community needs to ensure maximum availability of antiviral drugs and pandemic vaccine</td>
</tr>
<tr>
<td></td>
<td>Medical workers involved in direct patient care and vaccinations</td>
<td>Health care workers are required for quality medical care</td>
</tr>
<tr>
<td>2</td>
<td>Persons &gt;60 years old with one or more influenza high-risk conditions</td>
<td>These groups are at high risk of hospitalization and death</td>
</tr>
<tr>
<td></td>
<td>Persons 6 months to 59 years old with two or more influenza high-risk conditions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Persons 6 months or older with a history of hospitalization for pneumonia or influenza or other influenza high-risk condition in the past year</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Pregnant women</td>
<td>In past pandemics and for annual influenza, pregnant women have been at high risk; vaccination will also protect the infant who cannot receive vaccine</td>
</tr>
<tr>
<td></td>
<td>Household contacts of severely immunocompromised persons who would not be vaccinated due to likely poor response to vaccine</td>
<td>Vaccination of household contacts of immunocompromised and young infants will decrease the risk of exposure and infection among those who cannot be directly protected by vaccination</td>
</tr>
<tr>
<td></td>
<td>Household contacts of children &lt;6 months old</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Public health emergency response workers critical to pandemic response</td>
<td>It is critical to implement pandemic response measures, such as providing vaccinations and managing/monitoring response activities</td>
</tr>
<tr>
<td></td>
<td>Key government leaders</td>
<td>Preserving decision-making capacity is critical for managing and implementing a response</td>
</tr>
<tr>
<td>5</td>
<td>Healthy persons ≥60 years old</td>
<td>These groups are also at increased risk, but not as high as the population in tier 2</td>
</tr>
<tr>
<td></td>
<td>Persons 6 months to 59 years old with one high-risk condition</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Healthy children 6–23 months old</td>
<td></td>
</tr>
</tbody>
</table>

17 See an earlier section on recommendations for using influenza vaccine.
<table>
<thead>
<tr>
<th>TIER</th>
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<th>RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Other public health emergency responders</td>
<td>This group includes critical infrastructure groups that have impact on maintaining health, implementing a pandemic response, and maintaining societal functions</td>
</tr>
<tr>
<td></td>
<td>Public safety workers, including police, fire, 01-02-03-04 telephone dispatchers, and correctional facility staff</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Utility workers essential for maintenance of power, water, and sewage system functioning</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transportation workers transporting fuel, water, food, and medical supplies, as well as public transportation workers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Telecommunications/information technology for essential network operations and maintenance</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Other key government health decision-makers</td>
<td>These are other important societal groups for a pandemic response, but they are of a lower priority</td>
</tr>
<tr>
<td></td>
<td>Funeral directors</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Healthy persons 2–59 years old not included in the above categories</td>
<td>All persons not included in other groups based on objective to vaccinate all those who want protection</td>
</tr>
<tr>
<td></td>
<td>All persons not included in other groups based on objective to vaccinate all those who want protection</td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine procurement and distribution**

Each regional and rayon SES (hospital) will receive available vaccine in proportion to the size of its population in defined priority groups.

Local SES and health administrations should:

- Identify organizations that will provide vaccinations to persons in priority groups.
- Obtain written commitments from heads of each clinic or facility responsible for vaccinating a priority group.
- Work with the heads of these facilities to develop strategies for rapid distribution and administration of vaccines, taking into account vaccine security issues, cold chain requirements, and transport and storage issues.
- Estimate the size of the priority groups that will be vaccinated based on extrapolation from national data, or on local data where available.
- Develop procedures for collecting, removing, and disposing of used syringes, needles, and other vaccination supplies.
- Develop a plan for training vaccinators and other staff responsible for mass vaccination.
- Develop strategies for vaccinating hard-to-reach populations.

A vaccine against pandemic influenza will likely require two doses, administered at least a month apart, to provide a level of immunity comparable to that obtained with seasonal influenza vaccines. If two doses are required to achieve immunity, it will be necessary to ensure that vaccinated persons return for the second dose. Regional and district SES and health administrations should do the following:

- Arrange for information about the need for a second dose to be provided at the time of administration of the first dose.
- Ensure that planning for vaccine procurement and distribution to clinics and other facilities accounts for the need to use portions of future shipments for second doses, thus reducing the number of available first doses.
• Consider implementing a call-back system, immunization registry, or other management information system that would help accomplish the goals of pandemic vaccination.

**Vaccine monitoring and data collection**

Vaccine effectiveness will be assessed by comparing rates of influenza-related illness, hospitalization, and/or death among vaccinated and unvaccinated persons.\(^1\)\(^8\) Vaccine tracking will be implemented by regional and local health authorities who will have major responsibility for allocation decisions. Vaccine tracking may be used by decision-makers at the central and other levels to estimate adverse event rates and to determine if vaccine is being administered according to established priority groups for pandemic vaccine. Data will be collected from individual providers, collated at the district and regional levels, and reported to the Ministry of Health on a scheduled routine basis. At a minimum, tracking data should include:

- Number of doses administered, by date and age, priority group, and district.
- Number of doses that represent second doses, as applicable.

The Ministry of Health is working on the development of a system for monitoring vaccination rates and for reporting and investigating adverse effects following immunization with a pandemic vaccine.

**Public health communications**

The provision of vaccine information will be an important component of ongoing public health communication during a pandemic.

- Regional and local SES and health departments should work with the Ministry of Health to disseminate accurate, useful, and consistent public health messages on:
  - Rationale for prioritization and list of priority groups.
  - Phasing of vaccination, if any, after priority groups have been vaccinated.
  - When and where vaccination is available.
  - Importance of vaccination given the likelihood of subsequent pandemic waves.

In addition, all vaccine providers will need vaccine information sheets that describe the vaccination’s risks, benefits, and contraindications.

**Training**

Regional and district SES and health departments can assist health care partners in conducting training exercises to facilitate rapid and effective delivery and use of vaccines. Exercises and drills are essential to ensuring that emergency procedures are in place and that roles and responsibilities are well- understood. It may be useful, for example, to practice emergency implementation of mass vaccination (e.g., receiving large quantities of vaccine; storing and handling vaccine; setting up and staffing polyclinics; administering vaccine; testing information management systems; educating the public, media, and health care providers; targeting specific priority groups).

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\(^1\)\(^8\)Since influenza-related illnesses have non-specific clinical definitions, this needs to be supplemented with some type of laboratory surveillance, so at least a subset of cases are laboratory-confirmed and reasonable estimates can be made.
Annex 3


Acute Upper Respiratory Infections (J00–J06)

*Excludes:* chronic obstructive pulmonary disease with acute exacerbation NOS (J44.1)

**J00**  
*Acute nasopharyngitis [common cold]*
  - Coryza (acute)
  - Nasal catarrh, acute
  - Nasopharyngitis:
    - NOS
    - infective NOS
  - Rhinitis:
    - acute
    - infective

*Excludes:* nasopharyngitis, chronic (J31.1)
  - pharyngitis:
    - NOS (J02.9)
    - acute (J02.-)
    - chronic (J31.2)
  - rhinitis:
    - NOS (J31.0)
    - allergic (J30.1-J30.4)
    - chronic (J31.0)
    - vasomotor (J30.0)
  - sore throat:
    - NOS (J02.9)
    - acute (J02.-)
    - chronic (J31.2)

**J01**  
*Acute sinusitis*

*Includes:* abscess  
empyema  
infection  
*acute, of sinus (accessory) (nasal)*  
inflammation  
suppuration

Use additional code (B95–B97), if desired, to identify infectious agent.

*Excludes:* sinusitis, chronic or NOS (J32.-)

**J01.0**  
*Acute maxillary sinusitis*

Acute antritis

**J01.1**  
*Acute frontal sinusitis*
J01.2 Acute ethmoidal sinusitis
J01.3 Acute sphenoidal sinusitis
J01.4 Acute pansinusitis
J01.8 Other acute sinusitis
Acute sinusitis involving more than one sinus but not pansinusitis
J01.9 Acute sinusitis, unspecified

J02 Acute pharyngitis

Includes: acute sore throat

Excludes:
- abscess:
  - peritonsillar (J36)
  - pharyngeal (J39.1)
  - retropharyngeal (J39.0)
- acute laryngopharyngitis (J06.0)
- chronic pharyngitis (J31.2)

J02.0 Streptococcal pharyngitis
Streptococcal sore throat

Excludes: scarlet fever (A38)

J02.8 Acute pharyngitis due to other specified organisms
Use additional code (B95–B97), if desired, to identify infectious agent.

Excludes:
- pharyngitis (due to):
  - enteroviral vesicular (B08.5)
  - herpessimplex (B00.2)
  - infectious mononucleosis (B27.-)
  - influenza virus:
    - identified (J09, J10.1)
    - not identified (J11.1)

J02.9 Acute pharyngitis, unspecified
Pharyngitis (acute):
- NOS
- gangrenous
- infective NOS
- suppurative
- ulcerative

Sore throat (acute) NOS

J03 Acute tonsillitis

Exclude peritonsillar abscess (J36)

Sore throat:
- NOS (J02.9)
- acute (J02.-)
- streptococcal (J02.0)

J03.0 Streptococcal tonsillitis
J03.8  **Acute tonsillitis due to other specified organisms**  
Use additional code (B95–B97), if desired, to identify infectious agent.  
*Excludes:* herpesviral [herpes simplex] pharyngotonsillitis (B00.2)

J03.9  **Acute tonsillitis, unspecified**  
Tonsillitis (acute):  
· NOS  
· follicular  
· gangrenous  
· infective  
· ulcerative

J04  **Acute laryngitis and tracheitis**  
Use additional code (B95–B97), if desired, to identify infectious agent.  
*Excludes:* acute obstructive laryngitis [croup] and epiglottitis (J05.-)  
· laryngismus (stridulus) (J38.5)

J04.0  **Acute laryngitis**  
Laryngitis (acute):  
· NOS  
· oedematous  
· subglottic  
· suppurative  
· ulcerative  
*Excludes:* chronic laryngitis (J37.0)  
· influenzal laryngitis, influenza virus:  
· identified (J09, J10.1)  
· not identified (J11.1)

J04.1  **Acute tracheitis**  
Tracheitis (acute):  
· NOS  
· catarrhal  
*Excludes:* chronic tracheitis (J42)

J04.2  **Acute laryngotracheitis**  
Laryngotracheitis NOS  
Tracheitis (acute) with laryngitis (acute)  
*Excludes:* chronic laryngotracheitis (J37.1)

J05  **Acute obstructive laryngitis [croup] and epiglottitis**  
Use additional code (B95–B97), if desired, to identify infectious agent.

J05.0  **Acute obstructive laryngitis [croup]**  
Obstructive laryngitis NOS

J05.1  **Acute epiglottitis**  
Epiglottitis NOS
Acute upper respiratory infections of multiple and unspecified sites

Excludes: acute respiratory infection NOS (J22)

- influenza virus:
  - identified (J09, J10.1)
  - not identified (J11.1)

Acute laryngopharyngitis

Other acute upper respiratory infections of multiple sites

Acute upper respiratory infection, unspecified

Upper respiratory:

- disease, acute
- infection NOS

Influenza and Pneumonia (J09–J18)

Influenza due to identified avian influenza virus

Influenza caused by influenza viruses that normally infect only birds and, less commonly, other animals.

Influenza due to other identified influenza virus

Excl. Haemophilus influenzae [H. influenzae]:

- infection NOS (A49.2)

Excl. meningitis (G00.0)

- pneumonia (J14)

Influenza with pneumonia, other influenza virus identified

Influenzal (broncho)pneumonia, other influenza virus identified

Influenza with other respiratory manifestations, other influenza virus identified

- acute upper respiratory infection
- laryngitis
- pharyngitis
- pleural effusion

Influenza with other manifestations, other influenza virus identified

- Encephalopathy due to influenza

Influenzal:

- gastroenteritis
- myocarditis (acute)

Influenza, virus not identified
Includes: influenza, viral influenza

Excludes: Haemophilus influenzae [H. influenzae]:
- infection NOS (A49.2)
- meningitis (G00.0)
- pneumonia (J14)

J11.0 Influenza with pneumonia, virus not identified
Influenzal with pneumonia, unspecified or specific virus not identified

J11.1 Influenza with other respiratory manifestations, virus not identified
Influenza NOS
Influenzal:
- acute upper respiratory infection
- laryngitis
- pharyngitis
- pleural effusion

J11.8 Influenza with other manifestations, virus not identified
Encephalopathy due to influenza
Influenzal:
- gastroenteritis
- myocarditis (acute)

J12 Viral pneumonia, not elsewhere classified

Includes: bronchopneumonia due to viruses other than influenza viruses

Excludes: congenital rubella pneumonitis (P35.0)
- pneumonia:
  - aspiration (due to):
    - NOS (J69.0)
  - anaesthesia during:
    - labour and delivery (O74.0)
    - pregnancy (O29.0)
    - puerperium (O89.0)
  - congenital (P23.0)
  - in influenza (J09, J10.0, J11.0)
  - interstitial NOS (J84.9)
  - lipid (J69.1)
  - severe acute respiratory syndrome [SARS] (U04.9)

J12.0 Adenoviral pneumonia
J12.1 Respiratory syncytial virus pneumonia
J12.2 Parainfluenza virus pneumonia
J12.8 Other viral pneumonia
J12.9 Viral pneumonia, unspecified

J13 Pneumonia due to Streptococcus pneumoniae
Bronchopneumonia due to S. pneumoniae

Excludes: congenital pneumonia due to S. pneumoniae (P23.6)
- pneumonia due to other streptococci (J15.3-J15.4)
J14 Pneumonia due to Haemophilus influenzae
Bronchopneumonia due to H. influenzae
Excludes: congenital pneumonia due to H. influenzae (P23.6)

J15 Bacterial pneumonia, not elsewhere classified
Includes: bronchopneumonia due to bacteria other than S. pneumoniae and H. influenzae
Excludes: chlamydial pneumonia (J16.0)
   congenital pneumonia (P23.-)
   Legionnaires’ disease (A48.1)

J15.0 Pneumonia due to Klebsiella pneumoniae
J15.1 Pneumonia due to Pseudomonas
J15.2 Pneumonia due to staphylococcus
J15.3 Pneumonia due to streptococcus, group B
J15.4 Pneumonia due to other streptococci
Excludes: pneumonia due to:
   · streptococcus, group B (J15.3)
   · Streptococcus pneumoniae (J13)

J15.5 Pneumonia due to Escherichia coli
J15.6 Pneumonia due to other aerobic Gram-negative bacteria
Pneumonia due to Serratia marcescens
J15.7 Pneumonia due to Mycoplasma pneumoniae
J15.8 Other bacterial pneumonia
J15.9 Bacterial pneumonia, unspecified

J16 Pneumonia due to other infectious organisms, not elsewhere classified
Excludes: ornithosis (A70)
   pneumocystosis (B59)
   pneumonia:
      · NOS (J18.9)
      · congenital (P23.-)

J16.0 Chlamydial pneumonia
J16.8 Pneumonia due to other specified infectious organisms

J17* Pneumonia in diseases classified elsewhere
J17.0* Pneumonia in bacterial diseases classified elsewhere
Pneumonia (due to) (in):
   · actinomycosis (A42.0+)
   · anthrax (A22.1+)
   · gonorrhea (A54.8+)
   · nocardiosis (A43.0+)
   · salmonella infection (A02.2+)
   · tularaemia (A21.2+)
   · typhoid fever (A01.0+)
   · whooping cough (A37.-+)

J17.1* Pneumonia in viral diseases classified elsewhere
Pneumonia in:
· cytomegalovirus disease (B25.0+)
· measles (B05.2+)
· rubella (B06.8+)
· varicella (B01.2+)

J17.2* Pneumonia in mycoses
Pneumonia in:
· aspergillosis (B44.0-B44.1+)
· candidiasis (B37.1+)
· coccidioidomycosis (B38.0-B38.2+)
· histoplasmosis (B39.-+)

J17.3* Pneumonia in parasitic diseases
Pneumonia in:
· ascariasis (B77.8+)
· schistosomiasis (B65.-+)
· toxoplasmosis (B58.3+)

J17.8* Pneumonia in other diseases classified elsewhere
Pneumonia (in):
· ornithosis (A70+)
· Q fever (A78+)
· rheumatic fever (I00+)
· spirochaetal, not elsewhere classified (A69.8+)

J18 Pneumonia, organism unspecified
Excludes: abscess of lung with pneumonia (J85.1)
drug-induced interstitial lung disorders (J70.2-J70.4)
pneumonia:
· aspiration (due to):
  · NOS (J69.0)
  · anaesthesia during:
    · labour and delivery (O74.0)
    · pregnancy (O29.0)
    · puerperium (O89.0)
    · neonatal (P24.9)
    · solids and liquids (J69.-)
    · congenital (P23.9)
    · interstitial NOS (J84.9)
  · lipid (J69.1)
  pneumonitis, due to external agents (J67-J70)

J18.0 Bronchopneumonia, unspecified
Excludes: bronchiolitis (J21.-)

J18.1 Lobar pneumonia, unspecified

J18.2 Hypostatic pneumonia, unspecified

J18.8 Other pneumonia, organism unspecified

J18.9 Pneumonia, unspecified

Other Acute Lower Respiratory Infections (J20–J22)
Excludes: chronic obstructive pulmonary disease with acute:
· exacerbation NOS (J44.1)
· lower respiratory infection (J44.0)

**J20**  
**Acute bronchitis**

*Includes:* bronchitis:
- NOS, in those younger than 15 years of age
- acute and subacute (with):
  - bronchospasm
  - fibrinous
  - membranous
  - purulent
  - septic
  - tracheitis
  - tracheobronchitis, acute

*Excludes:* bronchitis:
- NOS, in those 15 years of age and older (J40)
- allergic NOS (J45.0)
- chronic:
  - NOS (J42)
  - mucopurulent (J41.1)
  - obstructive (J44.-)
  - simple (J41.0)
- tracheobronchitis:
  - NOS (J40)
  - chronic (J42)
  - chronic obstructive (J44.-)

**J20.0**  
Acute bronchitis due to Mycoplasma pneumoniae

**J20.1**  
Acute bronchitis due to Haemophilus influenzae

**J20.2**  
Acute bronchitis due to streptococcus

**J20.3**  
Acute bronchitis due to coxsackievirus

**J20.4**  
Acute bronchitis due to parainfluenza virus

**J20.5**  
Acute bronchitis due to respiratory syncytial virus

**J20.6**  
Acute bronchitis due to rhinovirus

**J20.7**  
Acute bronchitis due to echovirus

**J20.8**  
Acute bronchitis due to other specified organisms

**J20.9**  
Acute bronchitis, unspecified

**J21**  
Acute bronchiolitis

*Includes:* with bronchospasm

**J21.0**  
Acute bronchiolitis due to respiratory syncytial virus

**J21.8**  
Acute bronchiolitis due to other specified organisms

**J21.9**  
Acute bronchiolitis, unspecified

Bronchiolitis (acute)

**J22**  
Unspecified acute lower respiratory infection
Acute (lower) respiratory (tract) infection NOS

*Excludes:* upper respiratory infection (acute) (J06.9)
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