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FOREWORD

The African Union Inter-African Bureau for Animal Resources (AU-IBAR) in pursuit of its mandate and in the quest to become a centre of excellence for the enhancement of human welfare through improved management of Africa’s animal resources and the natural resources base upon which they depend, explores pragmatic strategies to assist AU member states and Regional Economic Communities to sustainably manage their animal resources.

A key strategic approach to achieving this outcome is the mobilization of technical and financial resources to enable the organization undertake necessary interventions that address specific bottlenecks to the realization of its goals.

As part of such continuing efforts the AU-IBAR and Centers for Disease Control and Prevention (CDC) of the United States signed a Memorandum of Understanding (MoU) to cement their common interest in the improvement of public health capacities of national human and animal health systems, broadly in relation to the prevention and control of zoonoses, and more specifically in the area of avian and pandemic influenza. The MoU has the potential to expand to cover other areas of common interest, especially emerging and re-emerging infectious diseases. It is instructive that the rapidly evolving one health concept further strengthens the need for such collaborative efforts in the betterment of public health services in general.

The MoU seeks to collapse the individual capacities of the organizations into one strong collaborative effort to support the strengthening of national capacities for the prevention and control of avian and pandemic influenza. Authored initially under the auspices of the Support Programme to Integrated National Action Plans on Avian and Human Influenza (SPINAP-AHI), the MoU has the objective to establish the guiding principles for cooperation between the CDC and the AU/IBAR for purposes of providing technical support to countries supported by the SPINAP-AHI programme.

This revised manual for the training of joint rapid response teams on avian and pandemic influenza is a product of joint effort between AU-IBAR and CDC technical teams. The manual will be used to train trainers from different countries initially in the SADC region, who in turn, are expected to use it for cascade training at national and sub-national levels in their own countries.

It is my sincere believe that as we move forward, greater opportunities will unfold for further collaboration between AU-IBAR the CDC in both programmatic as well as geographic scope. In the meantime, countries earmarked for this training are challenged to make the best use of the skills acquired in dealing with AHI, but other health emergencies as well.

Thank you.

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Training Manual for Joint Rapid Response Teams: Investigation and Containment of Avian and Pandemic Influenza

1. Background

Avian influenza (AI) is a highly contagious, often lethal, generalized viral disease affecting a wide range of domestic (e.g., chicken, ducks and turkeys) and wild birds and with public health importance. Influenza viruses infect many animal species including seals, whales, humans, horses, cats and swine and migrating waterfowl are primordial reservoirs. Influenza viruses are segmented, negative strand RNA viruses belonging to the family Orthomyxoviridae, and which are divided into three genera: Influenza virus A, B and C. Only influenza A viruses have been reported to cause natural infections in birds. Based on the antigenic relationships on the surface - glycoproteins hemagglutinin (H) and neuraminidase (N) - type A influenza viruses are further divided into subtypes. At present, 16 H subtypes (H1-H16) and nine neuraminidase subtypes (N1-N9) are recognized. Each virus has one H and one N antigen, virtually in any combination. All subtypes and the majority of possible combinations have been isolated from avian species.

According to the severity of the disease that they cause, influenza A viruses infecting poultry can be divided into two distinct groups.

i. The most virulent viruses cause Highly Pathogenic Avian Influenza (HPAI), a systemic infection, in which flock mortality in some susceptible species may be as high as 100%. These viruses have been individuated as some strains belonging to the H5 and H7 subtypes exhibit a multi-basic cleavage site at the precursor of the hemagglutinin molecule. HPAI is a dead-end infection in certain domestic birds (e.g., chickens and turkeys) and has a variable clinical behavior in domestic waterfowl and wild birds, in which it may cause clinical signs and mortality. To date, the potential role of wild birds and waterfowls as reservoirs of infection has been described only for the Asian HPAI H5N1 virus. The ecological and epidemiological implications of this unprecedented situation are not predictable.

ii. In contrast, viruses belonging to all subtypes (H1-H16), lacking the multi-basic cleavage site are perpetuated in nature in wild bird populations. Feral birds, particularly waterfowl, are natural hosts of these viruses and are therefore considered a constant source of viruses. The introduction of viruses into domestic bird populations may result in Low Pathogenic Avian Influenza (LPAI). This is a localized infection, resulting in a mild respiratory disease, depression and decrease in egg production. Current theories suggest that HPAI viruses emerged from H5 and H7 LPAI progenitors by mutation or recombination although there must be more than one mechanism by which this occurs. This is supported by phylogenetic studies of H7 subtype viruses, which indicate that HPAI viruses do not constitute a separate phylogenetic lineage or lineages, but appear to arise from non-pathogenic strains. It appears that such mutations occur only after the viruses have moved from their natural wild bird host to domestic poultry. However, the mutation to virulence is unpredictable and may occur very soon after introduction to poultry or after the LPAI virus has circulated for several months in domestic birds.
The scientific evidence collected in recent years leads to the conclusion that both HPAI and LPAI viruses of the H5 and H7 subtypes must be controlled in domestic populations since they represent HPAI precursors. Consequently, the World Health Organization (WHO) considers both HPAI and LPAI belonging to H5 and H7 subtypes notifiable diseases.

The continuing outbreaks of HPAI that began to spread in several Southeast Asian countries in 1997 and again late 2003, and that occurred in Eastern and Central Europe, and Western and Northern Africa, have been disastrous to the poultry industry in these regions and have raised serious global public health concerns. Despite the eradication of avian flu viruses among poultry in many countries, and the reduction in the prevalence of infection in other countries, the highly pathogenic H5N1 strain continues to threaten bird and human populations around the world. Since 2003, more than 250 million chickens have died or have been destroyed because of H5N1 infections. Four hundred and forty two (442) people have been infected with avian influenza and 262 have died (60% case fatality rate). Virtually all human cases were consequences of poultry-to-human transmission. However, as influenza viruses are highly adaptable, evolving constantly and rapidly through gene mutations and/or genome re-assortment with unpredictable biological results, the H5N1 virus may adapt to the human host, which would lead to a potential human influenza pandemic. The WHO has estimated that a minor pandemic might result in 2 to 7 million human deaths. Because of this threat, the transboundary nature of the highly infectious H5N1 influenza virus and the dramatic impact caused by HPAI on poultry production and trade, HPAI has become an important public concern.

The detection of high mortality in a poultry farm in Kaduna State in Northern Nigeria in February 2006 has marked the beginning of the HPAI crisis in Africa. Since then, Egypt, Niger, Nigeria, Cameroon, Burkina Faso, Sudan, Ivory Coast, Djibouti, and relatively recently Ghana, Togo and Benin have found infections, and the disease is still spreading in some of these countries. Legal and illegal poultry trade and uncontrolled movement of live animals seem to have played an important role in introducing the disease in Africa and these factors have contributed to its spread across countries.

Recent H5N1 outbreaks in Bangladesh, Vietnam, Thailand, Ghana, Togo, Czech Republic, Germany and France are a clear reminder that the virus is spreading to new or previously infected countries. The situation in Egypt, Indonesia and Nigeria are particularly serious; in Egypt, the government declared HPAI (H5N1) endemic in its poultry population in 2007. Consequently, containing and eradicating the virus will require a long-term financial and political commitment from governments, including modifying or changing high-risk poultry production systems and marketing practices to ensure safer supply. For these reasons, the international community has been mobilized to limit the potential negative impacts, particularly those that may affect human health and agriculture and food supply, and, as a consequence, the worldwide economy. At present, several national, sub-regional, regional and international initiatives have been taken to: (i) prevent the introduction of HPAI in disease-free countries; (ii) control and eradicate the disease where present; and (iii) prepare for the management and response to a potential human pandemic. Unfortunately, many developing countries, and in particular African countries, have limited resources - both financial and human - to implement these initiatives effectively.
From early April 2009, first cases of a new influenza A virus of swine-origin was reported by US CDC and in Mexico an increase of cases of severe respiratory infections were reported, which were later confirmed to be caused by the same novel influenza A H1N1. This virus is the result of a “quadruple reassortment” of the H1N1 virus from North American swine, North American avian, North American human and Eurasian swine. This novel influenza virus spread

**Figure 1:** Host and lineage origins for the gene segments of the 2009 A (H1N1) virus \(^{[26]}\).
rapidly first in the North America and later further into other regions of the world. WHO raised the pandemic alert phase to 4 and 5 end April 2009 and called out a phase 6 Pandemic of novel influenza A H1N1 on 11 June 2009. This influenza virus is more transmissible than seasonal influenza, but presents as a mild disease in most instances. Initially no cases were reported in animals and the first reported animal outbreak in Canada was caused by transmission from a farm worker who previously visited Mexico and fell ill and subsequently infected pigs on the farm. More recently there have been a few more similar outbreaks e.g. in Argentina in pigs and in Chile in turkeys and recently in Norway in pigs. It is assumed that poultry farms elsewhere in the world could also become infected. As the initial naming of the new virus was “Swine-origin Influenza”, there has been considerable confusion amongst the public on the nature of this novel infection. Figure 1 and 2 illustrate the genetic characteristics of the pandemic A (H1N1) virus and its relationship with other H1N1 viruses respectively.

As of 15 November 2009, WHO has reported over 378,223 confirmed cases and at least 6,770 deaths in 206 countries. For Africa, (AFRO and EMRO WHO sites), a total of 13,329 cases and 71 deaths were reported for pandemic H1N1 up to 22 September 2009. However, countries are no longer reporting all cases due to logistical constraints in testing all suspect cases. In addition, most cases are mild and do not present to health care facilities. This novel influenza virus has a low case fatality rate. Deaths occur mostly in persons with increased risk for complications due to underlying medical conditions. Pregnant women also appear to be at high risk (See Section 4.3).

In many developing countries the lack of effective surveillance systems for both animal
and human health, limited veterinary services hindering early detection and rapid response to outbreaks in livestock, as well as inadequately prepared public health systems unable of coping with outbreaks of human cases, are of great concern. Therefore, an adequate response to the global avian and human influenza (AHI) threat must entail collaboration among partners across all sectors, particularly animal and human health, including government, local and international organizations. Such an integrated approach should start with common objectives that bring together the human and animal health sectors to address zoonotic diseases more strategically, prevent the spread of AI among animals, and reduce the risk of a human infection or influenza pandemic. A schematic representation of the process involved in the early detection and response to AI or novel influenza subtypes of concern cases/outbreaks is provided in Figure 3.

The level of preparedness that allows early detection and response to HPAI (human and animal cases) and novel influenza strains with pandemic potential is dependent upon: (i) the strengthening of the surveillance and reporting system; (ii) the ability to investigate suspected cases/outbreaks in a timely and competent manner; (iii) the capacity to perform a
timely laboratory diagnosis of suspected cases; (iv) the ability to implement the necessary actions to prevent further spread and control the disease; and (v) the capacity to treat patients appropriately.

This manual provides the information needed to investigate suspected AI and novel influenza subtypes of concern cases/outbreaks and to implement the initial containment measures to prevent/slow down the spread of the disease.
2. Rapid Response Teams’ Responsibilities, Structure and Composition

The appropriate investigation of a suspected outbreak of AI or novel influenza subtypes of concern and its containment require specialized skills from different fields. Epidemiological intelligence is needed to trace the source of the infection, determine the extent of the infection, and forecast the spread. Veterinary and medical clinical skills are needed to perform a tentative diagnosis in the field to direct the initial control measures. This would also include special skills on identification, capturing ad sampling of wild birds. Laboratory expertise is required to collect, preserve and dispatch the appropriate samples to laboratories for diagnosis, and for in situ rapid tests where available and appropriate.

Furthermore, knowledge of the local situation (e.g. farming, market and production systems, social network and environment, health seeking behavior) and good communication skills are essential elements that will help: (i) collect the relevant information, (ii) sensitize the general public, (ii) predict the potential for spread of the disease, and (iii) enhance the support and collaboration of the communities in complying with the potential control/containment interventions. The composition of the rapid response teams (RRTs) should include human and animal health professions as well as laboratory and communication experts from national and local level to encompass all needed skills and expertise and to guarantee a sufficient geographical coverage and knowledge of the local situation. Communication with other relevant stakeholders (especially law enforcement agencies) should be maintained at all time for logistic support and enforcement of control interventions.

An example of Terms of Reference (for RRTs and each member of the team is provided in Annex I and Annex II respectively). Annex IV provides a list of equipment and supplies needed for the investigation and the initial containment of AI or other influenza subtypes of concern outbreaks in animals and humans.
3. Getting Ready for the Investigation

The RRTs will frequently be requested to investigate: (i) reported/suspected cases of AI or other influenza subtypes of concern in either animals, humans or both; or (ii) reported high mortality in birds or other animal species. In both instances, it is important to collect all information that may be already available before the team is mobilized. This will assist in better planning field investigation and the logistics of the mission. Before starting any field investigation it is important to get: (i) the exact location of the reported cases/outbreak(s); (ii) the contact details of the person that has reported the suspected case(s)/outbreak(s); and (iii) the location of the nearest referral hospital. Other important information that should be available before the beginning of the investigation includes:

- Animals
  - Geographical location and distribution of the suspected outbreaks;
  - Number of affected premises or number of suspected cases;
  - Morbidity and mortality rate within the infected premises/areas;
  - Species affected (e.g., poultry, duck, geese, fowl, wild birds);
  - Starting date of the event(s);
  - Clinical signs; and
  - Poultry (or other animals) production systems from which suspected cases have been reported.

- Humans
  - Number of suspected cases and deaths;
  - Geographical location and distribution of the suspected cases;
  - Starting date of the symptoms;
  - Clinical signs and symptoms; and
  - Contact or exposure to (HPAI or other subtype of concern) infected wild birds, domestic poultry or other infected animals, travel history and profession of the suspected case(s).

Before the mission begins, it is important to: (i) notify all relevant authorities, (ii) take care of the needed logistical aspects (e.g., car, fuel, per-diem, allowances, etc.) and (iii) prepare all needed equipment (Annex III). In general, the following authorities should be notified:

- Ministry of Agriculture (MoA) at national level
- Ministry of Health (MoH) at national level
- National Task Force
- Representative of the MoA at local level
- Representative of the MoH at local level
- Local administration and leadership
- Nearest referral hospital(s)
4. **Conducting the Clinical Examination**

In most cases, the RRT will be faced with the assessment of clinically suspected cases of AI or other influenza subtypes of concern in both animals and humans. The information gathered through clinical examination of suspected cases coupled with the data generated from the epidemiological investigation, especially in animal outbreaks, may assist the RRTs reach a tentative diagnosis of the disease under investigation. This will help identify the most appropriate control/containment interventions while waiting for laboratory confirmation. In suspected human outbreaks, a clinical tentative diagnosis is also extremely important in order to start appropriate treatment as early as possible, and to ensure that infection control measures are established to reduce possible spread of infection.

4.1. **Clinical and Post-Mortem Presentation of HPAI in Birds**

HPAI viruses can infect several species of birds. Chickens, quails and turkeys are especially susceptible, while ducks more commonly show no disease, but act as a reservoir for the virus. Other poultry species, including guinea fowls, pheasants and ostriches can also be affected.

Waterfowls and shorebirds are considered to be natural reservoirs for all AI subtypes. In general, most subtypes induce little or no disease. However, the H5N1 strain has, in recent years, caused varying degrees of mortality in wild birds in Asia and parts of Europe. This has been attributed to cross-transmission of the virus between domestic and wild bird species coupled with a combination of genetic drifts and shifts within the virus.[7, 25]

4.1.1. **Clinical Presentation and Case Definition of HPAI in Birds**

The clinical presentation of avian influenza in birds depends on the species affected and the virulence of the strain.[7]

- In peracute cases involving sudden death, clinical signs may not be seen and mortality occurs within hours after onset of depression. Overall mortality rates for peracute/acute cases nearing 100% have been reported.
- In acute cases, mortalities occur as early as 24 hours after the first sign of the disease, and frequently within 24 hours. In other cases, many diverse visible signs displayed and mortalities can be delayed for as long as a week.
- Clinical signs in chickens and turkeys include severe respiratory distress with excessively watery eyes and sinusitis, cyanosis of the combs, wattle and shanks, edema of the head and eyelids, ruffled feathers, diarrhea and nervous signs.
- Eggs laid after the onset of illness frequently have soft or no shells. Some severely affected hens may recover, but rarely come back to lay.
- The disease in turkeys is similar to that in chickens, but is often complicated by secondary bacterial infections such as fowl cholera (Pasteurella multocida), turkey coryza (Hemophilus gallinarum) or colibacillosis (Escherichia coli).

Due to practical constraints, the clinical signs may not be readily observed in wild birds under field conditions. Wild bird die offs may be the main presenting feature of HPAI infection.
Figure 4: Case definition: suspected HPAI in birds.

Table 1: provides the criteria for alert/suspicion of HPAI based on mortality rate for different farmed avian species.

Table 1: Criteria for alert/suspicion of HPAI based on mortality rate for different farmed avian species.
**Figure 5:** shows some of the most common symptoms observed during HPAI infections in chickens.

*Depression*  
*Nervous Signs*  
*Respiratory Distress*  
*Oedematous Comb and Wattle*  
*Ruffled Feathers*  
*Eggs with Soft or No Shell*  

**Figure 5:** Most common symptoms observed during HPAI infection in chickens.
The World Organization for Animal Health’s (OIE) definition of suspected HPAI is provided in Figure 4. However, progressive increase of mortality and cyanosis of the head and neck must be taken as an urgent warning.

Clinically inspected animals should be sampled for laboratory confirmation (see Section 6.1.1) and the observed clinical signs should be recorded in the appropriate sampling forms (Annex VII). Rapid tests could be used for preliminary diagnosis and to discriminate between other diseases with similar clinical presentations. However, the rapid tests generally have low sensitivity and specificity. Therefore, results should be interpreted cautiously and appropriate samples should be subjected to confirmatory tests. Clinical inspection of suspected cases should not be carried out without the appropriate Personal Protective Equipment (PPE). (See Section 10.)

4.1.2. Post-Mortem Presentation of HPAI in Birds

In many cases, poultry dying of the peracute form of the disease lack visible gross pathological lesions. With acute infections in chickens, there is severe lung congestion, hemorrhage and edema in dead chickens; other organs and tissues appear normal. More varied visible lesions are seen in chickens surviving 3 to 5 days, including congestion and/or cyanosis of the comb and wattles and swollen heads. The changes in the combs and wattles progress to depressed areas of dark red to blue areas of ischemic necrosis. Internally, the characteristic of acute infections with viruses causing HPAI are hemorrhagic, necrotic, congestive and transudative changes. The oviducts and intestines often have severe hemorrhagic changes.[7]

As the disease progresses, the pancreas, liver, spleen, kidney and lungs can display yellowish necrotic foci. Hemorrhages (petechial and ecchymotic) cover the abdominal fat, serosal surfaces and peritoneum. The peritoneal cavity is frequently filled with yolk from ruptured ova, associated with severe inflammation of the air sacs and peritoneum in birds that survive 7-10 days. Hemorrhages may be present in the proventriculus, particularly at the junction with the ventriculus (gizzard). In cases due to mild pathogenic avian influenza viruses, lesions may be seen in the sinuses, and are characterized by catarrhal, serofibrinous, mucopurulent or caseous inflammation. The tracheal mucosa may be edematous with exudates varying from serous to caseous. The air sacs may be thickened and have fibrinous to caseous exudates. Catarrhal to fibrinous peritonitis and egg yolk peritonitis may be seen. Catarrhal to fibrinous enteritis may be seen in the caeca and/or intestine, particularly in turkeys. Exudates may be seen in the oviducts of laying birds. Histopathological lesions seen in gross changes described above are not definitive for HPAI, although vasculitis in the brain and other organs may be highly suggestive of the disease.[7]
Figure 6: shows some of the most common gross pathological lesions observed during HPAI infections in chickens.

Figure 6: Most common gross pathological lesions observed in HPAI infected chickens.
These gross pathology signs may or may not be seen in wild birds exposed to HPAI.

Dead or sacrificed animals should be sampled for laboratory confirmation during autopsy (see Section 6.1.2) and the observed gross pathological lesions should be recorded in the appropriate sampling forms (Annex VII). Autopsy of suspected cases should not be carried out without the appropriate PPE. (See Section 10.)

4.1.3. Other Diseases that Manifest like HPAI in Birds

The described clinical signs and post-mortem lesions are not exclusive to HPAI. In this regard definitive diagnosis cannot be made on clinical and post-mortem findings alone. The following diseases must be considered in the differential diagnosis of virulent AI:

- Newcastle disease
- Infectious laryngotracheitis
- Duck plague
- Acute poisoning
- Other diseases causing swelling of the combs and wattles
- Acute flow cholera and other septicemic diseases
- Bacterial cellulitis of the comb and wattles

Less severe forms of the disease may be confused with many other diseases with respiratory or enteric signs. HPAI should be suspected in any disease outbreak in poultry that persist despite the application of preventive and therapeutic measures for other diseases, or when the epidemiological context is highly suggestive of the introduction of the infection.[7]

4.2. Clinical Presentation and Case Definitions of AI in Humans

The clinical picture of influenza infections can vary from no symptoms at all in seasonal influenza to fulminant (fully symptomatic) disease in pandemic strains that result in severe illness and death, even among previously healthy adults and children.

Seasonal influenza typically has an abrupt onset, with symptoms of fever, chills, fatigue, muscle aches, headache, dry cough, upper respiratory congestion, and sore throat. Time from exposure to disease onset is usually 1 to 4 days, with an average of two days. Most patients recover within 3 to 7 days. In adults, fevers usually last for 2 to 3 days, but may last longer in children. Cough and weakness can persist for up to 2 weeks.[10]

The highly pathogenic H5N1 avian influenza virus that caused outbreaks in Hong Kong, Thailand, Vietnam and Cambodia primarily resulted in disease in children and young adults. Hospitalized patients initially developed typical seasonal influenza symptoms such as high fever and cough, but unlike seasonal influenza, they presented with lower respiratory tract rather than upper respiratory tract symptoms. Because of the involvement of the lower respiratory tract,
Suspected Human Case of Influenza A (H5N1)

A person presenting with unexplained acute lower respiratory illness with:
- Fever (temperature > 38 °C) and
- Cough and/or
- Dyspnea (shortness of breath or difficult breathing)

... and one or more of the following exposures in the 7 days prior to symptom onset:

a. Close contact (within 1 meter) with a person (e.g. caring for, speaking with, or touching) who is a suspected, probable or confirmed H5N1 case;

b. Exposure (e.g. handling, slaughtering, defeathering, butchering, preparing for consumption) to poultry or wild birds or their remains or to environments contaminated by their faeces in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month;

c. 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;

d. Close contact with a confirmed H5N1 infected animal other than poultry or wild birds (e.g. cat or pig);

e. Handling samples (animal or human) suspected of containing H5N1 virus in a laboratory or other setting.

Figure 7: Case definition: suspected human case of influenza A (H5N1)

Probable Human Case of Influenza A (H5N1)

Probable Definition 1:
A person meeting the criteria for a suspected case and one of the following additional criteria:

a. Illness or evidence of an acute pneumonia on chest radiograph plus evidence of respiratory illness (hyponxia, severe tachypnea);

OR

b. Positive laboratory confirmation of an influenza A infection but insufficient laboratory evidence for H5N1 infection.

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

Figure 8: Case definition: probable human case of influenza A (H5N1)

Confirmed Human Case of Influenza A (H5N1)

A person meeting the criteria for a suspected or probable case and one of the following positive results conducted in a national, regional or international influenza laboratory whose H5N1 test results are accepted by WHO as confirmatory:

a. Isolation of an H5N1 virus;

b. Positive H5 PCR results from test using two different PCR targets, e.g. primers specific for influenza A H5 HA;

c. A fourfold or greater rise in neutralization antibody titre for H5N1 based on testing of an acute serum specimen (collected 7 days or less after symptom onset) and a convalescent serum specimen. The convalescent neutralizing antibody titre must also be ≥1:80 or higher;

d. A micro-neutralization antibody titre 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 haemagglutination inhibition titre of ≥1:80 or greater or an H5-specific western blot positive result.

Figure 9: Case definition: confirmed human case of influenza A (H5N1).
patients typically had shortness of breath and almost all patients developed viral pneumonia at the time of hospitalization. Also unlike typical seasonal influenza, diarrhea, abdominal pain, and vomiting were occasionally reported. Common laboratory finding were lymphopenia, thrombocytopenia and elevated aminotransferase levels[10].

Infections with the AI virus H5N1 can be confirmed only though appropriate laboratory diagnosis. However, the clinical symptoms and the epidemiological information collected about exposure of the patient to possible sources of infection can assist to categorize the patient as a suspected case according to the WHO classification. This has important implications in terms of notification and action to be undertaken. The WHO definitions of suspected, probable and confirmed cases are provided in Figures 7, 8 and 9 respectively.[17]

4.3. Clinical Presentation and Case Definitions of Pandemic Influenza A (H1N1) 2009 in Humans

Novel influenza A (H1N1) or pandemic influenza A (H1N1) 2009, presents mostly as mild cases of “flu” and many are not seen at health care facilities as disease resolves within a few days. However, some cases develop complications resulting in severe acute respiratory disease such as acute respiratory distress syndrome and need to receive intensive respiratory assistance (e.g ventilation). High-risk groups include pregnant women and persons with underlying chronic medical conditions.

Although data on the spectrum of illness is limited with pandemic H1N1, clinicians should expect complications to be similar to those seen with seasonal influenza, which include:
- Exacerbation of underlying chronic medical conditions;
- Upper respiratory tract disease (sinusitis, otitis media, croup);
- Lower respiratory tract disease primary viral pneumonitis progressing to Acute Respiratory Distress Syndrome (ARDS), bronchiolitis, pulmonary emboli with hypercoagulable state (particularly noted in obese patients);
- Cardiac disease (myocarditis, pericarditis, hypotension);
- Musculoskeletal disease (myositis, rhabdomyolysis);
- Neurologic disease (acute and post infectious encephalopathy - encephalitis and febrile seizures);
- Secondary bacterial pneumonia (particularly Streptococcus pneumoniae and Staphylococcus aureus), which may be severe, rapidly progressive and necrotizing;
- Rhabdomyolysis with renal failure, and
- Complications seen in pregnancy (especially in the third trimester) include spontaneous abortion and premature rupture of membranes.

As pandemic influenza H1N1 is widely transmitted in communities across the world, the earlier case definitions referring to a travel history or exposure to a traveler from areas affected by this novel virus are no longer useful.

The present case definitions (that can be used for mild, moderate and severe cases of suspected influenza infection and relate to the case-management for each category) are given in Figures 10 and 11.

Secondary bacterial pneumonia commonly with Streptococcus pneumoniae or Staphylococcus aureus. In young persons without co-morbidity, ARDS is a particular feature of
Influenza-Like Illness (ILI) – Mild Disease

An individual with:

a. sudden onset of fever (≥ 38°C)
   AND
b. cough OR sore throat

... in the absence of other diagnoses

Figure 10: Case definition: Influenza-Like Illness (ILI) – Useful to identify possible mild cases of pandemic H1N1.

Severe Acute Respiratory Illness (SARI) – Moderate to Severe Disease:

• Persons 2 days to < 2 months old:
  Any child with diagnosis of suspected sepsis or physician diagnosed lower respiratory tract infection (LRTI) irrespective of signs and symptoms. Patient presenting within 7 days of the onset of illness.

• Person ≥ 2 months to < 5 years old (following WHO Integrated Management of Childhood Illnesses protocol):
  Any child (age 2 months to 5 years) with:
  Cough OR difficulty breathing
  AND
  Any general danger sign*
  OR
  Tachypnea (2mo-1yr R>50, 1.5yr R>40)
  OR
  Chest inddrawing or stridor in a calm child

*General danger signs are: unable to drink or breast feed, vomits everything, convulsions, lethargy or unconsciousness.

• Person ≥ 5 years old:
  Any person presenting with:
  a. sudden onset of fever (≥38°C)
     AND
  b. cough OR sore throat
     AND
  c. shortness of breath or difficulty breathing

... with or without clinical or radiographic findings of pneumonia. Patient presenting within 7 days of the onset of illness.

Figure 11: Case definition: Severe Acute Respiratory Illness (SARI) – Useful to identify possible moderate to severe cases of pandemic H1N1.

Important Note: Rapid progression from mild ILI to SARI has been a feature of pandemic H1N1 infection in a subset of patients. Deterioration is due to viral pneumonia and/or
complicated disease. There are currently no clinical or laboratory predictors to identify which patients will progress to these complications. High fever, persistent vomiting, and marked prostration with progressive/persistent respiratory symptoms may suggest ongoing viral replication and progression to more severe illness.
5. Conducting the Epidemiological Investigation

For the purpose of this manual we will refer to the epidemiological investigation as the collection of relevant information on:
1. origin (where and when), geographic extent, affected species and magnitude (e.g., number of infected premises, number of cases, morbidity, mortality and case fatality rates) of an outbreak/epidemic;
2. prophylactic measures applied in the past for the control of poultry diseases (e.g., Newcastle disease, laryngotracheitis, infectious bronchitis);
3. estimation of the potential for further spread of the event under investigation.

However, generally, the collection of relevant samples for laboratory diagnosis, the analysis of the data and the preparation of a final report are all components of an epidemiological investigation. The collection of appropriate samples for laboratory confirmation is detailed in Section 6, while data analysis and reporting are covered in Sections 7 and 8 respectively.

The objective of the initial epidemiological investigation - as referred to in the manual – is to gather all relevant information that is needed to identify the source of the outbreak, its geographic extension and magnitude, and its potential for spread – both for animal and humans. This information gathering is essential to plan appropriate control and containment interventions. Most of the epidemiological information can be obtained through discussions with relevant key informants (e.g., poultry farm owner, wildlife ranger, person attending to the poultry in a household, suspected patient(s), relatives or friends of suspected patient(s), health care providers, etc.).

In most cases, the RRTs will be called to investigate reported or suspected avian and human influenza outbreaks (caused by H5N1, pandemic H1N1 or other novel influenza viruses) in wild birds, domestic poultry, humans or a combination of the three. For HPAI H5N1 the alert will most likely come from the animal surveillance system or network. However, the epidemiological investigation should focus on both animal and human health. It is also possible that an investigation will start from the report/suspicion of human case(s) only. The investigation teams should examine for epidemiological evidence of infections in both human and animal populations.

Annex V provides a checklist of relevant questions and information to be gathered during the implementation of the initial epidemiological investigation for both animal and human suspected cases/outbreaks.

5.1. Investigating Outbreaks in Birds

The investigation of suspected cases/outbreaks of HPAI in birds is essential to achieve the following:
• Confirm the diagnosis of infection with influenza A (H5N1);
• Identify the source of infection, extent and magnitude of the outbreak, risk factors and
potential for spread;
• Determine key epidemiological, clinical and virological characteristics of the disease including the mode(s) of transmission and manifestations of the disease in the area under investigation.

A successful investigation will inform public and animal health decision makers to take appropriate control/eradication interventions (see Sections 9.1.1 and 9.1.2) so as to reduce economic losses and the risk of human exposure and spread of infection.

The investigation of suspected HPAI in poultry should start at field level with a clear anamnesis (from the poultry owner), clinical examination and necropsy of the suspected cases (see Sections 4.1.1. and 4.1.2.). The anamnesis should include recent events in farms and the vaccination history for AI and other infectious poultry diseases. The latter can aid in differential diagnosis of the event under investigation. (see Section 4.1.2 for the list of diseases that should be considered for differential diagnosis. Collect this information for each species, and take note of the poultry production system(s) of the affected premise(s)).

A clinical diagnosis should always be confirmed by laboratory diagnosis through collection and testing of appropriate samples from live and dead birds (see Sections 6.1.1 and 6.1.2.). Use interviews with poultry owners/farmers, wildlife rangers and the public to establish the source of infection. In the case of animal outbreaks, the disease may be introduced in several ways:
• Introduction of infected animals from a nearby premise or household (e.g., animals bought or received as a gift);
• Importation of poultry and/or poultry products (legally or illegally) from infected countries for commercial purposes;
• Procurement of infected fertilizer or infected poultry food from commercial suppliers, infected farms, etc.
• Visits from farmers, neighbors, etc. coming from infected premises/areas;
• Cross-country movement of people carrying poultry or poultry products (e.g. movement of displaced people); and
• Contact of domestic poultry with infected wild birds.

To develop effective containment strategies against the infection, it is vital to estimate the potential for spread of the disease. This can be achieved though interviews with farmers, wildlife rangers and the public, and through observation of the situation on the ground. The following important information must be collected:
• Start date of the symptoms;
• Poultry production system(s) and level of bio-security applied;
• Records of poultry or poultry products sold to other farms, markets or neighbors during the seven days preceding the onset of symptoms, and throughout the duration of the outbreak;
• Poultry or poultry products given as gifts to friends or neighbors during the seven days preceding the onset of symptoms, and throughout the duration of the outbreak;
• Visits paid by friends or the general public to the farm during the seven days preceding the
onset of symptoms onset and throughout the duration of the outbreak;
• Disposal of contaminated material or infected carcasses in the environment;
• Contact of infected poultry/environment with wild birds;
• Density of wild birds and poultry (population at risk) in the area under investigation and their level of interaction; and
• Presence of poultry markets and important roads in the area under investigation.

When collecting this information, be sure to visit suspected farms, households or locations (e.g., poultry markets) to assess the actual situation on the ground. This will also assess the geographic extent and magnitude of the outbreaks, help identify the population at risk, and assist the zonation of the country according to the OIE guidelines for further control/containment interventions (see Sections 9.1.1 and 9.1.2.). An example of a Poultry Field Investigation and Sampling Form is provided in Annex VII.

Since poultry outbreaks can serve as a source of infection for humans it is crucial that all humans exposed to infected poultry or contaminated environment are clinically monitored for any development of symptoms for appropriate medical treatment. It is essential that close communication between public and animal health members of the team be maintained throughout the investigation.

5.2. Investigating Cases/Outbreaks in Humans

As with animal outbreaks, it is critical to identify the source of infection and potential for spread in suspected human cases or outbreaks. Specifically, investigation of human cases of influenza A with pandemic potential or those influenza virus infections causing sporadic but severe respiratory illness is essential to achieve the following:
• Confirm the diagnosis of recent infection with influenza A (H5N1) or other influenza subtypes of concern;
• Reduce morbidity and mortality through rapid identification, isolation, treatment and clinical management of cases and follow up of contacts;
• Reduce further spread through the identification of potential human, animal, and environmental sources of exposure, risk factors for infection, and implementation of appropriate prevention and control measures;
• Determine whether the risk for pandemic influenza has increased as evidenced by increased efficacy of human-to-human transmission;
• Determine key epidemiological, clinical and virological characteristics for cases, including the mode(s) of transmission and disease diagnosis, manifestations and response to treatment; and
• Ensure timely exchange of information among clinicians, investigators of public and animal health, and government officials to facilitate critical and informed decision-making at sub-national, national and international levels during the investigation.

Investigation of ill persons will usually be undertaken in the context of established or highly suspect influenza A infection of a subtype of concern in humans, birds or other animals.
The possible source(s) of the infectious agent need to be identified as early as possible. This will be reflected in the case definition for suspected and confirmed cases.

The likelihood of A (H5N1) infection for ill persons is increased if exposure to birds or environment contaminated with bird droppings or consumption of uncooked poultry products occurred. However, it is important to note that human cases of A (H5N1) infection have been diagnosed in some locations where illness or death in bird populations had not been reported previously (e.g., Djibouti). In the setting of confirmed or highly suspected A (H5N1) infection in domestic or wild bird populations, the urgency of initiating an investigation is increased when: [20]

- Two or more persons presenting with manifestations of unexplained acute lower respiratory illness with fever (>38ºC), (or who died of an unexplained respiratory illness) are detected with onset of illness in a two-week period and in the same geographical area and/or are epidemiologically linked;
- Health-care workers with only occupational exposure risks develop unexplained acute lower respiratory illness with fever after providing care to patients with either known A (H5N1) infection or unexplained acute respiratory illness with fever;
- People working with birds/animals or travelling from an affected areas within 7 days from symptoms onset present with unexplained acute respiratory illness with fever; and
- Routine seasonal influenza surveillance detects influenza-like illness with an unusual distribution by age group, high frequency of pneumonia, or unexplained acute moderate-to-severe respiratory illness in previously healthy adults or adolescents.

The above is also valid for other influenza viruses which may present in humans, and have pandemic potential.

During an investigation, the case patient and family members (if the patient is too ill to be interviewed or has died) should be interviewed within the first 24 to 48 hours of the investigation to collect basic demographic, clinical and epidemiological information. First, the date of the case patient’s illness onset needs to be ascertained. Exposures to potential sources of influenza A (H5N1 or other subtype of concern) in the seven days before illness (symptom) onset should be sought. If the diagnosis of influenza A (H5N1 or other subtype of concern) infection has not been confirmed, collection and testing of appropriate clinical samples (see Section 6.2) from the case patient(s) is an immediate priority. [20] Annex VIII provides an example of a sample collection form from suspected case patient(s).

It is important that investigators obtain, and verify first-hand, as much information as possible. This usually includes visiting the case patient’s home during which a number of key actions should be undertaken:

- Confirm the family and household composition and identify contacts of the case patients including:
  - Household and other contacts in work, school, and community settings who had close, unprotected (i.e., not wearing PPE) contact in the first day before the infection through 14 days after the case patient’s symptoms onset; and
Contacts in traditional and non-traditional in- and out-patient health-care settings before initiation of appropriate infection control measures.

- Inquire about possible bird/animal exposure for the case patient in the seven days prior to illness onset including exposure to ill or dead poultry, wild birds, contaminated environments and other animals regardless of their clinical status;
- Inquire about illness or death in birds, cats, swine, or other animals in the household and neighboring areas.
- Inquire about travel to infected areas, visits to bird markets, etc.
- Examine the house and its surroundings for evidence of domestic poultry. Note whether poultry and other animals were allowed to enter the house, had access to household water and food storage areas, and if persons – especially children – were
6. **Collecting, Preserving, Storing and Shipping Appropriate Samples for Laboratory Confirmation**

The final confirmation of a suspected case/outbreak of H5N1 or other influenza subtypes of concern in animals and humans can be achieved only through laboratory confirmation. In this regard it is essential to collect and preserve the appropriate samples from suspected cases in a proper manner, and safely ship them to the reference national, regional or international laboratories for testing. The contact list of influenza reference laboratories convenient for shipping samples from Africa is provided in Annex III.

6.1. **Collecting and Preserving Samples from Birds**

It is important to collect quality samples and in a sufficient number to increase the chances of successfully detecting the HPAI H5N1 virus or other influenza subtypes of concern if present. Whenever possible, it is important to collect the following for each species affected: (i) up to 5 birds that have recently died (less than 24 hours); (ii) up to 5 birds suffering respiratory, neurological or gastro-intestinal disease; and (iii) up to 5 apparently healthy birds in direct contact with currently sick birds.[7] Do not handle and sample birds without the appropriate PPE (see Section 10) and without regard to necessary biosecurity measures.

i. 6.1.1. **Collecting and Preserving Samples from Live Birds**

The following samples should be collected from live birds for the laboratory diagnosis of the HPAI virus: (i) blood samples; (ii) tracheal swabs; and (iii) cloacal swabs. In the high-risk areas, particular attention should be paid to ducks (domestic and/or wild) as they can act as silent reservoirs, excreting large quantities of highly pathogenic virus yet showing few if any signs of illness.

- **Blood Sampling**

  Blood can be collected from the jugular vein (right side of the bird’s neck), branchial/ulnar vein (wing vein) or medial metatarsal vein (leg vein shown in Figure 12) using a 22, 23, 25 or 27 g hypodermic or butterfly needle and a 12, 10, 6, 3 or 1 ml syringe, depending on the size of the bird and the amount of blood to be collected. In general, it is safe to collect 0.3-0.6 cc of blood per 100 g of body mass from live birds. After blood is collected, cover the venipuncture site with gauze and apply pressure until bleeding stops (30-60 sec.)[7]

  Then immediately transfer blood from the syringe to a serum (red top) gel separator tube. Serum samples should be allowed to clot at environmental temperature and then be kept refrigerated or in a cool water bath until centrifugation. After centrifuging, serum should be transferred to a cryovial with a sterile transfer pipette or, if unavailable, carefully poured into the cryovials and then frozen.[5,7] All cryovials should be labeled with the date, species and ID number. Ensure that labels are marked with pencil or permanent ink, which will not dissolve when they get wet or are placed in liquid nitrogen, or temperatures of -70 °C or below.[7]
Tracheal and Cloacal Swabs

Swabs taken from the cloacae (vent) and trachea (in-between the two cartilage structures in the back of the mouth of the bird that open and close with breathing) and stored in a transport medium can be used for viral culture or RT-PCR to detect the presence of a variety of viral pathogens(7). Tracheal and cloacal swabs are collected as follows:

a. Properly restrain the bird;
b. Unwrap a Dracon swab from the stem-end of the packaging and be careful not to touch the swab tip;
c. Remove swab and insert the entire tip of the swab into the cloaca. Use gentle pressure and in a circular motion, swab the inside of the cloaca two to four times and shake off any large (> 0.5 cm) pieces of feces;
d. Open the cryovial and place the swab tip in the transport media approximately ¾ of the way toward the bottom of the cryovial;
e. Cut or snap the stem of the swab so that the swab remains in the vial and the cap can be screwed on tightly. The entire swab end and a portion of the stem should be left in the cryovial;
f. Wipe scissors with 70% alcohol if they were used to cut the swab stem;
g. Label the tube with appropriate information (sample ID and type of sample: cloacal vs. tracheal) making sure that the ID on the tube can be cross referenced to the datasheet where additional information about the sample is recorded;
h. Record sample tube number, on data sheet along with ID number, date, species, type of sample, age, sex, location, etc. (Annex VII);
i. For tracheal swabs, repeat steps “a” to “b”, however instead of steps “c” and “d”. Gently insert the swab tip into the trachea, waiting until the bird breath and the cartilage protecting the trachea opens to allow the passage of air. Gently touch the swab tip to the back and sides of the trachea and remove it. Then follow steps “e” to “h”.

A variety of viral transport media (VTM) exist, and these can either be prepared locally at a laboratory, or, commercial kits can be purchased. VTM can be prepared as follows: (i) 2.5% veal infusion broth, 0.5% BSA, 100 µg/ml gentamicin sulphate, 2 µg/ml amphotericin B in distilled water; or (ii) brain-heart infusion added with penicillin (10 000 IU/ml) streptomycin (200 – 10 000 - µg/ml) gentamicin sulphate (10 000 µg/ml) and kanamicin sulphate (650 µg/ml). Some commercial viral transport media are stable at room temperature such as the TBD Universal Viral Transport Media. The latter can also be obtained as a kit (Cellmatics® Viral Transport Pack) containing a sterile rayon-tipped swab and a vial of medium.(70)

6.1.2. Collecting and Preserving Samples from Dead Birds

When performing an investigation of a suspected AI outbreak it is very likely that several birds will be dead at the time of investigation. Birds that died within 24 hours before the start of the investigation are suitable for autopsy and sample collection. If no birds are found dead, or the death occurred more than 24 hours prior to the investigation, it is recommended that one euthanize a certain number of sick birds for autopsy and sample collection. In general, it is best to euthanize birds suspected of suffering from avian influenza by cervical dislocation (neck wringing) or application of Burdizzo clamps.(7)

If possible, the autopsy should be performed in a well-equipped and easy-to-disinfect post mortem room. In this regard, carcasses should be transported in sealed bags, and in a space well separated from the occupants of the vehicle. The best method to collect a dead bird is to invert a plastic bag around your gloved hand and then surround the animal with the bag so that you do not directly touch the animal. Seal the bag tightly (use a double bag if required for strength and cleanliness) and clearly and indelibly label the bag with an animal identification number, species, date, time and location. After the autopsy is performed the carcasses should be maintained frozen (-70 °C) until a diagnosis has been established, and then they should be disposed of in a means approved by local regulations.(7) If it is not possible to perform the autopsy in a post-mortem room, the autopsy should be performed in the field, in an isolated and shaded place observing all needed biosecurity measures. The carcasses should be appropriately disposed after the autopsy (see Section 9.1.2).

During the post-mortem, samples should be collected of pieces (at least 2 cm x 2 cm, but larger if possible) of at least spleen, lungs, ceca and intestine, and any obviously abnormal tissue placed in sterile vials and frozen. If possible, all the following tissues should be collected, placed in sterile vials and frozen: liver, kidney, trachea, lung, air sacs, brain, spleen, pancreas, proventriculus, heart, ceca and intestine. If possible, the following tissues should also be formalin fixed (pieces of 0.5 cm; formalin to tissue ratio 10:1): brain, trachea, lung, heart, liver, kidney, spleen, pancreas, bursa of Fabricius (if present), proventriculus/ventriculus, duodenum,
ceca, thyroid/parathyroid and skin, including feather follicles. No autopsy and/or samples collection from dead birds should be carried out without the appropriate personal protection equipment (see Section 10). An autopsy protocol is detailed below:

a. Spray or dip the carcass in a diluted solution of detergent to wet the feathers and reduce the risk of aerosoling infectious particles.

b. Cut across the upper beak at the level of the oral commissure to examine the nares and sinuses. Cut through the mandible and make an incision in the skin extending from the mandible to the thoracic inlet. Cut the esophagus from the oral cavity, through the crop and down to the level of the thoracic inlet.

c. Examine the soft palate, larynx and syrinx. Longitudinally incise the trachea beginning at the larynx and proceeding to the level of the thoracic inlet.

d. Incise the skin from the thoracic inlet to the vent. Disarticulate the coxofemoral joints. Reflect the skin off the abdomen and breast.

e. Make serial incisions into the pectoral musculature to rule out the presence of lesions. Remove the sternum by cutting through the abdominal muscles, ribs, coracoid bones and furcula.

f. As soon as the internal body cavity is exposed, use clean instruments to collect fresh tissue samples. Carefully lift the ventriculus and intestine to investigate the abdominal air sacs and reproductive organs. In chicks, check the navel and yolk sac for evidence of infection.

g. Begin to examine the tissues of the body while collecting and placing 2 cm x 2 cm samples of each organ into 10% buffered formalin and into a sterile vial for culture.

h. Examine the circulatory system and immune system. Examine and sample the thyroid glands as they disappear quickly upon dissection of other organs.

i. Remove the heart by severing the major vessels at the base of the heart. Make a transverse cut along the apex of the heart to expose the ventricular chambers and valves.

j. Cut the esophagus at the bifurcation of the trachea. Grasp the caudal esophagus with forceps and gently lift it as you cut the peritoneal membrane that attaches the liver and intestinal tract to the dorsal body wall. Reflect the liver and intestinal tract onto the table beyond the cloaca. Stretch out the intestine tract and examine the serosal surface carefully. Examine the pancreas and spleen.

k. Test the patency of the bile duct by expressing the gall bladder or bile duct prior to removing the liver from the intestinal mass. Create serial sections through the liver to observe the integrity of the hepatic parenchyma and biliary system.

l. Peel out the lung. Examine the pulmonary parenchyma and incise several major bronchi.

m. Examine the adrenal glands and gonads. Open the oviducts if one is present. Examine the kidneys and ureters. Attempt to find the bursa of Fabricious, which is only present in young birds.

n. Starting at the proventriculus, cut through the wall of the intestinal tract, including the ceca. Examine the digestive tract for evidence of normal or abnormal ingesta, hemorrhage, necrosis, ulceration, parasites or vascular accident.

o. Examine the skin, integument, muscles, bones, and joints. Disarticulate and remove the head from the cervical spine. Using scissors or bone rongeous gently snip away the dorsal portion of the cranium beginning at the foramen magnum. Grossly examine the cranial vault and place half of the brain in formalin and freeze the other half.
Sterilize instruments between each necropsy by immersing in alcohol and flaming them.

6.2. Collecting and Preserving Samples from Humans

Whenever a patient is considered a suspected case according to the WHO case definition (see Section 4.2), the appropriate sample for laboratory confirmation should be collected. No samples should be collected without the appropriate personal protective equipment (see Section 10). The most appropriate samples are:

- **Upper Respiratory Tract**
  - Posterior pharyngeal (throat) swabs are currently the highest yield upper respiratory tract specimen for detection influenza A (H5N1) and possibly other influenza viruses causing acute lower respiratory disease.
  - 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 and therefore useful if the influenza is not due to influenza A (H5N1).

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

- **Blood**
  - Serum (acute and convalescent if possible).

In order to increase the chance of laboratory diagnosis the sample should be collected at the appropriate time. The variation in viral load and antibody titers for influenza A (H5N1) over time is illustrated in Figure 13.

![Figure 13: Virus excretion, viral RNA in blood and antibody response in H5N1 infection in humans](image-url)
A throat swab should be taken (if possible) within three days of onset of symptoms. Note that the virus is generally detectable in throat swabs from most patients from the point of onset of symptoms (or even just before) until toward the end of the second week.\(^{(16)}\)

An acute phase serum sample should be taken seven days or less after symptom onset, and a convalescent sample after three to four weeks. A single serum sample can be collected at day 14 or later, after symptom onset since the likelihood of detecting neutralizing antibodies increases over time, certainly during the first three to four weeks after onset of symptoms. Blood serum for the detection of viral RNA should be taken during the first seven to nine days after the development of symptoms because the patient is most likely to be RNAemic at that time.\(^{(16)}\)

Initial specimens (respiratory and blood) should ideally be collected from suspected patients before antiviral therapy is begun but treatment must not be delayed in order to take specimens. In order to collect samples from the respiratory tract, choose a sitting position for adults and a supine position for infants and younger children. Children often find sampling from the respiratory tract very distressing and need to be reassured. They may also need to be restrained during the sampling process.

If the children’s parents or guardians are present, they must be fully informed of what is to take place, and must be made aware that the children may become distressed. The parent(s) should not usually be in the room during the sampling procedures. It is also usually not appropriate for a parent to help restrain the child. The procedures to collect the appropriate samples properly are as follows:\(^{(16)}\)

- **Posterior Pharyngeal Swab:**

  Posterior pharyngeal swabs are the best upper respiratory tract samples to take because the evidence suggests that they are more likely to be positive than anterior nasal swabs in sporadic A (H5N1) illness. However, if difficulty is experienced in obtaining the former (e.g., from babies and young adults) nasopharyngeal swabs should be obtained instead. The sampling procedures are detailed below:
  a. Communicate with patient on procedure as there may be a need to restrain patient if a child;
  b. Unwrap a Dracon swab from the stem-end of the packaging and be careful not to touch the swab tip;
  c. Hold the tongue out of the way with a tongue depressor;
  d. Remove swab and insert the entire tip of the swab into the throat. Use gentle sweeping motion to swab the posterior pharyngeal wall (not the tonsils or the tongue). Have the subject say “aahh” to elevate the uvula. Avoid swabbing the soft palate and do not touch the tongue with the swab tip;
  e. Open the cryovial and place the swab tip in the viral transport media approximately three-quarters of the way toward the bottom of the cryovial;

\(^{(16)}\) Always use full PPE for suspected H5N1 cases and gloves, mask and goggles for suspected pandemic H1N1.
f. Cut or snap the stem of the swab so that the swab remains in the vial and the cap can be screwed on tightly. The entire swab end and a portion of the stem should be left in the cryovial;
g. Wipe scissors with 70% alcohol if they were used to cut the swab stem; and
h. Label the tube with appropriate information making sure that the ID on the tube can be cross referenced to the datasheet where additional information about the sample exist (Annex VIII).

Figure 14 shows the sampling area for the Posterior Pharyngeal Swab.

Figure 14: Sampling area for the posterior pharyngeal swab.

• Nasopharyngeal Swab:
  a. Communicate with patient on procedure as there may be the need to restrain the patient, especially if in the case of children;
  b. 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 swab is inserted following the base of the nostril toward the auditory pit and will need to be inserted at least 5-6 cm in adults to ensure that it reaches the posterior pharynx. Do not use rigid shafted swabs for this sampling method – a flexible shafted swab is essential;
  c. Leave the swab in place for a few seconds;
  d. Withdraw slowly with a rotating motion;
  e. Open the cryovial and place the swab tip in the viral transport media approximately three-quarters of the way toward the bottom of the cryovial;
  f. Cut or snap the stem of the swab so that the swab remains in the vial and the cap can be screwed on tightly. The entire swab end and a portion of the stem should be left in the cryovial;
g. 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;
h. Wipe scissors with 70% alcohol if they were used to cut the swab stem; and
i. Label the tube with appropriate information making sure that the ID on the tube can be cross referenced to the datasheet where additional information about the sample is recorded (Annex VIII).

Figure 15 shows the sampling area for the Nasopharyngeal Swab.

• 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 (e.g. HIV or Hepatitis B). The collection of blood specimens should be performed as follows:

a. Place a tourniquet above the venipuncture site, palpate and locate the vein;
b. Disinfect the venipuncture site meticulously with 70% alcohol (an alcohol swab) or 10% polyvidone iodine by swabbing the skin concentrically from the centre of the venipuncture site outwards. Let the disinfectant evaporate. Do not re-palpate the vein;
c. Perform venipuncture. Loosen tourniquet. If withdrawing blood with conventional disposable syringes, withdraw 3-5 ml of whole blood from adults and older children and 1 ml from infant. Under asepsis, transfer the specimen to appropriate transport tubes. If withdrawing
blood with a vacuum system (e.g., Vacutainer®), withdraw the desired amount of blood
directly into each transport tube.

d. Remove the tourniquet. Use a cotton swab to apply pressure to the venipuncture site until
bleeding stops and apply a band-aid.

e. After taking all the samples, label the tubes and complete the appropriate data sheet. (See
Annex VIII)

Blood samples need to be centrifuged for at least 5 minutes at 1500g. If a basic sampling
tube without any additive is used, the clot can be allowed to form overnight. Whichever type
of tube is used, once the serum has been separated it should be pipetted off. Then put the serum
into a cryovial.

6.3. Storing Samples

After the samples from animals and/or humans have been collected, they need to be
properly stored and shipped to the reference laboratories. Repeated freezing and thawing of
specimens must be avoided to prevent loss of infectivity. Certain types of freezers are designated
frost-free and these should NOT be used for specimen storage as the temperature cycling
involved in keeping them free of ice accumulation can damage specimens.(16)

If specimens in viral transport medium (VTM) or blood sera for viral isolation can be taken to
the laboratory within four 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 and because these fridges
often have freeze/thaw cycles.

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 should be frozen at -70 °C for PCR and at -20 °C or lower for antibody detection
but they can be stored at +4 °C for approximately one week.

Specimens for influenza virus isolation should not be stored or shipped in dry ice 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. Table 2 provides the different
storage and shipment conditions that can be used, and shows which method is recommended.

(14,16)
Table 2: Suitability of various storage/shipment conditions for different specimens types\textsuperscript{(16)}

<table>
<thead>
<tr>
<th>Storage/ Shipment Conditions</th>
<th>Swabs or other specimens in VTM for virus isolation</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 detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>-70 °C or Dry Ice or Liquid N2</td>
<td>SR</td>
<td>SR</td>
<td>N/A</td>
<td>SR</td>
<td>SR</td>
<td>SR</td>
</tr>
<tr>
<td>-20 °C</td>
<td>NR</td>
<td>NR</td>
<td>N/A</td>
<td>NR</td>
<td>A</td>
<td>SR</td>
</tr>
<tr>
<td>+ 4 °C</td>
<td>A*</td>
<td>A</td>
<td>A</td>
<td>A***</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Room temperature</td>
<td>NR</td>
<td>A</td>
<td>A</td>
<td>NR</td>
<td>A*</td>
<td>A*</td>
</tr>
</tbody>
</table>

Where: SR: Strongly recommended method; A: Adequate method; NR: Not recommended method; N/A: Not applicable; * For up to 7 days storage; ** Where refrigerator is not available; *** For up to 4 days storage.

6.4. Shipping Samples

All human and animal samples collected in the field have to be transported to the national reference laboratories for testing. This should be done in the shortest possible time in order to guarantee a timely laboratory confirmation of the field findings, which will lead to appropriate control/containment interventions. One aliquot of the samples will be also sent to the WHO (human samples) and the Food and Agriculture Organization (FAO) and OIE (animal samples) reference laboratories for confirmation of the results and genotyping. The receiving laboratories should be notified before shipment of specimens in order to arrange for proper reception and obtain the needed movement/import permits. The contact details of international reference laboratories for Avian Influenza are provided in Annex III.

When dealing with infectious substances potentially harmful to animal and humans it is important to prevent any contact of the potentially infectious substances (e.g., specimens collected in the field) with the susceptible hosts. All samples should be transported or shipped in appropriate packages that can prevent the leakage of infectious substances into the environment. Samples from HPAI or other influenza subtypes of concern suspected cases shipped for diagnostic purposes fall into the Category B infectious substances according to the IATA international standards\textsuperscript{[5,13,14,16,21]} For this category of substances the packaging should consist of three components:

a. Leak-proof primary receptacle(s);
b. Leak-proof secondary packaging; and
c. Outer packaging of adequate strength for its capacity, mass and intended use, and with at least one surface having minimum dimensions of 100 mm x 100 mm.

For liquids, absorbent material in sufficient quantity to absorb the entire contents should be placed between the primary receptacle(s) and the secondary packaging so that any leak of a liquid substance during transportation will not reach the outer packaging and will not compromise
the integrity of the cushioning material. When multiple fragile primary receptacles are placed in a single secondary packaging, they should be either individually wrapped or separated to prevent contact between them. An example of a triple packaging system is provided in Figure 16.

![Figure 16: Example of the triple packaging system for the packing and labeling of Category B infectious substances.](image)

The package should be marked as UN 3373 and display the following information:

- The shipper’s (sender’s, consignor’s) name, address and telephone number;
- The telephone number of a responsible person, knowledgeable about the shipment;
- The receiver’s (consignee’s) name, address and telephone number;
- The proper shipment name (“DIAGNOSTIC SPECIMENS” or “CLINICAL SPECIMENS” or “BIOLOGICAL SUBSTANCE CATEGORY B”); and
- Temperature storage requirements (optional).

The following shipping documents are also required:

- A packing list/proforma invoice that includes the shipper’s and the receiver’s address, the number of packages, detail of contents, weight, value (Note: the statement “no commercial value” should appear if the items are supplied free of charge);
- An import and/or export permit and/or declaration if required;
- An airway bill.

The responsibility for shipping aliquots of the collected human and/or animal samples to WHO and/or FAO/OIE reference laboratories lies with the national reference laboratories.
7. **Analyzing Collected Data**

7.1. **Analyzing Animal Data**

A descriptive analysis of the outbreaks by species should be performed. This should include: (i) observed morbidity, mortality and case fatality rates; (ii) a description of the production system of the affected premises; and (iii) the geographic extent of the outbreak(s). Key epidemiological parameters (e.g., observed clinical symptoms, severity of the diseases among different avian species, mode of transmission between premises and species, involvement of wildlife) should be characterized to understand the dynamic of the epidemic in the area under investigation.

The population at risk by production system and species should also be estimated and reported in order to forecast the potential for spread of the infection and to identify appropriate control/containment interventions (see Sections 9.1.1 and 9.1.2). The population at risk should include avian populations as well as other susceptible animal species. Presence of wild/migratory birds should also be reported.

Moreover, the investigator should indicate the contact rate between avian and other susceptible animal species and the human population to provide baseline data on the likelihood of animal-to-human transmission. Common practices on poultry production systems and habits related to the consumption of poultry and poultry products should also be provided. The vaccination history of the infected premises for AI and/or other infectious poultry diseases should be collected in order to aid in differential diagnosis of the event under investigation while waiting for laboratory confirmation.

An epidemic curve – showing the number of newly infected premises over time – should be developed to monitor the spread of the epidemic. Spatial and temporal clusters of the disease should be reported and thoroughly investigated, to estimate the likelihood of established endemicity of the disease in the area under investigation.

In case the suspected outbreak is reported in wild birds the analysis should adopt more an ecosystem approach including wild bird movements, interaction with domestic birds, species affected and the population at risk.

7.2. **Analyzing Human Data**

A descriptive analysis of cases should be performed in terms of person, place and time based on well-maintained and updated line-lists. For investigations that yield multiple cases, graphical and/or tabular descriptions of cases by date of onset (i.e., epidemic curve), geographical location (e.g., maps of the locale, case patient’s home) should be developed. Key epidemiological (e.g., estimation of an incubation period, description of transmission patterns, attack rates by age, occupation, blood relation) and clinical (e.g., underlying chronic medical conditions; pregnancy status; spectrum of illness severity; treatment information; proportion
of cases who develop pneumonia require hospitalization, require ventilation, die) parameters should be characterized to enhance understanding of the spectrum and dynamics of disease associated with influenza A (H5N1 or other subtype of concern) infection.\(^{[20]}\)

Another key objective of the investigation is to ascertain whether there is any evidence that the virus may have increased its ability to cause more severe human disease or enhance its transmissibility. Examples of situations that might indicate a change in the transmission pattern of Influenza A (H5N1 or other subtype of concern) include:

- Sharp increase in the number of Influenza A (H5N1 or other subtype of concern) cases despite adequate control measures in the animal population;
- Absence of exposure to bird or animals among confirmed or possible Influenza A (H5N1 or other subtype of concern) 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; and
- Changes in epidemiological characteristic (e.g., age distribution, severity of disease).

Detection of two or more cases of confirmed, probable or suspect Influenza A (H5N1 or other subtype of concern) infection with onset of illness in the same two-week period and who are in the same geographical area and/or are epidemiologically linked, requires careful and detailed investigation to assess if transmission was likely due to a common source of exposure or to human-to-human transmission.\(^{[20]}\)

To date, there is little evidence of human-to-human transmission of A (H5N1). Settings where persons have direct, prolonged and unprotected contact with a symptomatic person may facilitate human-to-human transmission such as household and extended families, health-care settings, schools, places of work and residential institutions such as prisons, military barracks, recreational camps, refugee/displacement locations or orphanages.\(^{[20]}\)

Evaluation of clusters of cases requires collection of extremely detailed information about how the cases are related in time and space (e.g., familial or workplace relationships, dates of contact with other cases, the location, circumstances and type of contact, the time interval between contact and onset of illness). It also requires details of all other exposures that cases may have had with infected animals or contaminated environments, also through travel from an affected area. If human-to-human transmission is suspected, secondary attack rates among household and other close contacts and the serial interval (i.e. number of days between the onset of illness for each case) should be calculated. It may be helpful to display data using graphs or transmission tree/cluster diagrams.\(^{[20]}\)

In practice, it can be very difficult to differentiate between human-to-human transmission and a common source of exposure. Human-to-human transmission may be indicated in the setting of:

- Well-documented exposure to a confirmed, probable or suspected human case (see Section 4.2. for case definition);
and

The time interval between contact with a human case and illness onset is 7 days or less (2-7 days);

and

Absence of an alternative source of exposure such as exposure to birds, animals, feathers, droppings, fertilizers made of fresh bird droppings, contaminated environments or laboratory specimens.

OR

• Several generations of transmission linked to a primary case.

In line with the International Health Regulations (2005), WHO should be notified if the investigation suggests that human-to-human transmission is occurring as described above.
8. Reporting and Notifying

During the investigation, frequent (possibly daily) situation reports and efficient and timely communication with relevant authorities at local, national and international level (e.g., relevant ministries at local and national levels; international institutions like OIE, FAO and WHO) and other stakeholders (e.g., the public and the media, Red Cross, security, other partner organizations) is crucial.

8.1. Reporting and Notifying Avian Influenza in Birds

The detection of a possible case of HPAI (H5N1) in avian populations should trigger immediate notification of local, sub-local and national animal and human health authorities to make immediate decisions about the launching of an investigation and possibly implement appropriate control/eradication interventions.

HPAI in avian species (domestic and wild) is a notifiable disease for the OIE\(^6\). The suspicion or confirmation of HPAI outbreak(s) in the country should trigger the notification of the event to the OIE within 24 hours. Epidemiological data (including number of outbreaks, affected species, morbidity and mortality, population at risk, geographical location(s) of the outbreak(s) and laboratory confirmation with recognized laboratory tests) should be part of the notification.

Updates on the evolution of the outbreak(s) and implemented control measures must also be reported to the OIE on weekly basis. If the system is operational in the country, the OIE should be notified by the authorized OIE country focal point (usually the Chief Veterinary Officer) through the World Animal Health Information System (WAHIS).

8.2. Reporting and Notifying Avian Influenza and Other Influenza Subtypes of Concern in Humans

The detection of a possible case of HPAI (H5N1) in human populations should trigger immediate notification of local, sub-local and national human and animal health authorities to make immediate decisions about the launching of an investigation. This in turn should result in notification of health-care providers (traditional and non-traditional), hospitals and outpatient facilities, community leaders in the area where the case patient resided and/or traveled as part of active case-finding efforts.

In line with the International Health Regulations (2005)\(^7\), the national health authority must notify WHO of any human case of A (H5N1) or other new human influenza subtypes and should disseminate to WHO Collaborating Centers any relevant information and biological materials in a timely and consistent manner.\(^{20}\)

Under the IHR (2005), immediate reporting to WHO is required for human influenza

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due to a new influenza subtype including the pandemic H1N1 virus. Reports should be sent by the national IHR Focal Point to the relevant WHO IHR Contact Point at the WHO Regional Office, the WHO Country representative (where applicable) and WHO headquarters in Geneva should be copied on the correspondence.
9. Containing and Controlling Avian and Human Influenza Outbreaks

The containment and control of AI or other influenza subtypes of concern outbreaks in animals and humans is not the sole responsibility of the RRTs. However, the rapid response teams are responsible for coordinating and supervising the containment control interventions. Furthermore, the RRTs are responsible for the application of the initial control measures that shall be applied in case of high suspicion of HPAI or other influenza subtypes of concern in animals and humans. In fact, while waiting for the laboratory confirmation, if the epidemiological investigation and the clinical examination are highly suggestive of an AI outbreak in animal and/or humans, then initial control measures shall be implemented to prevent the further spread of the disease.

9.1. Containing and Controlling Avian Influenza Outbreaks in Birds

9.1.1. Control Measures in Case of Suspected Avian Influenza Outbreaks in Birds

Whenever an HPAI outbreak is suspected, the following containment measures should be implemented:[3,4,6,7]

a. Immediately impose quarantine of the suspected areas (premises or villages);
b. Restrict the movement of persons and vehicles (in and out of the infected premises);
c. Investigate and collect samples for laboratory confirmation;
d. Decontaminate sheds and other poultry housing areas;
e. Keep sick and dead birds out of the human food chain; and
f. Temporarily close markets until the laboratory confirmation of HPAI is available.

These measures are not easy to implement and they require the cooperation of the community and, in most cases, the support of the police forces that should be notified along with the local authorities and local and national human and animal health authorities as soon as an HPAI outbreak is suspected.

Quarantines should be imposed on all farms/villages on which infection is either known or suspected and should be strictly policed to ensure that no one, including the residents, owners, staff and other visitors, leave without changing clothes and footwear. Effective quarantine of an area requires around-the-clock security to ensure that only authorized personnel in protective clothing are allowed to enter. It will be necessary to supervise the movements of residents onto and off the property and to ensure that all pets are confined.[6,7]

9.1.2. Control Measures in Case of Confirmed Avian Influenza Outbreaks in Birds

Whenever an HPAI outbreak in birds is confirmed though laboratory diagnosis, appropriate measures to control the outbreak should be implemented. This is not the sole responsibility of the RRTs. The animal health authorities, police and relevant stakeholders should all be involved. Based on country regulations, the control measures to be implemented after the confirmation of HPAI can be summarized as follows:

a. Report the outbreak(s) on national radio and television;
b. Develop a zoning strategy;
c. Issue an order declaring an outbreak and recommending that movement in the area be restricted;
d. Implement an epidemiological investigation in order to determine the source of the infection;
e. Prohibit the movement of birds or their products from the area where infection has been detected;
f. Close poultry and poultry products markets in the entire area where infection is detected;
g. Implement active epidemiological surveillance of all poultry farms in the area, and sampling of poultry and wild birds for submission to the reference laboratories;
h. Implement appropriate control measures (e.g., stamping-out, vaccination, disinfection of farm buildings and premises);
i. Monitor movement within the country; and
j. Quarantine suspected farms/villages.

According to the epidemiological situation of the country, the available human and financial resources and the available information the following interventions can be implemented:

1. Stamping out involving the destruction of affected and in-contact birds in all affected locations followed by disposal of carcasses and disinfection of infected premises

   All poultry species in suspected or infected premises must be slaughtered whether they are obviously diseased or apparently healthy. Birds should be slaughtered by methods that consider animal welfare and the safety of operations, preferably without moving the animals from the site. Given the scarce availability of resources in many African countries, the recommended method for slaughtering is dislocation of the neck (using Burdizzos, bone cutters or bare hands). Burdizzos are particularly useful when large numbers of poultry with strong necks (e.g., geese, ducks) are to be destroyed.[6,7]

   Disposal of dead birds, poultry litter and other contaminated waste can be performed in different ways. Burning/incinerating is a practical method that can be utilized for this purpose. The principle is to place carcasses on top of sufficient combustible material, ensuring the arrangement of fuel and carcasses allows adequate airflow to enter the pyre from below, thus achieving the hottest fire and the most complete combustion in the shortest time.[6,7]

   When loading the carcasses is complete and weather conditions are suitable, saturate the fire-bed and carcasses with diesel or heating oil (NOT PETROL), and prepare ignition points along the length of the fire-bed. These can be made of rags soaked in kerosene. Move all vehicles, personnel and other equipment well away from the fire-bed. Start the fire by walking into the wind and lighting the ignition points along the way. The fire must be attended at all times and re-fuelled as necessary. Ensure that all carcasses or parts thereof that fall off the fire are repositioned on the fire. A well-constructed fire will burn all carcasses within 48 hours. The ashes should be buried and the site restored as soon as possible.[6,7]

   Soapy water and detergents are the first choice for decontamination. Washing contaminated surfaces should always be with detergents (soapy water or disinfectants). The most difficult materials to decontaminate are bird droppings since the virus can survive in moist environments with high organic content. It is essential to thoroughly clean and disinfect items that have been in contact with bird droppings – cages, shoes, clothes – before working with poultry or entering a place where poultry are kept.[6,7]

2. Mass immunization
Vaccination as a support strategy may be considered when the disease has spread to such an extent that it has overwhelmed the resources of the disease control authorities, or, the economic cost of a widespread slaughter campaign cannot be borne. It can also be considered at an earlier stage when veterinary services’ infrastructures and capacities prove to be very weak and insufficient to curb the spread of the disease. The available vaccines provide excellent protection against clinical disease in chickens by reducing mortality and production losses. Vaccination of poultry also reduces the viral load in the environment, thus decreasing the risk of transmission to poultry and humans.\(^6\) Vaccination, when it is applied, must be done in combination with other disease control measures, including the slaughter of infected flocks. Efforts to control the disease by vaccination alone, without slaughtering affected birds to reduce the virus load in the environment, will probably not be successful.

3. Targeted vaccination (vaccination in a well-defined zone/territory in a country)

This strategy consists of creating a sanitary cordon preventing the spread of the disease in disease-free countries, but which border infected countries.

The RRTs will be responsible for coordinating and supervising all field operations. In case of a confirmed outbreak, a zoning approach for containment and control shall be applied. In order to attempt to contain HPAI outbreaks rapidly, three areas should be considered and defined: (i) infected area; (ii) restricted area; and (iii) control area. The geographic extent of the different areas should take into consideration the epidemiological characteristics of the outbreak, physical and geographical barriers, poultry density and farming systems.\(^6,7\) An example of the zoning strategy for the control of avian influenza is provided in Figure 17.

![Figure 17: Example of zoning strategy for the control of avian influenza](image)

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In each area, specific control measures should be implemented as follows:

- **Infected area**

  An area classified as infected area (IA) will be a defined area (e.g., village, farm) in which HPAI has been detected. Infected premises shall be subject to quarantine and all susceptible animals shall be destroyed (see Section 9.1.2).

- **Restricted area**

  A restricted area (RA) is a relatively small declared area (compared to the control area) around infected places, which is subject to intense surveillance and movement controls. Movements out of the RA should be prohibited, while movement into the area should only be through regulatory approval. The RA does not need to be circular but can have an irregular perimeter depending on the physical and geographical barriers, markets, poultry density and farming systems. The distance will vary according to the size and nature of the potential source of virus, but will be approximately 1 to 5 km around the infected premise, depending on the density of poultry premises.

- **Control area**

  The control area (CA) will be a larger declared geographical area around one RA where restrictions will reduce the risk of disease spreading from the RA. The boundary of the CA will be adjusted as confidence about the extent of the outbreak becomes clearer. Surveillance and movement control will be less intense and animals and products may be permitted to move under permit from the area.

  The declaration of a CA also helps to control the spread of the outbreak from within the RA. The perimeter of the CA is a buffer zone between the RA and the rest of the country. The boundary does not have to be circular or parallel to that of the RA, but should be 2 to 10 km from the boundary of the RA. The movement of possibly contaminated materials and equipment within the CA is allowed, but movement out of the CA is prohibited without the approval of the Chief Veterinary Officer. This type of control area allows reasonable and safe commercial activities to continue.

**9.2. Containing, Mitigating and Controlling Avian Influenza and Other Influenza Sub-types of Concern in Humans**

While at present Avian Influenza is not easily transmitted from human-to-human, pandemic H1N1 is highly transmissible and has spread across the world in a short time. A human influenza pandemic caused by a highly virulent and transmissible influenza virus represents a potential risk that each country should be ready to face.

Key to preventing the emergency of a human pandemic strain of influenza virus is the early detection of human cases and the resulting prevention of the spread of the infection. In this regard, two actions are required: (i) the timely treatment of the suspected or confirmed case(s) of AI or other influenza subtypes of concern such as novel influenza A H1N1; and (ii) the prevention of the spread of infection.

The RRTs are not directly responsible for the treatment of suspected/confirmed cases of AI or another influenza viral infection of concern. However, the RRTs are responsible for
the initial follow up of individuals at risk, the implementation of sensitization and awareness campaigns, and the coordination of the disinfection and sanitization activities of the hospitals and houses where suspected or confirmed cases are found. The RRTs are also responsible for providing guidance to health-care workers on the best practices for the use of PPE and the implementation of standard and droplet precaution measures for infection control.

9.2.1. **Pharmaceutical Interventions**

Two drugs (in the neuraminidase inhibitors class), Oseltamivir (commercially known as Tamiflu®) and Zanamivir (commercially known as Relenza®) can reduce the severity and duration of illness caused by seasonal influenza. The efficacy of the neuraminidase inhibitors depends on the early administration (within 48 hours after symptoms onset). Oseltamivir was initially developed for treatment of the most frequently occurring subtype of influenza A. It binds to one of the two large molecules on the surface of all influenza viruses, including the avian influenza virus. When the body’s cells are infected with influenza, the virus uses the cell’s own biochemical reactions to reproduce. New virus particles are formed and released from the cell, and infect other cells. The release of new virus particles from the infected cells depends on neuraminidase. Hence, treatment with Oseltamivir counteracts the release of newly formed virus particles from infected cells, thereby limiting the spread of the infection in the body. Tests on patients infected with seasonal influenza A have shown that Oseltamivir can reduce the disease course by approximately 36 hours if the treatment is initiated no more than 48 hours after the first symptoms. The need for hospitalization and, for example, antibiotic treatment of sequela of the influenza is also reduced.

For cases of human infection with H5N1, the drugs may improve prospects of survival if administered early, but clinical data are limited. The H5N1 virus is expected to be susceptible to the neuraminidase inhibitors. No actual clinical trials have been performed with Oseltamivir for treatment of humans infected with AI. The only experience of the drug stems from the use of Oseltamivir in a local outbreak of disease from bird to human, and from animal trials. This experience indicates a positive outlook of Oseltamivir suitability for both prevention and treatment of the bird flu or a pandemic based on this virus. Antiviral resistance to neuraminidase inhibitors has been negligible so far. Resistance was reported in a few H5N1 infected patients treated with Oseltmavir; no transmission from human to human of this Oseltamavir resistant H5N1 virus was noted.

For pandemic H1N1, Oseltamivir has been used extensively during the onset of the 2009 pandemic. As of 30 October, resistance of Novel H1N1 to Oseltamivir has been reported in thirty-nine cases, of which 7 cases were immuno-compromised patients on treatment for pandemic H1N1 (WHO Wkly Epidemiol Rec 2009;84:453-9). Rational use of antivirals must be considered, with priority given to severely and moderately ill patients with a high risk for complications (See Section 4.3). Patients with infection of oseltamivir resistant virus (with the H275Y mutation in the neuraminidase) should be treated with zanamivir.

The recommended Tamiflu® treatment dosage for H5N1 or pandemic H1N1 patients is as follows:\[24\]:

- Adults:
  - 75 mg. twice daily for 7-10 days.
- Children:
  - <15 kg: 30 mg. twice daily;
  - 15 - <23 kg: 45 mg. twice daily;
For prophylaxis (in case of potential exposure to H5N1) the recommended dose should be administered once a day for 5 to 7 days. In general, WHO is not recommending post-exposure prophylaxis for pandemic H1N1. Instead it advises close monitoring of symptoms and promptly administering antiviral treatment if symptoms develop. This will reduce the risk of sub-optimal dose used in patients already infected at the time chemoprophylaxis starts and it ensures the treatment is administered only when needed. Chemoprophylaxis with Tamiflu® for pandemic H1N1 is recommended only in the case of high risk for complications as with underlying chronic medical conditions (see Section 4.3).

Tamiflu® is not authorized for children under the age of one year. No trials involving treatment of pregnant women have been done, but the substance has not caused malformation in animal trials. In general, pregnant woman should not use Tamiflu®, unless their general practitioner believes that the advantages outweigh the risk involved. However, pregnant women, especially those in 2nd and 3rd trimester, have proven to be at higher risk for severe complications and death due to pandemic H1N1 infection. Pregnancy was also identified as a risk factor during the 1918/19 and 1957/58 pandemics. Clinical trials for pandemic H1N1 vaccines have been carried out and more are underway. The vaccine is currently available and some countries (USA) have started mass campaign vaccination. They are expected to be on the market by end 2009, and would be best used for prevention of pandemic H1N1 infection in high risk groups.

Patients using Tamiflu® only rarely have stopped their treatment due to adverse reactions. The most frequent adverse reactions are nausea and vomiting, which occur in almost 8% of all patients treated. Few severe psychiatric adverse reactions have been reported. Adverse reactions to Tamiflu®, as with all drugs, need to be monitored.

For the neuraminidase inhibitors, the main constraints – which are substantial – involve limited production capacity and a price that is prohibitively high for many countries. At present manufacturing capacity, which has recently quadrupled, it will take a decade to produce enough Oseltamivir to treat 20% of the world’s population. The manufacturing process for Oseltamivir is complex and time-consuming, and is not easily transferred to other facilities.

Other neuraminidase inhibitors such as Zanamivir (Relenza) and Peramivir are under further study for parenteral treatment of Influenza A (H5N1) patients. Zanamivir is used in seasonal flu patients, is inhaled by mouth once in morning and evening in patients >5 years of age but has side effects of wheezing and breathing difficulties. Stringent infection control measures in treatment of hospitalized Influenza AH5N1 patients with nebulized Zanamivir would be needed, and parenteral Zanamivir or Peramivir may prove to be a better choice, second only to Oseltamivir.

So far, most fatal pneumonia in cases of H5N1 infection or novel influenza subtypes have resulted from effects of the virus. However, since influenza is often complicated by secondary bacterial infection of the lung, antibiotics could be life-saving in the case of late onset of pneumonia and antibiotic treatment is indicated for suspected bacterial co-infection. Bacteria frequently reported include Streptococcus pneumoniae and Staphylococcus aureus, including methicillin-resistant strains in some cases. WHO regards it as prudent for countries to ensure adequate supplies of antibiotics as part of Influenza pandemic preparedness and response.
An older class of antiviral drugs, the M2 inhibitors Amantadine and Rimantadine, could potentially be used against pandemic influenza, but resistance to these drugs could develop rapidly and this could significantly limit their effectiveness against novel pandemic influenza. Some currently circulating H5N1 viruses are fully resistant to these M2 inhibitors. However, should a new virus emerge through reassortment, the M2 might be effective.

Combination therapy (e.g., two neuraminidases or Oseltamivir with Rimantadine, or a neuraminidase with probenicid (to double the systemic exposure following conventional dosage of Oseltamivir or a neuraminidase with Ribavirin) may also be an option when more than one virus strain is circulating and the viruses have different antiviral susceptibilities, to decrease treatment failure of monotherapy. There will be continuous monitoring for drug susceptibility, to guide treatment choice.\(^\text{24,25}\)

Vaccines are produced each year for seasonal influenza, but do not provide cross-immunity to pandemic influenza A H1N1 nor to H5N1. H5N1 vaccines are continuing to be developed by manufacturers (using clade 1 and 2 viruses - including from Egypt (A/Egypt/2321-NAMRU3/2007) - that have been modified by reverse transcriptase) and stockpiles of clade 1 and 2 vaccines are being acquired by a number of countries. Clinical trials for H5N1 are now under way to test whether experimental vaccines will be fully protective and to determine whether different formulations can economize on the amount of antigen required. Vaccine trials are underway in a number of countries for influenza A/H5N1.

For Pandemic influenza H1N1, vaccines were developed in various countries, following the emergence of the pandemic virus. Live-attenuated and inactivated vaccines have been developed. Some inactivated vaccines are adjuvanted (enhanced, allowing manufacturers to use less vaccine and thus have larger supplies). In the Northern Hemisphere, mono-valent vaccine, both nasal and injectable, have been produced. WHO has recommended Trivalent vaccine (pandemic A/H1N1 as one of 3 vaccines, other influenza A H3N2 and influenza B), for the Southern Hemisphere winter seasonal vaccine. For the monovalent vaccine, one vaccine suffices except for young children <10 years (two doses needed). Protection from influenza vaccination can be expected from 10-14 days post vaccination. Pandemic H1N1 vaccine was produced using A/California/7/09(H1N1) strain. Production is based on virus isolation on cell culture on eggs; a slow process, which limits the amount of vaccine available.

The safety of Pandemic H1N1 vaccines is similar to that of seasonal vaccines. It is contraindicated for same groups as for seasonal influenza vaccination (e.g. children under 6 months of age; people with moderate-severe illness with a fever - these need to wait until they recover to vaccinate; history of anaphylaxis/sever allergic reaction to vaccine constituents or previous influenza vaccine; history of Guillan-Barré following influenza vaccination). Side-effects as for vaccine e.g. swelling, redness or pain; and less frequently fever, headache, fatigue and muscle aches, have been noted.

No Clinical trials for pandemic A/H1N1 vaccine have been carried out in Pregnant women but due to the fact that pregnant women, particularly those in the 3rd trimester, are at higher risk for complicated influenza infections\(^\text{81}\), countries are recommending vaccination in pregnant women in 2nd and 3rd trimester.

\(^{8}\)To date (WHO, 30 Oct 09) studies do not show harmful effects from pandemic influenza vaccine with respect to pregnancy, fertility or a developing embryo or fetus, birthing or post-natal development. Pregnant women are at higher risk for complicated influenza (10 times higher chance to require hospitalization in ICU than H1N1 infected general population).
Monitoring of Adverse Events is very important. In particular, severe side effects and deaths need to be monitored. Guillan-Barré syndrome has been seen in 10 cases following 85 Million vaccinations of pandemic H1N1 (WHO 19 November 2009). This number correlates with normal baseline rates. China administered 11 million pandemic H1N1 vaccines and reported 15 cases of severe side effects and 2 deaths following vaccination. The 2 deaths were reviewed and autopsies were done; underlying medical conditions were determined as the cause of death (WHO 19 November 2009).

Concerning the policy for prioritized vaccination groups, countries may decide to focus on Front-Line Health Care Workers (e.g. emergency care givers, ICU) and on High Risk Groups for Pandemic H1N1 (those developing severe complications: Pregnant Women (esp. 3rd trimester); Young Children (esp. <2years) and Persons with Underlying Chronic Medical Conditions (esp. Chronic Lung disease incl. asthma; and other).

9.2.2. Non-Pharmaceutical Interventions

Non-pharmaceutical interventions include all interventions that aim at preventing the spread of the disease without using available curative or prophylactic treatments. Patients that are suspected (according to a standard case definition) or confirmed as infected with H5N1 or an influenza subtype of concern should be treated with antivirals. If possible, patient(s) should be referred to the nearest referral hospital to receive an appropriate antiviral treatment (see Section 9.2.1) and severely ill patients may need supportive treatment. Once a suspected or confirmed case is hospitalized, it is very important that all health-care workers are informed, before exposure to the case. Necessary preventative precautions must be implemented. The patient must be isolated. Contacts between patients and family members, friends, other patients and health-care workers should be minimized.

When suspecting infections with highly infectious influenza of a virulent sub-type, standard and droplet precautions must be implemented. These include (i) using gloves and facial protection (nose, mouth and eye) as part of full Personal Protective Equipment (PPE) by health-care workers when providing care to suspect or confirmed infected patients; (ii) practicing hand hygiene before and after patient contact and after removing gloves and PPE; (iii) implementing standard operating procedures when handling and disinfecting patient care equipment, patient rooms, and soiled line; and (iv) addressing environmental cleaning, spills-management and handling of waste.[10,18]

- Infection Control in Health-Care Facilities

Available evidence suggests that transmission of human influenza viruses occurs through multiple routes including large droplets, direct and indirect contact, and droplet nuclei. However, observational studies conducted in health-care facilities suggest that droplet transmission is the major mode of transmission in these settings and standard plus droplet precautions are recommended for the care of patients infected with human influenza of a virulent nature. Standard and droplet precautions should be also the minimum level of precaution to be used in all health-care facilities providing care of patients with acute respiratory illness, regardless of whether AI or other influenza subtype of concern infection is suspected. The most critical elements of these precautions include facial protection and hand hygiene and these precautions should be prioritized. The use of PPE (see Section 10) is needed for the care of suspected/confirmed AI or other influenza subtype of concern patients.
Suspected and confirmed patients should be placed in an adequately ventilated, preferably negative pressure isolation room, or airborne infection isolation room if available. If a negative pressure isolation room is not available, a room with cross-ventilation of open windows may suffice (ensure windows lead to unoccupied space). A fan on a low-standing table will assist with ventilation, and create negative pressure. (Figure 18)

If single rooms are not available, patients infected with the same organism can be cohorted. These rooms should be in a well-defined area that is clearly segregated from other patient care areas used for uninfected patients. The beds should be placed at least one meter apart. Increasing spatial distance between patients may theoretically be helpful in preventing transmission of droplet-transmitted diseases. Whenever possible health-care workers assigned to cohorted patient-care units should be experienced hospital staff and should not “float” or be assigned to other patient-care areas. The recommended infection control precautions should be implemented during the time the patient is infectious:

- Adults and adolescents > 12 years of age: implement precautions at time of admission and continue for 7 days after resolution of fever;
- Infants and children ≤ 12 years of age: implement precaution at time of admission and continue for 21 days after symptom onset.

Children may take longer to shed influenza viruses (up to 21 days). In addition, immune-compromised persons may take longer to shed influenza viruses.

Visitors should be strictly limited to only those necessary for the patient’s well-being and care. Visitors should also be advised about the possible risk of AI/influenza subtype of concern transmission. Visitors should be provided, instructed and monitored in the use of PPE and in hand hygiene practices prior to entering the patient isolation room/area. A list of visitors and staff working with patients need to be kept to monitor contacts.

The movement and transport of patients out of the isolation room/area should be for
essential purposes only. The receiving area should be informed of the patient’s diagnosis as soon as possible prior to the patient’s arrival, of the precautions should be taken. The patient must wear a surgical mask if leaving the isolation room.

Standard precautions must be implemented when working with solid waste that may be contaminated with AI or other influenza subtype of concern virus outside the isolation room/area. Clinical (infectious) waste includes waste directly associated with specimens processing, human tissues, including material or solutions containing blood. All waste generated in the isolation room and area should be removed from the room and area in suitable containers or bags that do not allow spillage or leakage of contents. When transporting waste outside the isolation room and area, use gloves followed by hand hygiene. Standard precautions must also be applied when handling dishes, utensils, linen and laundry.

Environmental cleaning and disinfection must be applied in the isolation room and area. Cleaning must precede disinfection. The AI or other influenza subtype of concern viruses are inactivated by a range of disinfectants, including (i) phenolic disinfectants; (ii) quaternary ammonia compounds; (iii) peroxygen compounds; (iv) sodium hypochlorite (household bleach); (v) alcohol; and (vi) other germicide with a tuberculocidal claim on the label. Patient’s rooms and surrounding areas should be cleaned daily and terminally at discharge. In addition to daily cleaning of floors and horizontal surfaces, special attention should be given to cleaning and disinfecting frequently touched surfaces and dedicated equipment (e.g., stethoscope).

Health-care workers should be (i) vaccinated against seasonal influenza; (ii) monitored for vaccine uptake; (iii) monitored for influenza-like illness (including self-reporting and self-isolation); (iv) receiving prophylactic treatment whenever possible in the case of working with suspect or confirmed AI or other influenza subtype of concern viruses; and (v) reminded regularly on infection control measures.

• Infection Control outside Health-Care Facilities

In order to early detect new cases for timely treatment and to prevent the spread of the disease, it is also important to follow-up on individuals at risk as identified during the initial epidemiological investigation of the reported outbreak. Individuals that have been exposed to a potential source of infection (either animal or human), but do not present any sign of the disease at the time of the investigation, should be closely monitored (for at least 7 days following exposure) to detect early signs of the disease.

The successful containment of an outbreak is very often determined — among other factors — by the level of collaboration of the community and the public. In this regard, appropriate sensitization is required. Individuals at risk should be mentored about the possible risk of infection. They should be informed about the possible clinical manifestation of the disease, and encouraged to report any symptom that they may develop, particularly fever. They should also be instructed about the standard precautions (see also Infection Control in Health Care Facilities) that they should take in order to prevent the potential transmission of the infection to relatives, friends and other people. This should include the potential for transmission by contact, droplets, (e.g., sneezing, coughing) or by objects. Social distancing and voluntary quarantine should be recommended for identified contact cases. During the investigation of a suspected or confirmed outbreak of HPAI in birds, it is possible that no human cases are reported. However, the public should be sensitized about the risk of contracting AI through contact with infected birds, handling and consumption of infected uncooked carcasses, etc.
10. Using Personal Protective Equipment

When implementing an investigation of suspected and reported outbreaks of HPAI in animals or other influenza subtype of concern in humans, the RRTs members must protect themselves from possible infection though the use of Personal Protective Equipment (PPE) and the implementation of standard precautions. Human infection from H5N1 HPAI occurs only because of direct exposure to live viruses in droplets, airborne particles or contaminated fluids and objects. Influenza may infect humans via contact with any mucous membrane (e.g., inhalation, introduction into the eyes, via open skin wounds and theoretically through ingestion). Exposed or contaminated skin should be washed with soap and water. Influenza-like illness within 7 days of working with birds should be viewed as suspected AI infection and treated appropriately by a medical doctor. [7,10]

During the investigation of suspected outbreaks of AI in animals (see Section 5.1.) and humans (see Section 5.2.), PPEs must be worn during the following activities: (i) clinical investigation of any bird (sick or apparently healthy) in suspected premises/areas; (ii) autopsy of any bird in suspected premises/areas; (iii) disposal of carcasses; (iv) disinfection of premises and equipment; (v) clinical examination of confirmed, suspected and at risk patients; and (vi) treatment of suspected/confirmed patients.

The first line of defense against transmitting or contracting infection is hand washing. Wash your hands with hot water and soap before putting gloves on, and after removing them.

- Wearing PPEs:

There are four key items of PPE that you need to wear in any occasion:

» Face masks (N-95 or FFP2) are recommended for the examination of animals or humans with signs of severe acute respiratory illness or in locations where H5N1 HPAI has been found in either poultry or wildlife;
» Goggles face shield, or protective glasses;
» Gloves (need not be sterile); and
» Long-sleeve gown or coverall (plastic apron if splashing is foreseen).

When using PPE, wash your hands then put on your PPE in the following order (Figure 19):

1. Coverall.
2. Plastic apron.
4. Mask – fit the mask ensuring that it is secure around the face, especially around your nose. Test by inhaling and noting indentation.
5. Goggles.
6. Gloves (Ideally wear two sets of gloves, making sure that the cuffs of the outer gloves go up and over the cuffs of your coverall.)
Once the task is completed, it is important that you remove your PPE in such a way as not to expose yourself or others to potential infectious matter. Have your disposal bag and container for reusable ready. Remove your PPE in the following order (Figure 20):
1. Outer gloves, goggles (these are recyclable and should be put into your container for disinfection).
2. Apron (the thick PVC style aprons are recyclable and should be put into your container for disinfection).
4. Mask (do not touch the front of your mask; remove it by taking hold of the straps at the back of your head, first bring the bottom strap up and over your head and finally the top strap, lifting the mask away from your face and into the disposal bag).
5. Remove your hair cover.
6. Wash your hands.

All waste produced from handling and examining birds and humans with signs of infectious disease must be treated as potentially contaminated. Disposable gloves, coverall, shoe covers, masks and hair covers should be used once only. In field situations, reusable clothing should be washed with detergent and hot soapy water and disinfected. Citric acid (0.2% weight/volume for 30 minutes) is a good disinfectant for clothing and body. (7,10)
Figure 20: Order for removing personal protection equipments(7)
11. Effectively Communicating During Rapid Response Interventions

Effective communication is essential for successful management of any emergency. In particular, during the implementation of rapid response interventions, communication is crucial to achieve the following objectives:

• To win confidence, support and active participation from the stakeholders;
• To accurately inform stakeholders about the event that triggers the investigation and about findings;
• To avoid panic;
• To provide the relevant information to minimize risk of infection and spread through promoting appropriate behavior;
• To obtain accurate and reliable information from the stakeholders;
• To ensure effective coordination among team members and relevant sectors;
• To ensure timely and coordinated flow of information vertically and horizontally;
• To ensure effective engagement of communication actors, especially the media.

Good communication is an essential component of all stages of rapid response interventions, namely:

• Pre-Investigation Stage
• Investigation Stage
• Mitigation Stage
• Follow-up Stage

It is essential that the right messages are conveyed to the right target audiences and in a timely manner. Information needs and communication tools may vary according to the stage of intervention and target audience. Effective communication should also generate required information and provide feedback to the RRT through interactive processes involving the RRT and the stakeholders.
### Pre-Investigation Stage

<table>
<thead>
<tr>
<th>Target Audience/ Source</th>
<th>Information Needs</th>
<th>Suggested Communication Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>• RRT Members</td>
<td>Findings of daily activities, challenges encountered and way forward.</td>
<td>Telephone calls, and daily meetings</td>
</tr>
<tr>
<td>• National Task Force and Relevant Departments</td>
<td>Update on progress and findings</td>
<td>Telephone calls and emails</td>
</tr>
</tbody>
</table>
| • Local Authorities (LA) of the Affected Areas | **To the KI:** Introduction of the RRT, update on progress and findings and provision of appropriate messages for the community and the technical management of the outbreak.  
**From the KI:** Update on the situation in the field and anamnestic and epidemiological information. | Telephone calls (when possible), interpersonal communication, provision of RRT contact details, administration of questionnaires/semi-structured interviews, provision of technical and communication materials (e.g. pamphlets, posters, technical guidelines, etc.) and TV, radio spots and other local media. |
| • Community (civil society organizations, farmers, traders, households, schools, religious/cultural groups, etc) | **To the Community:** Introduction of the RRT, update on progress and findings and provision of appropriate messages for the community.  
**From the Community:** Report of cases and contact information. | On-site briefings, telephone calls, provision of RRT contact details, communication materials (e.g. pamphlets, posters, etc.) and TV, radio spots and other local media. |
| • Media | Introduction of the intervention, update on progress and findings and provision of appropriate messages for the community. | Scheduled press briefings/releases through official communication channels. |
### Mitigation Stage

<table>
<thead>
<tr>
<th>Target Audience/Source</th>
<th>Information Needs</th>
<th>Suggested Communication Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RRT Members</strong></td>
<td>Epidemiological findings to support mitigation interventions, challenges encountered and way forward.</td>
<td>Telephone calls, and daily meetings</td>
</tr>
<tr>
<td><strong>National Task Force and Relevant Departments</strong></td>
<td>Update on progress and findings, RRT needs, proposed mitigation strategy and authorization.</td>
<td>Telephone calls, emails and official communication of authorized mitigation strategies to RRT and local authorities.</td>
</tr>
<tr>
<td><strong>Local Authorities (LA) of the Affected Areas</strong></td>
<td><strong>To the LA:</strong> Update on progress, findings and proposed mitigation measures, provision of appropriate messages for the community and required support. <strong>From the LA:</strong> Update on the community perception and reaction to the mitigation measures and supportive actions taken.</td>
<td>Interpersonal communication, telephone calls (when possible), provision of RRT contact details, provision of communication materials (e.g. pamphlets, posters, speeches, etc.).</td>
</tr>
<tr>
<td><strong>Key Informants (KI) from the Affected Areas (e.g. Local Animal and Human Health Professionals; Affected Farmers, Patients, etc.)</strong></td>
<td><strong>To the KI:</strong> Update on progress, findings and proposed mitigation measures, provision of appropriate messages. <strong>From the KI:</strong> Update on the situation in the field and perception of the efficacy of the mitigation measures.</td>
<td>Telephone calls (when possible), interpersonal communication, provision of RRT contact details, provision of technical and communication materials (e.g. pamphlets, posters, technical guidelines, etc.) and TV and radio spots.</td>
</tr>
<tr>
<td><strong>Community (civil society organizations, farmers, traders, households, schools, religious/cultural groups, etc.)</strong></td>
<td><strong>To the Community:</strong> Update on progress, findings and proposed mitigation measures, provision of appropriate messages. <strong>From the Community:</strong> Update on the situation in the field and perception of the efficacy of the mitigation measures.</td>
<td>On-site briefings, telephone calls, provision of RRT contact details, communication materials (e.g. pamphlets, posters, etc.) and TV, radio spots and other local media.</td>
</tr>
<tr>
<td><strong>Media</strong></td>
<td>Update on progress, findings and proposed mitigation measures, provision of appropriate messages and FAQ.</td>
<td>Scheduled press briefings/releases through official communication channels.</td>
</tr>
</tbody>
</table>
## Follow-up Stage

<table>
<thead>
<tr>
<th>Target Audience/Source</th>
<th>Information Needs</th>
<th>Suggested Communication Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>• RRT Members</td>
<td>Summary of findings and implemented mitigation measures</td>
<td>Review meeting</td>
</tr>
<tr>
<td>• National Task Force and Relevant Departments</td>
<td>Update of findings and implemented mitigation measures and proposed follow-up.</td>
<td>Mission report and briefing.</td>
</tr>
<tr>
<td>• Local Authorities (LA) of the Affected Areas</td>
<td><strong>To the LA:</strong> Update of findings and implemented mitigation measures and proposed follow-up.</td>
<td>Mission report, telephone calls (when possible) and interpersonal communication.</td>
</tr>
<tr>
<td></td>
<td><strong>From the LA:</strong> Update on the community perception and reaction to the mitigation measures and new developments.</td>
<td></td>
</tr>
<tr>
<td>• Key Informants (KI) from the Affected Areas (e.g. Local Animal and Human Health Professionals; Affected Farmers, Patients, etc.).</td>
<td><strong>To the KI:</strong> Update of findings and implemented mitigation measures and proposed follow-up.</td>
<td>Telephone calls (when possible), interpersonal communication, provision of RRT contact details, provision of technical and communication materials (e.g. pamphlets, posters, technical guidelines, etc.) and TV, radio spots and other local media.</td>
</tr>
<tr>
<td></td>
<td><strong>From the KI:</strong> Update on the community perception and reaction to the mitigation measures and new developments.</td>
<td></td>
</tr>
<tr>
<td>• Community (farmers, traders, households, schools, religious/ cultural groups, etc)</td>
<td><strong>To the Community:</strong> Update of findings and implemented mitigation measures and proposed follow-up.</td>
<td>On-site briefings and TV and radio spots.</td>
</tr>
<tr>
<td></td>
<td><strong>From the Community:</strong> Update on the situation in the field and perception of the efficacy of the mitigation measures.</td>
<td></td>
</tr>
<tr>
<td>• Media</td>
<td>Update of findings and implemented mitigation measures and proposed follow-up.</td>
<td>Scheduled press briefings/releases through official communication channels and debriefing report on websites.</td>
</tr>
</tbody>
</table>
To effectively communicate and build ownership with stakeholders:

- **Build confidence and trust:** Be polite. Use phrases like, “I know how you feel” or “I understand.” Sit on the same level that the family is sitting.
- **Tell people about control efforts:** Keep explanations simple. Do not provide too much technical information, but be clear about the actions they can take to protect themselves from avian influenza or other influenza subtypes of concern, and why everyone needs to participate.
- **Leave behind leaflets (if you have them):** even if they cannot read. The act of leaving something will remind them after you have gone. School-going children in the family also may be able to relay the information.
- **Ask for their participation and support:** Reiterate that they can help protect the whole community. Thank the family for their cooperation and time.
- **Be reassuring but honest about the situation:** People may be frightened and confused. Be patient.
- **Listen carefully:** Listen more than you talk, and respond sympathetically to their concerns.
- **Motivate:** Tell them people’s actions are key to controlling the spread of influenza.
- **Reinforce messages:** People can protect themselves, their families and neighbors by taking action.
- **Be honest:** If you do not know the answer to a question, tell people you will return or contact them later with a response.
- **Explain if you have to take notes:**

**TO EFFECTIVELY COMMUNICATE AND BUILD OWNERSHIP WITH STAKEHOLDERS DO NOT:**

- Get angry or act impatient.
- Use phrases such as “You are wrong,” or “that is ignorant.”
- Blame the family.
- Make a gesture of disapproval when they are expressing an opinion.
- Answer questions when you do not know the answer.
- Threaten the family.
- Act arrogant or insult the family.

**EXAMPLES OF TALKING POINTS TO USE WHEN COMMUNICATING TO FAMILIES ABOUT AVIAN OR PANDEMIC H1N1 INFLUENZA**

- As in other countries, avian influenza or pandemic H1N1 is now a problem in our country.
- Any person who comes into close contact with sick or dead birds is at risk for avian influenza. You usually cannot tell if a bird is sick from avian flu or from another disease, so you should always take precautions. Some birds, such as ducks, may not show symptoms at all.
- Pandemic H1N1 is not acquired from pigs or other animals, but it is easily transmitted from human to human.
- So far, avian influenza does not seem to transmit easily from person to person.
- Drippings, blood, saliva, and nose secretions of infected birds and poultry can carry the virus, and the virus can survive for many hours on surfaces (and for many days in the environment). Boiling water, soap and detergents can kill the virus.
- Pandemic H1N1 is easily transmitted by droplets and contact with infected persons or...
objects. To prevent spread cough/sneeze in disposable tissues or on your elbow and wash hand frequently.

- Everyone must participate to protect each other from the spread of this disease.

EXAMPLE OF FIVE ACTIONS TO SUGGEST FOR REDUCING THE RISK OF GETTING AVIAN INFLUENZA FROM BIRDS IN AN INFECTED AREA:

1. Avoid close contact with all birds
   - Keep your children away from all birds and from collecting eggs, if possible.
   - Do not allow poultry in your house. If poultry must be kept indoors, keep them in a specific area that is away from where the family sleeps and eats.

2. Do not touch sick or dead birds – report them to the authorities immediately
   - If you come across any dead or sick birds, do not touch them unless you are wearing gloves.
   - Do not slaughter or prepare sick or dead poultry for food.
   - If you develop fever within days after being in contact with sick or dead poultry, seek immediate health care treatment.

3. Practice good hygiene
   - Wash your hands with soap and water or ash before and after handling any poultry – and especially before and after you prepare poultry or eggs for eating.
   - Wear gloves and a mask (or towel/cloth/handkerchief) over your mouth when cleaning or sweeping any area where poultry are kept and wash your hand after – poultry droppings, feed and feathers can all be infected with the avian influenza virus.

4. Cook chicken and eggs thoroughly before eating.
   - Do not eat runny eggs or poultry meat (or blood) that is not well-cooked.
   - Wash your hands with soap and water or ash before and after preparing poultry or eggs for eating.

5. Be careful if you go to farms, markets, or other areas where poultry are kept.
   - Wash hands with ash or soap and water before entering and after leaving an area where poultry are kept.
   - Brush off and disinfect clothing, shoes-sandals, and the wheels of bikes/motorcycles/other vehicles after leaving, and especially before going indoors, remove droppings

EXAMPLES OF FIVE ACTIONS TO SUGGEST FOR REDUCING THE RISK OF GETTING/SPREADING PANDEMIC H1N1 INFLUENZA:

1. Avoid overcrowded places whenever possible
   - Avoid closed environments with poor ventilation

2. Maintain distance from persons with flu-like symptoms
3. Practice good hand hygiene
   • Wash your hands frequently with soap and water
   • Clean utensils and surfaces properly in the house.

4. Practice cough etiquette.
   • Cough/Sneeze in a disposable tissue, dispose it immediately and wash hand afterward. If tissues are not available cough/sneeze in your elbow.

5. Stay at home if sick (with influenza-like symptoms).
   • If you develop influenza-like symptoms stay at home (away from work or school) for at least 24 hrs after resolution of fever.
   • While at home, drink plenty of fluids and take rest.
   • If symptoms persist or get worse contact your health care provider
REFERENCES


WHO (2009). Guidelines for Pharmacological Management of Pandemic (H1N1) 2009 Influenza and Other Influenza Viruses.


Other Useful References


- International Health Regulations (IHR): http://www.who.int/csr/ihr/en/

- UN: http://un-influenza.org

- CDC: http://www.cdc.gov/flu
Annex I: Terms of Reference for the Rapid Response Teams (Example)

The primary responsibility of the RRT is to investigate suspected cases or outbreaks of AI and other influenza subtypes of concern in both human and animals to confirm the nature of the event under investigation. It is also the responsibility of the RRT to undertake the preliminary control/containment measures needed to prevent further spread of the disease. Specific duties of the RRT are:

1. To adequately sensitize the stakeholders on the purpose of the investigation and the roles and responsibilities of the team members;
2. To conduct a preliminary epidemiological/anamnestic investigation aiming at identifying the origin/source, extent and potential for spread of the event under investigation. All information should be properly recorded in appropriate investigation forms;
3. To conduct a clinical examination of the subjects (animals or humans) affected by the event under investigation. A post-mortem can also be carried out in the event that dead animals are encountered or sick animals can be euthanized to add information to the clinical examination through post-mortem findings;
4. To collect relevant samples from the suspected cases (animal and human) for laboratory confirmation. All information related to the samples should be recorded in appropriated sampling forms;
5. To dispatch collected samples and the accompanying sampling forms to the relevant laboratories for confirmation as quickly as possible;
6. To immediately notify the relevant authorities about the findings/results of the investigation and to recommend possible interventions;
7. To carry out the preliminary containment and control measures as appropriate according to the findings in the field;
8. To prepare a detailed report of the investigation mission and submit it to the relevant authorities;
9. To support and coordinate follow-up containment and control measures according to finding/results and in line with the national intervention policies;

Events that can trigger the mobilization of RRT are: (i) report(s) of suspected AI animal/human cases or outbreaks received from the animal or human health authorities, private practitioners or the public; (ii) report(s) of elevated mortality in wild or domestic birds received from the animal health authorities, private practitioners or the public; and (iii) increased incidence of reports of Acute and Severe Respiratory Infections and/or influenza-like sickness according to the data generated from the routine passive human surveillance.
Annex II: Terms of Reference for the Rapid Response Teams’ Members (Example)

Veterinary Epidemiologist / Team Leader

The Veterinary Epidemiologist / Team Leader will be an experienced veterinarian from the Ministry of Agriculture (MoA) based at the MoA headquarters. S/he will possess practical experience on the epidemiological investigations of outbreaks of infectious diseases in animals in the country. He/She will respond directly to the Head of Department (Chief Veterinary Officer) and will strongly liaise with the Ministry of Agriculture, Ministry of Health and the National Task Force. The specific duties of the Veterinary Epidemiologist / Team Leader are:

• To coordinate all activities of the RRT, starting with preparation to the implementation of all field missions related to the investigation and containment of AI or other influenza subtypes of concern outbreaks;
• To liaise with all stakeholders involved in the investigation and response of AI or other influenza subtypes of concern suspected or confirmed outbreaks in collaboration with the human epidemiologist;
• To alert and collect all available information from the provincial (sub-national) focal points (veterinarians) prior to the field mission;
• To alert all relevant national animal health authorities (e.g., Ministry of Agriculture, National Task Force) prior to the field mission;
• To conduct epidemiological investigation of all suspected and confirmed outbreaks of AI in animals;
• To collate and analyze the animal data generated during the field investigation and to identify the required follow-up measures in collaboration with the human epidemiologist;
• To prepare a final mission report in collaboration with the other RRT members;
• To notify the animal national and international relevant authorities (e.g., Ministry of Agriculture, National Task Force, OIE and FAO) about the field findings related to animal outbreaks and to recommend the needed follow-up measures; and
• To coordinate all follow-up measures with the relevant national and international institutions in collaboration with the human epidemiologist.

\(^{91}\) In case of emergence of pandemic viruses with sustained human-to-human transmission, the leadership should be under the Ministry of Health.
Wildlife Expert: Veterinarian / Ornithologist

The Wildlife Expert will be an experienced professional with practical experience on identification, capture and handling of wild birds. Preferably, the expert should also have an understanding of the ecology of migratory birds species, a good knowledge of diseases of wild birds and the ability to conduct investigations of disease outbreaks in wildlife. He/She will respond directly to the Team Leader and strongly liaise with the relevant authorities from the wildlife sector. The specific duties of the Wildlife Expert are:

- To identify, capture and handle wild birds in line with international standards, as need may arise;
- To conduct clinical (including necropsy) investigation of all suspected and confirmed outbreaks of AI in wild birds;
- To ensure the proper collection, storage and transportation of samples from the field to laboratories for confirmation of diagnosis.
- To ensure that proper biosecurity measures are taken by the RRT.
- To collect, collate and analyze relevant ecological and epidemiological data related to the outbreak in wild birds.
- To identify required follow-up measures in collaboration with the veterinary and human epidemiologist and advise the relevant authorities;
- To prepare a final mission report in collaboration with the other RRT members;
Human Epidemiologist

The Human Epidemiologist will be an experienced medical doctor from the Ministry of Health (MoH) based at the MoH headquarters. S/he will possess practical experience on the epidemiological investigations of outbreaks of infectious diseases in humans in the country. S/he will respond to the Head of Department (Chief Medical Officer) and to the Veterinary Epidemiologist/Team Leader during the implementation of all field missions related to AI or other influenza subtypes of concern. He/she will strongly liaise with the Ministry of Health and the National Task Force. The specific duties of the Human Epidemiologist are:

- To coordinate the activities of the RRT related to the investigation and containment of suspected or confirmed outbreaks of AI or other influenza subtypes of concern in humans;
- To liaise with all stakeholders involved in the investigation and response of AI or other influenza subtypes of concern suspected/confirmed outbreaks in collaboration with the Veterinary Epidemiologist / Team Leader;
- To collect all available information from the provincial (sub-national) focal points (human doctors) prior to the field mission and prepare the logistic of the mission in collaboration with the Veterinary Epidemiologist / Team Leader;
- To alert all relevant national human health authorities (e.g., Ministry of Health) prior to the field mission;
- To conduct the epidemiological investigation of all human AI or other influenza subtypes of concern suspected or confirmed outbreaks;
- To collate and analyze the human data generated during the field investigation and to identify the needed follow-up measures in collaboration with the Veterinary Epidemiologist / Team Leader;
- To prepare a final mission report in collaboration with the other RRT members;
- To notify the human national and international relevant authorities (e.g., Ministry of Health and WHO) about the field findings related to human outbreaks and to recommend the needed follow-up measures;
- To coordinate all follow-up measures with the national and international relevant institutions in collaboration with the Veterinary Epidemiologist / Team Leader.
Animal Laboratory Expert

The Animal Laboratory Expert will be an experienced laboratory technologist from the National Veterinary Laboratory (NVL). S/he will possess practical experience on the collection, preservation, storing and shipment of relevant samples from live and dead birds for the diagnosis of AI. He/she will also possess practical experience on the laboratory diagnosis of AI suspected animal cases. He/She will respond to the NVL Director and to the Veterinary Epidemiologist / Team Leader during the implementation of all field missions related to AI. The specific duties of the Animal Laboratory Expert are:

- To maintain an inventory at NVL of: (i) all sampling, preservation, storing and shipping materials for AI animal sampling (for live and dead birds); (ii) equipment, reagents and consumables for avian influenza diagnosis; (iii) investigation/sampling forms and stationery needed for the investigation of animal suspected outbreaks; and (iv) PPE and disinfection material and equipment;
- To be responsible for the timely restocking/supply of all needed materials, equipment and consumables;
- To keep record of all material, equipment and consumables available at provincial (sub-national) veterinary posts and assist the provincial (sub-national) focal points (veterinarians) for timely restocking;
- To keep contact with the regional and international AI reference laboratories for the confirmation of animal suspected cases;
- To be responsible - in collaboration with the provincial (sub-national) focal points (veterinarians) and the Veterinary Epidemiologist / Team Leader - for the collection, labeling (according to the laboratory labeling system), preservation and storing of all samples for the laboratory confirmation of AI suspected cases (live and dead birds);
- To properly fill the relevant clinical, post-mortem and sampling forms and to ship the collected samples to the NVL;
- To prepare an aliquot of the collected samples and to timely ship them to the regional and/or international AI animal reference laboratories;
- To carry out the test for the laboratory diagnosis of AI animal suspected cases at NVL and to timely report the results to the Veterinary Epidemiologist / Team Leader; and
- To prepare a final mission report in collaboration with the other RRT members.
Human Laboratory Expert

The Human Laboratory Expert will be an experienced laboratory technologist from the National Human Laboratory (NHL). S/he will possess practical experience on the collection, preservation, storing and shipment of relevant samples from humans for the diagnosis of AI or other influenza subtypes of concern. He/she will also possess practical experience on the laboratory diagnosis of AI or other influenza subtypes of concern suspected human cases. He/She will respond to the NHL Director and to the Human Epidemiologist during the implementation of all field missions related to AI or other influenza subtypes of concern. The specific duties of the Human Laboratory Expert are:

- To maintain an inventory at NRL of: (i) all sampling, preservation, storing and shipping materials for AI or other influenza subtypes of concern human sampling; (ii) equipment, reagents and consumables for avian influenza diagnosis; (iii) investigation/sampling forms and stationery needed for the investigation of human suspected outbreaks; and (iv) PPE and disinfection material and equipment;
- To be responsible for the timely restocking/supply of all needed materials, equipment and consumables;
- To keep record of all material, equipment and consumables available at the provincial Hospitals and assist the provincial (sub-national) focal points (medical doctors) for timely restocking;
- To keep contact with the regional and international AI or other influenza subtypes of concern reference laboratories for the confirmation of human suspected cases;
- To collaborate with the provincial (sub-national) focal points (medical doctors) and the Human Epidemiologist for the collection, labeling (according to the laboratory labeling system), preservation and storing of all samples for the laboratory confirmation of AI or other influenza subtypes of concern suspected cases;
- To properly fill the relevant clinical and sampling forms and to ship the collected samples to NHL;
- To prepare an aliquot of the collected samples and to ship them to the regional and/or international AI or other influenza subtypes of concern human reference laboratories;
- To carry out the test for the laboratory diagnosis of AI or other influenza subtypes of concern human suspected cases at NHL and to timely report the results to the Human Epidemiologist; and
- To prepare a final mission report in collaboration with the other RRT members.
Provincial (Sub-National) Focal Points – Veterinarians (Clinicians)

The provincial focal points (veterinarians) will be experienced veterinary clinicians from the provincial (sub-national) veterinary posts. They will possess sound knowledge of the poultry farming system and wild birds’ situation of their province (sub-national) and practical experience on the clinical examination and implementation of autopsies in birds. They will also possess practical experience on the procedures for carcasses disposal, vaccination and decontamination of premises in case of infectious diseases outbreaks. They will respond to the Veterinary Epidemiologist / Team Leader during the implementation of all field missions related to AI. The specific duties for the Provincial Focal Points (Veterinarians) are:

- To maintain an inventory at the Provincial (Sub-National) Veterinary Posts of: (i) all sampling, storing and shipping materials for AI animal sampling; (ii) investigation/sampling forms and stationery needed for the investigation of animal suspected outbreaks; and (iv) PPE and disinfection material and equipment;
- To regularly forward the inventory to the Animal Laboratory Expert for timely restocking of material, equipment and consumables;
- To timely report all AI animal suspected outbreaks in the Province (Sub-National) to the Veterinary Epidemiologist / Team Leader, carry out a preliminary assessment of the situation in the field, collect all relevant preliminary information and timely transmit them to the Veterinary Epidemiologist / Team Leader before the central RRT members are mobilized;
- To keep an updated register of the relevant animal health authorities and local administrations in the province and alert them before the investigation begins;
- To perform the clinical and post mortem examination of birds in suspected premises/areas and assist the Animal Laboratory Expert to collect the relevant samples from live and dead birds;
- To implement and supervise all carcasses disposal, vaccination (if policy) and decontamination activities in the infected premises/areas;
- To assist the Veterinary Epidemiologist / Team Leader in the investigation of the extension of the outbreak and the zonation of the area according to his/her knowledge of the local situation;
- To assist the Veterinary Epidemiologist / Team Leader to coordinate all containment/control interventions and follow-up measures; and
- To prepare a final mission report in collaboration with the other RRT members.

Provincial Focal Points – Medical Doctors (Clinicians)

The provincial (sub-national) focal points (medical doctors) will be experienced clinicians from the provincial (sub-national) hospitals. They will possess sound knowledge of the health care system of their province and practical experience on the clinical examination and management of influenza patients. They will also possess practical experience on the procedures for sanitary precautions and disinfection of health care facilities and other premises in case of infectious diseases outbreaks. They will respond to the Human Epidemiologist during the implementation of all missions related to AI or other subtypes of concern. The specific duties for the provincial (sub-national) focal points (medical doctors) are:
To maintain an inventory at the provincial (sub-national) hospitals of: (i) all sampling, storing and shipping materials for AI or other influenza subtypes of concern human sampling; (ii) investigation/sampling forms and stationery needed for the investigation of human suspected outbreaks; and (iv) PPE and disinfection material and equipment;

To regularly forward the inventory to the AI or other influenza subtypes of concern Human Laboratory Expert for timely restocking of material, equipment and consumables;

To timely report all AI or other influenza subtypes of concern human suspected cases/outbreaks in the province (sub-national) to the Human Epidemiologist, carry out a preliminary assessment of the situation, collect all relevant preliminary information and transmit them in a timely manner to the Human Epidemiologist before the Central RRT members are mobilized;

To keep an updated register of the relevant human health authorities and local administrations in the province and alert them before the investigation begins;

To perform the clinical examination of suspected patients and assist the Human Laboratory Expert to collect the relevant samples from suspected patients;

To implement and supervise all disinfection activities in the health care facilities or other premises where suspected/confirmed cases are found;

To assist the Human Epidemiologist in the identification of the contact (at-risk) cases and their follow-up according to his/her knowledge of the local situation and costumes;

To assist the Human Epidemiologist to coordinate all containment/control interventions and follow-up measures and to supervise the treatment of suspected/confirmed patients; and

To prepare a final mission report in collaboration with the other RRT members.
Communication Expert

The Communication Expert will be experienced in community sensitization and preparation of awareness material and messages for the media and the press. He/she will respond to the Veterinary Epidemiologist / Team Leader and the Human Epidemiologist during the implementation of all missions related to AI or other influenza subtypes of concern. The specific duties for the Communication Expert are:

- To keep an updated register of the relevant media and press institutions to be contacted in case of AI or other influenza subtypes of concern outbreaks in the country;
- To prepare appropriate sensitization and awareness materials related to AI or other influenza subtypes of concern (prior to outbreak);
- To help the other RRT members interact with the community and other relevant local authorities and administrations;
- To assist the Veterinary Epidemiologist / Team Leader and the Human Epidemiologist to gather the relevant epidemiological information during the investigation of the suspected outbreaks;
- To assist the Veterinary Epidemiologist / Team Leader and the Human Epidemiologist in preparing specific messages for the media and the press;
- To assist the Agriculture and Human Authorities to gain the support and the confidence of the communities and the general public for the implementation of the needed control/containment measures in case of AI or other influenza subtypes of concern outbreaks; and
- To prepare a final mission report in collaboration with the other RRT members.
Annex III: Contact List of AI Reference Laboratories Convenient for Shipping Samples from Africa

OIE/FAO AI Reference Laboratories (convenient for shipping samples from Africa):

Contact: Dr. Marco ROMITO
Institution: ARC – Onderstepoort Veterinary Institute
Address: Private Bag X05 Onderstepoort 0110, Pretoria – SOUTH AFRICA
Title: Project Leader / AI Focal Point
Tel.: +27-(0)12-529.94.16
Fax: +27-(0)12-529.92.49
Email: romitom@arc.agric.za

Contact: Dr. Ilaria CAPUA
Institution: Istituto Zooprofilattico Sperimentale delle Venezie, Laboratorio di Virologia
Address: Via Romea 14/A, 35020 Legnaro, Padova - ITALY
Title: Virologist / AI Focal Point
Tel.: +39-(0)49-808.43.69
Fax: +39-(0)49-808.43.60
Email: icapua@izsvenezie.it

Contact: Dr. Nancy COX
Institution: Influenza Division; National Centres for Infectious Diseases; Centres for Disease Control and Prevention
Address: 1600 Clifton Road, Mailstop G16, Atlanta, Georgia 30333 – USA
Title: Director
Tel.: +1-404-639.35.91
Fax: +1-404-639.23.34

WHO AI Reference Laboratories (convenient for shipping samples from Africa):

Contact: Dr. Marietjie VENTER
Institution: National Institute for Communicable Diseases
Address: Private Bag X4 2131 Sandringam – SOUTH AFRICA
Title: AI Responsible
Tel.: +27-11-386.60.00
Fax: +27-11-882.05.96
Email: marietjiev@nicd.ac.za

Contact: Dr. A. HAY
Institution: National Institute for Medical Research
Address: The Ridgeway, Mill Hill, London NW7 1AA – UNITED KINDOM
Title: AI Director
Tel.: +44-208-959.36.66
Fax: +44-208-906.44.77
Contact: Dr. Nancy COX
Institution: Influenza Division; National Centers for Infectious Diseases; Centers for Disease Control and Prevention
Address: 1600 Clifton Road, Mailstop G16, Atlanta, Georgia 30333 – USA
Title: Director
Tel.: +1-404-639.35.91
Fax: +1-404-639.23.34
Email: nje1@cdc.gov
Annex IV: List of Material and Equipment for the Investigation and Containment of AI or Other Influenza Subtypes of Concern

The following material should be available at all time at the identified premises in order to guarantee a timely investigation and response of suspected/confirmed AI outbreaks in animal and/or humans.

- Sampling and Autopsy Equipment

<table>
<thead>
<tr>
<th>Item</th>
<th>Ministry of Agriculture</th>
<th>Ministry of Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heavy duty rubbish bags</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>String</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Burdizzo’s clamps</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Knives and steel (knife sharpener)</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Scalpel handle</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Disposable scalpel blades</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Forceps</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Scissors</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Poultry shears or large bandage scissors</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Syringes (1, 3, 6, 10, 12, 20 ml)</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Syringes’ needles (17 through 27 G)</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Vacutainer Holder</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Vacutainer Needles (20 G)</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Vacutainer no additives</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Transfer pipettes</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Flexible and sterile polyester swab</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Tourniquet</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Cotton swabs</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>10% polyvidone iodine</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Tongue depressor</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Stethoscopes</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Sterile plastic bottles – 90 ml</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Sterile cryovials – 2 and 5 ml</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Zip-lock bags</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>One liter plastic container filled with 10% neutral buffered formalin</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>100 ml of 70-90% ethanol</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Sterile polyester swabs</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Viral transport medium</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cooler (with ice packs)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Liquid-nitrogen container</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Three-packaging shipping container</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Clinical/Sampling forms (for human or animal cases)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Post-mortem forms</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Semi-structured interview templates (for human or animal cases)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Stationery (pen; notepads; permanent markers small and big tips; masking, cello &amp; tapes, etc.)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>List of contacts</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Notification forms</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>GPS unit</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Digital camera</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
- **Personal Safety Equipment**

<table>
<thead>
<tr>
<th>Item</th>
<th>Ministry of Agriculture</th>
<th>Ministry of Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coveralls</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>PVC Apron</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Latex gloves</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Goggles or face shields</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Surgical face masks</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Rubber boots</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Boots/shoes cover</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Disposal bag</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Antiviral</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

- **Decontamination and Disinfection Equipment**

<table>
<thead>
<tr>
<th>Item</th>
<th>Ministry of Agriculture</th>
<th>Ministry of Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heavy duty rubbish bag</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Wash bucket</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Nail brush</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Antiseptic soap</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Disinfectant for cloths (Citric acid (0.2% weight/volume for 30 minutes))</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Sodium hypochlorite (2-3% available chlorine)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Pressure Sprayer</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Foot bath</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Shovels</td>
<td>X</td>
<td>-</td>
</tr>
</tbody>
</table>
# Annex V: Checklist for the Epidemiological Investigation of AI Outbreaks (Example)

## Checklist of Relevant Information to be Collected during the Epidemiological Investigation of AI Suspected Outbreaks / Cases

### Domestic Fowls
- Exact location of the outbreak (Province, District, County, Physical Address and GPS Coordinates - if available)
- Type of Premises (e.g. Farm: Intensive, Semi-Intensive, Open Air, Backyard Production, etc.)
- Fowl species owned
- Number of owned domestic fowls by species
- Number of affected domestic fowls by species
- Symptoms by species
- Morbidity and mortality by species
- Date of beginning of the symptoms / mortality by species
- Recent introduction (received as a gift, purchased, etc.) of new domestic fowls
- Place of origin of newly introduced domestic fowls (details)
- Recent disposal (given as a gift, sold, etc.) of domestic fowls from the premise
- Place of destination of disposed domestic fowls (details)
- Recent purchase of domestic fowls for food
- Place of origin of domestic fowls’ food
- Contact between domestic fowls from neighbor premises.
- Contact between domestic and wild fowls
- Domestic fowls’ morbidity in the area
- Wild fowls’ morbidity in the area
- Any other relevant information

### Humans
- Exact location of the investigation (Province, District, County, and GPS Coordinates - if available)
- Type of Premises (e.g. Hospital, Clinic, Home, etc.)
- Demographic information of the patient(s)
- Contact history with potential sources of infection (e.g. sick poultry, poultry carcasses, infected premises, suspected/probable confirmed human cases, etc.)
- Recent travel history of the patient(s)
- Profession of the patient(s)
- Symptoms of the patient(s)
- Date of beginning of the symptoms
- Recent "contact" history of the patient(s) in order to identify contact-cases
- Any other relevant information

### Wild Fowls
- Exact location of the outbreak (Province, District, County, Physical Address and GPS Coordinates - if available)
- Description of the area under investigation (e.g. National Park, Wetland, etc.)
- Wild fowl species involved in the outbreak
- Number of affected wild fowls by species
- Symptoms by species
- Morbidity and mortality by species
- Date of beginning of the symptoms / mortality by species
- Presence of domestic fowls in the area
- Contact between domestic and wild fowls
- Any other relevant information
Annex VI: Avian Influenza – Contact Follow-Up Form (Example)

<table>
<thead>
<tr>
<th>Case Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Name:</td>
</tr>
<tr>
<td>First Name:</td>
</tr>
<tr>
<td>Address:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>Contact’s Details</th>
<th>Contact’s Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Family Name:</td>
<td>Contact Seen:</td>
</tr>
<tr>
<td></td>
<td>First Name:</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Address:</td>
<td>Date Contact First Seen:</td>
</tr>
<tr>
<td>1</td>
<td>Age:</td>
<td>Contact Status at Subsequent Visits (Days after the First Visit)**</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Contact Type: D</td>
<td>R</td>
</tr>
<tr>
<td></td>
<td>Relationship with Case:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date of Last Contact:</td>
<td>J</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>Contact’s Details</th>
<th>Contact’s Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Family Name:</td>
<td>Contact Seen:</td>
</tr>
<tr>
<td></td>
<td>First Name:</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Address:</td>
<td>Date Contact First Seen:</td>
</tr>
<tr>
<td>2</td>
<td>Age:</td>
<td>Contact Status at Subsequent Visits (Days after the First Visit)**</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Contact Type: D</td>
<td>R</td>
</tr>
<tr>
<td></td>
<td>Relationship with Case:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date of Last Contact:</td>
<td>J</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>Contact’s Details</th>
<th>Contact’s Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Family Name:</td>
<td>Contact Seen:</td>
</tr>
<tr>
<td></td>
<td>First Name:</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Address:</td>
<td>Date Contact First Seen:</td>
</tr>
<tr>
<td>3</td>
<td>Age:</td>
<td>Contact Status at Subsequent Visits (Days after the First Visit)**</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Contact Type: D</td>
<td>R</td>
</tr>
<tr>
<td></td>
<td>Relationship with Case:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date of Last Contact:</td>
<td>J</td>
</tr>
</tbody>
</table>

* Close Contact (from less than one meter); R: Household Contact (less than one meter); P: Health Care Worker; L: Other Contact
** W: Not Seen; H: Healthy; ILI: Illness-like Illness
Annex VII: Avian Influenza – Specimen Collection Form – Birds (Example)

### Avian Influenza - Specimen Collection Form - Animal Specimens

**General Information**

- **Location Description/Address of infected premises:**
- **Date of Investigation:** __/__/__
- **Contact Name:** ____________________________
- **Contact Tel.:** ____________________________
- **Name on report:** __________________________

### Mortality and Morbidity Rates by Species

<table>
<thead>
<tr>
<th>Species</th>
<th>Total by Species</th>
<th>Survived/Infected</th>
<th>Sick</th>
<th>Dead</th>
<th>Approximate Age of Affected Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2)</td>
<td></td>
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<td>(3)</td>
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<td>(5)</td>
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<tr>
<td>(6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(7)</td>
<td></td>
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### Description of the Outbreak and Contact History

Include any relevant information about the geographical location, and magnitude of the outbreak. Include also information related to recent introduction or movement of domestic fowl, premises, and plans for caging and vaccination, contact with wild birds, vaccination history, and any other relevant information.
# Specimen Collection Form - Live Animal Section

<table>
<thead>
<tr>
<th>No.</th>
<th>Animal ID</th>
<th>Species</th>
<th>Sex*</th>
<th>Approximate Age**</th>
<th>Clinical Symptoms***</th>
<th>Samples****</th>
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</tbody>
</table>

* M: Male; F: Female

** C: Chick; J: Juvenile; A: Adult

*** D: Depression; N: Nervous Signs; RD: Respiratory Disease; OCW: Ocular Erosion & Wate; RF: Ruffled Feathers; Dl: Diarrhea

**** S: Swab; TS: Tissue Swab; CS: Cloacal Swab
## Specimen Collection Form - Post-Mortem Animal Sector

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<tr>
<th>No.</th>
<th>Animal ID</th>
<th>Species</th>
<th>Status*</th>
<th>Sex**</th>
<th>Approximate Age***</th>
<th>Gross Pathology Findings****</th>
<th>Tissues Collected (Specify)*****</th>
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<td>FR FF</td>
</tr>
</tbody>
</table>

* E: Experienced; D24: Dead within 24 hours
** M: Male; F: Female
*** Ct: Chick; J: Juvenile; A: Adult
**** 3B: Oedema of the Trachea; P: Pneumonia; PA: Pneumonia on the anterior Fat; PH: Pneumonia on the Heart; H: Hemorrhages of the Ovary; HI: Hemorrhages of the Intestine
***** FF: Fresh Tissue; F: Formalin Fixed Tissue; Then specific collected tissue types (e.g., intestine, lung, liver, trachea, etc.)
Annex VIII: Avian Influenza – Specimen Collection Form – Human Cases (Example)

### Avian Influenza - Specimen Collection Form - Human Cases

#### Patient's Details

<table>
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<tr>
<th>Field</th>
<th>Details</th>
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<td>Family Name</td>
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<tr>
<td>First Name</td>
<td></td>
</tr>
<tr>
<td>Date of Birth / Age</td>
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<tr>
<td>Sex</td>
<td>Male</td>
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<td>Female</td>
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<td>Address</td>
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<td>Date of Onset of Illness</td>
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<td>Unique ID Number</td>
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#### Clinical Symptoms

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<th>Symptom</th>
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<th>No</th>
<th>Unknown</th>
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<td>Date of Symptom Onset</td>
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<tr>
<td>Hospitalisation</td>
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<td>Date</td>
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<td>Fever</td>
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<td>Cough</td>
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<td>Shortness of Breath</td>
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<td>Diarrhoea</td>
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<td>Vomiting</td>
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<td>Sore Throat</td>
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<td>Headache</td>
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<td>Other (Specify)</td>
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#### Travel History (During the 10 Days Prior to Illness Onset)

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<th>Country (Specify)</th>
<th>Country (Specify)</th>
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#### Exposure History (During the 10 Days Prior to Illness Onset)

<table>
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<tr>
<th>Contact or proximity (&lt; 1 meter) with any live domestic or wild birds</th>
<th>Yes</th>
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<tbody>
<tr>
<td>Contact with recently/bloodied poultry.</td>
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<tr>
<td>Visit or stay in the same household with anyone with pneumonia or fever in the illness.</td>
<td>Yes</td>
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<tr>
<td>Visit or stay in the same household with anyone with suspected human influenza (A/H1N1) case</td>
<td>Yes</td>
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<tr>
<td>Visit or stay in the same household with anyone with known human influenza (A/H5N1) case</td>
<td>Yes</td>
<td>No</td>
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#### Results (For Laboratory Use Only!!)

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<thead>
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<th>Specimen</th>
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