



Strengthening the intersectoral work for Influenza at the  
Human Animal Interface in the Region of the Americas

---

## Technical Questions & Answers

**PAHO**



**SARInet plus**

Red de infecciones respiratorias agudas graves



# PAHO

## Strengthening the intersectoral work for Influenza at the Human Animal Interface in the Region of the Americas

May 2023

### Technical Questions & Answers

Given the increasing detection of outbreaks of highly pathogenic avian influenza (HPAI) in birds registered in countries of the Region of the Americas, the confirmation of human infections of influenza A(H5N1) in Latin America and the Caribbean, and the increase of cases in mammals, the Pan American Health Organization/World Health Organization (PAHO/WHO) has developed a regional document on technical questions and answers on zoonotic influenza, which reiterates its guidance on surveillance, laboratory diagnostics in human and animal samples and other public health considerations. PAHO/WHO recommends strengthening surveillance of respiratory disease in animal and human populations, thorough investigation of all zoonotic infections, considering the preparedness for an increase in zoonotic infections as well as pandemic influenza preparedness.

---

**Suggested citation:** Pan American Health Organization / World Health Organization. Strengthening the intersectoral work for Influenza at the Human Animal Interface in the Region of the Americas. May 2023, Washington, D.C.: PAHO/WHO; 2023



# PAHO

## Content

**Case detection and reporting of animal influenza in humans .....5**

    Question: What is the current risk of zoonotic influenza to human health? .....5

    Question: What are the main surveillance pathways for the detection of a case of zoonotic influenza (human infected with animal influenza) and what are required components of a surveillance system capable of detection of a case? ..... 6

    Question: What steps can a Member State take to enhance human influenza surveillance in preparation for introduction/occurrence of zoonotic influenza?.....7

    Question: How and when should Member States begin health worker sensitization for case detection of zoonotic influenza in humans?..... 8

    Question: What are the recommended considerations for intra-country reporting mechanisms for suspected and confirmed? cases of zoonotic influenza? ..... 8

    Question: What are the national level considerations for international reporting of suspected/confirmed cases of avian influenza in humans?..... 8

**Case investigation of zoonotic influenza ..... 10**

    Question: What elements should the investigation of a zoonotic influenza case include? .....10

    Question: What are the case definitions of suspected and confirmed cases of zoonotic influenza for case finding during an investigation?.....10

    Question: What are the key variables required for line listing of suspect/confirmed human cases?..... 11

    Question: What are the risk levels of different exposures to zoonotic influenza? .....12

    Question: Who are considered close contacts of suspected zoonotic influenza cases? ..... 13

    Question: How should contact tracing be carried out? .....13

    Question: Should humans directly or indirectly exposed to infected animals be monitored?.....14

    Question: How should humans exposed to infected animals be monitored? .....14

**Cases and contacts management ..... 15**

    Question: Should oseltamivir be used to treat suspected/confirmed cases? .....15

    Question: Should chemoprophylaxis be provided to contacts?.....15

    Question: Should suspected and confirmed cases be put in isolation? If yes, how?.....16

    Question: What infection prevention measures are required in a health-care setting? .....16

**Animal health considerations ..... 17**

    Question: What is the current risk to animal health?..... 17



# PAHO

Question: What are the main surveillance pathways for the detection of cases of zoonotic influenza in animals and what are required components of a surveillance system capable of detection of a case? .... 17

Question: What steps can a Member State take to enhance animal influenza surveillance in preparation for introduction/occurrence of zoonotic influenza viruses in animals? .....18

Question: What are the national level considerations for intra-country reporting of detections of zoonotic influenza viruses in animals?.....18

Question: What are the national level considerations for international reporting of detections of zoonotic influenza viruses in animals? .....18

Question: What steps should be taken by Member States to control an influenza outbreak in animals? 19

Question: What PPE is needed for farm workers and cullers doing culling and cleaning operations for flocks infected with influenza viruses? .....19

Question. What steps might be taken by the Member State to enhance animal surveillance and prevent disease transmission along the border with a MS reporting an animal influenza event? ..... 20

**Laboratory considerations for diagnosis and surveillance in humans..... 21**

Question: Which samples should be collected from humans to be tested? ..... 21

Question: What is the recommended sampling and testing strategy for a human with high risk exposure to avian influenza? ..... 22

Question: What are the recommended laboratory protocols for influenza detection in humans?..... 22

Question: What are the recommended sample flow and laboratory testing algorithms for suspected avian influenza cases in humans?.....23

Question: How should results be interpreted for avian influenza A(H5) detection in humans? .....23

Question: If the result is influenza A positive but is not influenza A(H5). How should be the testing algorithms?..... 24

Question: How should an unusual result in influenza A subtyping be interpretate? ..... 24

Question: Could animal specimens be tested and processed in the same laboratory where human specimens are processed? .....25

Question: Which laboratories should test specimens of human suspected avian influenza cases? ..... 26

Question: How to ship influenza A(H5)-positive human sample to the WHO-CC at US-CDC? ..... 26

Question: How to ship influenza A(H5)-positive animal sample to the WHO CC at St. Jude Children’s Hospital? ..... 26

Question: Should the NIC report the situation to the WHO Global Influenza Surveillance and Response System (GISRS)? ..... 27



# PAHO

**Laboratory considerations for diagnosis and surveillance in animals** ..... 27

    Question: What laboratory findings in animal specimens should be reported to WOA by Member States and when it should be reported? ..... 27

    Question: What should be reported to WOA by MS and when it should be reported? ..... 27

**Genomic sequencing considerations** ..... 27

    Question: Which genetic group of influenza A(H5) is being recently detected in the Americas region? .. 27

    Question: Is there a candidate virus available for the human zoonotic influenza A(H5) vaccine? ..... 28

    Question: Do the influenza A(H5) viruses detected in the Americas present resistance to antivirals? .... 28

    Question: What are the recommendations for sequencing influenza A(H5) viruses? isolated from human samples?..... 28

    Question: What are the recommendations for the influenza sequences nomenclature? ..... 28

**Considerations on vaccination**..... 29

    Question: What are the recommendations on the use of human H5N1 influenza vaccines to prevent zoonotic influenza in the interpandemic period? ..... 29

    Question: Can the seasonal influenza vaccine be used to prevent infection from influenza A(H5) virus? 29

    Question: What are the recommendations on the use of veterinary influenza A(H5) vaccines to prevent against avian influenza in animals? ..... 30

**Considerations on Risk communication and community engagement**..... 31

    Question: What are the main recommendations regarding risk communication messages for preparedness to animal influenza outbreaks? ..... 31

    Question: What are the main recommendations regarding risk communication messages for preparedness and response to animal influenza outbreaks? ..... 31

**References** ..... 33



## Case detection and reporting of animal influenza in humans

### Question: What is the current risk of zoonotic influenza to human health?

Answer: Ongoing circulation of some avian influenza viruses in animals, such as but not limited to A(H5), A(H7) and A(H9) viruses, are of public health concern as these viruses can cause severe disease in humans and if an animal virus acquired the ability to transmit efficiently from human to human, it could cause a pandemic as the population would have little to no immunity to the virus. To date, although limited human-to-human transmission of these viruses is thought to have occurred in some instances when there had been close or prolonged contact with a patient, there has been no sustained human-to-human transmission identified. Whether currently circulating avian, swine and other zoonotic influenza viruses will result in a future pandemic is unknown. However, the diversity of animal influenza viruses that have caused human infections, together with the large extension of influenza viruses in birds worldwide and with unusual occurrence in mammals, is alarming and necessitates strengthened surveillance in both animal and human populations, thorough investigation of every zoonotic infection and pandemic preparedness planning.

### Avian influenza

The number of reported human infections with avian influenza remains low, and they are linked to close contact with infected birds and contaminated environments. At the moment there is no evidence of sustained human-to-human spread. So, overall, the risk to public health is low but vigilance is required on the public health front. Surveillance of the circulating viruses in animals is critical to pick up any significant changes early, laboratories need to be alert and if anything is to change, information must be shared quickly so that the needed public health actions can be taken.

### Swine influenza

Swine influenza viruses circulate in swine populations in many regions of the world. Depending on geographic location, the genetic characteristics of these viruses differ. Most human cases are result of the exposure to swine influenza viruses through contact with infected swine or contaminated environments. When swine viruses are detected in people, they are referred to as "variants"; these viruses (e.g. A(H3N2)v and A(H1N2)v and A(H1N1)v) must be monitored closely in swine and when infecting humans. Human infection tends to result in mild clinical illness. Since these viruses continue to be detected in swine populations, further human cases can be expected. However, the likelihood of sustained human-to human transmission of these viruses remains low, as these viruses have currently not acquired the ability for sustained transmission among humans.

Further information available at:



[Influenza \(Avian and other zoonotic\) \(who.int\)](https://www.who.int)

[Assessment of risk associated with recent influenza A\(H5N1\) clade 2.3.4.4b viruses \(who.int\)](https://www.who.int)

[Influenza at the Human-Animal Interface: PAHO Recommendations to Strengthen Intersectoral Work for Surveillance, Early Detection, and Investigation, 9 July 2020](https://www.who.int)

<https://www.who.int/publications/m/item/standardization-of-terminology-for-the-influenza-virus-variants-infecting-humans-update>

**Question: What are the main surveillance pathways for the detection of a case of zoonotic influenza (human infected with animal influenza) and what are required components of a surveillance system capable of detection of a case?**

Answer:

Pathway*	Component
Through an investigation carried out following the identification of an influenza outbreak in the animal sector. The investigation should include the monitoring and follow up of persons exposed to infected poultry flocks or those in contact with infected wildlife (including handling carcasses).	Targeted human surveillance linked to animal surveillance: studies carried out in populations with increased risk of exposure following the detection of influenza in animals.
Individual(s) that present to health services with an unusually severe acute respiratory infection, especially if they test negative for laboratory tests indicated according to the differential diagnosis.	Universal/national surveillance of unusual cases/ events. (Mandatory notifiable diseases*)
Individual(s) with flu-like illness (both mild and severe) that present to health services in areas where outbreaks of avian influenza in animals have been reported, and who report recent exposure to animals during anamnesis.	Universal/national surveillance of unusual cases/ events. (Mandatory notifiable diseases*)
Clusters of atypical severe cases detected in the community or a healthcare setting.	Universal/national surveillance of unusual cases/ events. (Mandatory notifiable diseases*)  Community surveillance and/or monitoring of media.



Individual(s) with SARI/ILI that present to a sentinel site where laboratory tests using the surveillance algorithm suspect zoonotic influenza.	Sentinel surveillance of ILI/SARI.
Rumors or unofficial information in the media about possible humans infected with animal influenza in the community or health facilities.	Community surveillance and/or monitoring of media.

*Some examples of different pathways are provided however cases may appear under other circumstances.*

\* Four critical diseases are deemed always to be unusual or unexpected and may have serious public health impact, and hence must be notified to WHO in all circumstances. Human influenza caused by a new subtype, and severe acute respiratory syndrome (SARS) are included among them so countries must have surveillance models allowing its rapid detection and notification at national and international levels.

Further information regarding the four diseases requiring notification to WHO in all circumstances under the IHR (2005) is available at: [Case definitions for the four diseases requiring notification to WHO in all circumstances under the IHR \(2005\)](#)

Further information about International Health Regulations available at: [International Health Regulations \(2005\) – Third edition \(who.int\)](#)

Further information about other complementary surveillance models and approaches is available at: [WHO Mosaic Respiratory Surveillance Framework](#)

**Question: What steps can a Member State take to enhance human influenza surveillance in preparation for introduction/occurrence of zoonotic influenza?**

**Answer:** Member State Ministries of Health may consider enhancing all the surveillance components for case detection especially in those areas where zoonotic influenza has been detected in animals - or in those areas where there is greater risk of its occurrence - including health worker sensitization. Additionally, countries may consider the reinforcement of surveillance in their borders.

Other additional measures for preparedness to an avian influenza outbreak include:

- Review of plans for the investigation of cases including contact tracing.
- Review of plans for the use of oseltamivir and clinical management of human cases
- Review of plans for the use and availability of PPE
- Review of plans for the collection and shipment of samples
- Review of risk communication plans for zoonotic influenza or updating of current plans to include zoonotic influenza





## Question: How and when should Member States begin health worker sensitization for case detection of zoonotic influenza in humans?

Healthcare personnel in areas where transmission of zoonotic influenza in animals is taking place should be alerted about the possibility of infection in people exposed to these viruses. PAHO/WHO acknowledges that many countries already have disease notification systems in place that will be used for communication regarding unusual events.

Sensitization should begin as soon as possible BEFORE the first case is detected or suspected. Countries should convene a technical working group consisting of representatives from each health worker category (as appropriate to the country's situation and health system structure). This working group could produce and implement a training plan that covers the following components:

1. Case identification – including case definitions and the importance of exposure history.
2. Specimen collection
3. Notification protocols
4. Personal Protection and Infection Prevention and Control
5. Immediate case management

## Question: What are the recommended considerations for intra-country reporting mechanisms for suspected and confirmed cases of zoonotic influenza?

**Answer:** Countries should reinforce all the components of their surveillance system for the detection of human infections with animal influenza through the different surveillance pathways.

Public health authorities in countries need to define and reinforce the main channels and flows for reporting to the national level suspected/confirmed cases of zoonotic influenza detected at the local level. Suspected/confirmed zoonotic influenza cases should be immediately reported through mandatory notifiable diseases' surveillance channels.

When cases of zoonotic influenza are detected, national authorities should inform their counterparts in the animal sector to conduct the corresponding investigations and perform joint assessments.

## Question: What are the national level considerations for international reporting of suspected/confirmed cases of avian influenza in humans?

**Answer:** A confirmed case of human avian influenza infection should be reported immediately via two channels—the WHO International Health Regulations (IHR) Regional Contact Point ([ihr@paho.org](mailto:ihr@paho.org)) via the IHR National Focal Point, and the WHO Global Influenza Surveillance and Response System (GISRS) managed by PAHO and WHO ([flu@paho.org](mailto:flu@paho.org)). The report should include all available results from the epidemiological case investigation and the virological characteristics of the virus.



A **suspected** case of human avian influenza infection should be **reported immediately** to GISRS ([flu@paho.org](mailto:flu@paho.org)) and information about the suspected case can be shared with the WHO IHR Regional Contact Point ([ihr@paho.org](mailto:ihr@paho.org)), given it is an unusual event. The report should include all available results from the epidemiological case investigation and the virological characteristics of the virus.

If there is uncertainty regarding how to proceed or if there is inadequate information to complete the decision instrument, members states may keep the WHO apprised of the situation and obtain support via the National IHR Focal Point.

Further information regarding IHR available at: [International Health Regulations \(2005\) – Third edition \(who.int\)](#)

Further information about GISRS available at: [Global Influenza Surveillance and Response System \(GISRS\) \(who.int\)](#)

Question: What are the main public health actions when animal influenza viruses are detected in humans?

**Answer:**

- A thorough epidemiologic investigation of the history of exposure to animals (particularly to poultry, swine or wild birds and mammals), travel, and ill contacts should be conducted, even while awaiting confirmatory testing. (Expanded information in the section: Case investigation of zoonotic influenza in humans).
- Enhance surveillance through all the different components.
- Undertake animal health and environmental investigations: investigators in public health and animal health need to work together to assess the role of animals as sources of human exposure and infection. Field visits to investigate the occurrence of illness among animals or the circulation of the pathogen in animals can include visits to:
  - the case's home and surroundings;
  - farms and live animal markets;
  - local areas where food is produced to be consumed raw or unpasteurized; and
  - places frequented by wild animals (e.g. caves or watering holes). Information should be collected on animal illnesses and deaths, as well as animal housing, feeding and handling practices.

Investigators should coordinate their activities so that human and animal specimens can be linked and compared. Guidance from the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (WOAH) should be consulted regarding technical issues related to surveillance, prevention and control of disease in animals.



- Conduct Risk communication and community engagement activities. (Expanded information in the section: Considerations on Risk communication and community engagement)

## Case investigation of zoonotic influenza

**Question: What elements should the investigation of a zoonotic influenza case include?**

- A thorough epidemiologic investigation including definition of cases, history of exposure to animals (particularly related to poultry, swine and wild birds and mammals), travel, and ill contacts should be conducted, even while awaiting confirmatory testing.
- The epidemiologic investigation should include early identification of additional unusual respiratory events (or other relevant signs and symptoms especially in people with increased exposure risk) that could signal person-to-person transmission of the novel virus.
- Clinical samples collected from the time and place that the case occurred should be tested and sent to a WHO CC for further characterization within the first week of detection.
- Standard infection prevention and control (IPC) procedures and standard precautions should always be applied, and personal protective equipment (PPE) used according to risk, to protect the health of the investigators.
- The epidemiological investigation should include information from the official veterinarian services (OVS) and (animal production) private sector about the origin of the animals and the records of movements in and out of the premise. This information will contribute to define the scope (location) of investigations on humans exposed to the infected animals.
- Information from OVS could inform about potential episodes of influenza (both notifiable and non-notifiable) occurring in the area and farms related to the event.

Further information about how to investigate non-seasonal influenza and other emerging acute respiratory diseases available at: [Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases \(who.int\)](https://www.who.int/publications/m/item/protocol-to-investigate-non-seasonal-influenza-and-other-emerging-acute-respiratory-diseases)

**Question: What are the case definitions of suspected and confirmed cases of zoonotic influenza for case finding during an investigation?**

**Answer:** Case definitions should be applied systematically and without bias to all persons under investigation. Working case definitions should be developed using information obtained from the initial interview and home visit of the case patient, along with known information about the pathogen and its epidemiological characteristics. The case definitions should be sensitive enough during the initial stages of the investigation to capture most cases. As the investigation evolves and more information is obtained, it may be desirable to refine the definition to increase its sensitivity and specificity.



For avian influenza A(H5N1) and A(H7N9), WHO has recommended case definitions primarily for standardized international investigation and reporting of cases. The following case definitions are proposed for further adaptation for this purpose:

**Suspected case:** A person with acute onset of at least one of the following symptoms: cough, sore throat, shortness of breath or coryza.

AND/OR fever

AND with onset within the last 10 days in a person with at least one of the following epidemiological exposures in the two weeks prior to symptom onset in [Area X] since/during [date Y/date Y to Z]:

- exposure to animals (including sick or dead animals) or their remains or to environments contaminated by their excreta (faeces, blood, respiratory tract secretions, etc.) in an area where there has been an outbreak of an influenza A virus in domestic poultry, wild birds or other animals in the past two weeks, or
- consumption or handling of raw or undercooked animal products in an area where influenza infections in animals or humans (other than seasonal influenza virus subtypes) have been suspected or confirmed in the past two weeks, or
- close contact (within 1 metre) with an animal or human confirmed to be infected with a zoonotic influenza A virus.

**Confirmed Case:** Laboratory confirmation of a recent<sup>1</sup> infection with a zoonotic influenza A virus infection in a person.

Further information about case definitions available at: <https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2018.2>

Further information about case definitions available at: [Zoonotic Influenza A Virus Outbreak Toolbox \(who.int\)](#)

**Question: What are the key variables required for line listing of suspect/confirmed human cases?**

**Answer:** For suspected and confirmed cases : Unique ID number, Case status (suspected, confirmed); First name; Last Name; Address; Sex; Date of Birth; Contact number; Date of symptom onset; Date of first health facility visit; Date of initial hospitalization, Outcome; Symptoms and onset (fever, chills, cough, sore throat, runny nose, vomiting, diarrhoea, headache, shortness of breath, other); Comorbid conditions (list); Date of last influenza vaccination; Date of last SARS-CoV-2 vaccination; Occupation; Exposure to wild, domestic, or commercial animals; Type of animal; Nature of contact (groom, feed, slaughter); any sick or dead animals



in past 2 weeks in the environment; Specimen collection date; Specimen type; Type of test; Lab test result (positive/negative); Pathogen(type, sub-type).

Further information about case investigation forms available at: [Zoonotic Influenza A Virus Outbreak Toolbox \(who.int\)](#)

Further information about case investigation forms available at: [generic-respiratory.pdf \(who.int\)](#)

### **Question: What are the risk levels of different exposures to zoonotic influenza?**

**Answer:** risk levels of exposure may vary depending on the pathogen, and for this reason early investigations are needed to determine the main exposures associated with risk of infection. For avian influenza H5N1 risk exposures have been defined as:

#### **High risk** exposure groups:

- Household or close family contacts of a strongly suspected or confirmed H5N1 patient, because of potential exposure to a common environmental or poultry source as well as exposure to the index case.

#### **Moderate risk** exposure groups:

- Personnel involved in handling sick animals or decontaminating affected environments (including animal disposal) if personal protective equipment may not have been used properly.
- Individuals with unprotected and very close direct exposure to sick or dead animals infected with the H5N1 virus or to particular birds that have been directly implicated in human cases.
- Health care personnel in close contact with strongly suspected or confirmed H5N1 patients, for example during intubation or performing tracheal suctioning, or delivering nebulized drugs, or handling inadequately screened/sealed body fluids without any or with insufficient personal protective equipment. This group also includes laboratory personnel who might have unprotected exposure to virus- containing samples.

#### **Low risk** exposure groups:

- Health care workers not in close contact (distance greater than 1 metre) with a strongly suspected or confirmed H5N1 patient and having no direct contact with infectious material from that patient.
- Health care workers who used appropriate personal protective equipment during exposure to H5N1 patients.
- Personnel involved in culling non-infected or likely non-infected animal populations as a control measure.



- Personnel involved in handling sick animals or decontaminating affected environments (including animal disposal), who used proper personal protective equipment.

Further information about risk levels according to exposure available at: [WHO rapid advice guidelines on pharmacological management of humans infected with avian influenza A \(H5N1\) virus](#)

### **Question: Who are considered close contacts of suspected zoonotic influenza cases?**

Contacts are persons who had contact with individuals fitting the case definition during the presumptive incubation period. For respiratory disease pathogens for which modes of transmission, periods of infectivity and incubation periods are not known, a contact may be defined as a person who came within 1 m distance from the case without PPE (for at least 15 minutes) in the 1 day before the onset of the case's illness until 14 days after the onset of the illness. It may be necessary to trace contacts for suspect cases if the capacity to determine probable or confirmed case status is limited.

Further information about identification and monitoring of contacts available at: <https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2018.2>

### **Question: How should contact tracing be carried out?**

#### **Answer:**

There are four key steps in a contact investigation:

- Decide how a contact will be defined (clinic-epidemiologic factors)
- Identify and list potential contacts
- Based upon the definition of a contact, identify the contacts that will need to be monitored
- Follow-up with each contact during the period specified.

A line-listing of all contacts and exposed persons should be maintained.

The number of days for monitoring contact health status depends on the incubation period of the pathogen. Contacts of cases infected with avian influenza A(H5N1) virus should be monitored for 7 days from the last unprotected contact, whereas contacts of cases infected with avian influenza A(H7N9) virus should be monitored for 14 days. If the incubation period and period of infectivity are unknown, an alternative approach is to monitor contacts for up to 14 days, until information about these epidemiological features is determined and the contact follow-up period can be revised.

Monitoring of contacts can be done through:

- a. self-reporting each day by the contact to the field staff with a predefined frequency
- b. telephone call by the field staff to the contact with a predefined frequency



- c. household or virtual visit by the field staff to the contact to check for symptoms with a predefined frequency
- d. self-reporting by the contact to the field staff only if develop symptoms.

Factors influencing this choice include the feasibility of telecommunication, availability of human and logistical resources to conduct physical visits daily, likelihood of contacts recognizing and self-reporting illness, likelihood of symptomatic contacts fleeing from health authorities and consequences of missing cases

Further information about identification and monitoring of contacts available at: [Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases \(who.int\)](https://www.who.int/publications/m/item/protocol-to-investigate-non-seasonal-influenza-and-other-emerging-acute-respiratory-diseases)

### **Question: Should humans directly or indirectly exposed to infected animals be monitored?**

**Answer:** People directly or indirectly exposed to infected animals (domestic, wild, or captive) are at risk of contracting infections, (for example, poultry keepers who maintain close and regular contact with infected birds or the personnel involve in the slaughter or cleaning and disinfection of affected farms). Exposed persons should have their level of risk assessed and isolation measures taken as stated below. It is important that employers maintain a list of people working on farms or involved in culling and cleaning operations for monitoring. Information should be made available to them regarding what to do if symptoms.

### **Question: How should humans exposed to infected animals be monitored?**

**Answer:** When zoonotic influenza is circulating, for individuals who have interactions with potentially ill or dead animals the risk of exposure should be assessed. If the risk is moderate-high (see section above), these individuals should be monitored.

The number of days for monitoring depends on the incubation period of the pathogen, in case of avian influenza A(H5N1) virus the person should be monitored for 7 days from the last unprotected contact, whereas in case of avian influenza A(H7N9) virus the person should be monitored for 14 days. If the incubation period and period of infectivity are unknown, an alternative approach is to monitor contacts for up to 14 days, until information about these epidemiological features is determined and the contact follow-up period can be revised.

The clinical signs and symptoms that can be used to monitor the exposed persons can be influenza-like illness (ILI) and severe acute respiratory infection (SARI). The constellation of signs and symptoms might be expanded to include any of the following: fever, diarrhea, cough, nausea, sore throat, vomiting, runny or stuffy nose, fatigue, sneezing, seizures, muscle or body aches, rash, headaches, eye tearing, redness, irritation, difficulty breathing, among others.



Further information about identification and monitoring of contacts available at: [Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases \(who.int\)](#)

## Cases and contacts management

### Question: Should oseltamivir be used to treat suspected/confirmed cases?

In suspected and confirmed zoonotic influenza cases, neuraminidase inhibitors should be prescribed as soon as possible (ideally, within 48 hours following symptom onset) to maximize therapeutic benefits. However, given the significant mortality currently associated with A(H5) and A(H7N9) subtype virus infections and evidence of prolonged viral replication in these diseases, administration of the drug should also be considered in patients presenting later in the course of illness. The standard dose of oseltamivir is 75 mg twice daily for 5 days. However, the optimal duration and dose are uncertain for severe or complicated influenza. Influenza A (H5N1) and A (H7N9) viruses have been shown to be associated with higher virus loads and more sustained viral replication. Longer courses of treatment (e.g., 10 days) should be considered for severely ill hospitalized patients with infections with novel influenza A viruses that cause severe disease.

Further information about the clinical management of zoonotic influenza cases is available at:

[Influenza \(Avian and other zoonotic\) \(who.int\)](#)

[Guidelines for the clinical management of severe illness from influenza virus infections \(who.int\)](#)

[WHO rapid advice guidelines on pharmacological management of humans infected with avian influenza A \(H5N1\) virus](#)

[Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases \(who.int\)](#)

### Question: Should chemoprophylaxis be provided to contacts?

**Answer:** The use of chemoprophylaxis, if available, depends on the event context and risk assessment. As per guidance for outbreaks of avian influenza A(H5N1) virus infection:

- In high-risk exposure groups, including pregnant women, oseltamivir should be administered as chemoprophylaxis, continuing for 7–10 days after the last exposure (strong recommendation); zanamivir could be used in the same way (strong recommendation) as an alternative.
- In moderate-risk exposure groups, including pregnant women, oseltamivir might be administered as chemoprophylaxis, continuing for 7-10 days after the last exposure (weak recommendation); zanamivir might be used in the same way (weak recommendation).
- In low-risk exposure groups oseltamivir or zanamivir should probably not be administered for chemoprophylaxis (weak recommendation). Pregnant women in the low risk group should not receive oseltamivir or zanamivir for chemoprophylaxis (strong recommendation).





Further information about the use of chemoprophylaxis in the context of zoonotic influenza available at: [WHO rapid advice guidelines on pharmacological management of humans infected with avian influenza A \(H5N1\) virus](#)

**Question: Should suspected and confirmed cases be put in isolation? If yes, how?**

**Answer:** If the patient has an ambulatory illness, the case can be isolated voluntarily at home while febrile; personal hygiene and infection prevention and control at home should be applied carefully for 21 days after onset. Variables to take into consideration when consider isolation are the possibility for the person to self-isolate, the person's understanding about the potential of transmitting a potentially dangerous disease to others, and if there is a possibility to isolate the person in a health care setting.

For severe cases requiring hospitalization, isolation following standard, droplet and contact precautions are required.

Further information about isolation and IPC measures for zoonotic influenza cases available at: [Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases \(who.int\)](#)

[Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care \(who.int\)](#)

**Question: What infection prevention measures are required in a health-care setting?**

**Answer:** Standard, droplet, and contact precautions should be used.

Ministries of Health are encouraged to identify and designate appropriate isolation facilities and mechanisms for cohorting patients in in-patient and outpatient health facilities BEFORE the first case is identified.

Health care workers should wear appropriate PPE (gloves, masks, eye protection, and long-sleeved-gown as per standard, droplet, and contact precautions) when within 1 metre of the patient.

For hospitalized patients, the patient should be placed in a single room (when available) or cohorted, separated from others by at least 1 metre. There should be limited movement out of the hospital room with use a medical-surgical mask if they must move outside of the isolation area. Cleaning and disinfection of the patient environment and patient-care equipment, and Laundry and waste management should be conducted in keeping with recommended protocols.

Airborne precautions are required if aerosol generating procedures (aspiration or open suctioning of respiratory tract secretions, intubation, cardiopulmonary resuscitation, bronchoscopy, aerosolized nebulizer, non-invasive ventilation (NIV), high flow oxygen are being done. These include:

- *Health care worker:* Uses a particulate respirator, gown, eye protection, gloves.



- *Patient*: Placed in single room; Avoid unnecessary individuals in the room
- *Airborne precaution room characteristics*: Natural ventilation with at least 160 l/s/patient air flow, Negative pressure rooms with at least 12 air changes per hour, and Controlled direction of airflow.

Further information about IPC measures for zoonotic influenza cases in healthcare settings available at: [Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care \(who.int\)](https://www.who.int/publications/m/item/infection-prevention-and-control-of-epidemic-and-pandemic-prone-acute-respiratory-infections-in-health-care)

## Animal health considerations

### Question: What is the current risk to animal health?

**Answer:** The risk evaluation for H5N1 needs to consider the subregional epidemiological scenario and the country context including different potential routes of introduction (e.g. imported poultry, wild birds, etc.)

There is uncertainty about the evolution of the current H5N1 virus risk, as there is comparable historical data with this level of occurrence of highly pathogenic avian influenza in the region, although traditionally the Pacific route had more impact for other subtypes. Additionally, it is difficult to compare scenarios from other regions, due to the different epidemiological contexts, poultry population, wild bird species and distribution. It should be considered the possibility of the virus being maintained in resident wild birds (or bridge birds) with some primary incursions into backyards or farms with low biosecurity.

Thus, while the virus is maintained in the wild bird population the risk of introduction through migratory wild birds into countries is moderate/high and the impact will depend on the type of birds exposed.

Some key factors in the region to be considered in the risk evaluation are migration routes for wild birds, "bridge wild birds", high dependence on protein from poultry origin, backyard, poor biosecurity, game birds, and multispecies (ducks).

Further information available at: <https://www.fao.org/3/cc4720en/cc4720en.pdf>

### Question: What are the main surveillance pathways for the detection of cases of zoonotic influenza in animals and what are required components of a surveillance system capable of detection of a case?

**Answer:** Countries need to implement adequate surveillance strategies to detect AI, targeting the different avian components, i.e. commercial units, backyard, breeders/genetic units and wild birds. For HPAI viruses such as H5N1, it is necessary to have an adequate system for passive surveillance in poultry, where all the sensors, such as (birds' keepers, farmers or local vets) should be able to recognize the disease, communicate the suspicions to the official veterinary services (OVSs) getting a rapid response to this notification to confirm or rule out the suspicions. This strategy requires adequate sensors 'conscientization to detect and report suspicion. The surveillance should also target wild populations, particularly to investigate unusual mortalities or sick animals in partnership with national wildlife actors.



Further information available at:

<https://www.fao.org/documents/card/en/c/de4959ee-b8c2-58c7-b180-907d9d87761d/>

[https://www.woah.org/fileadmin/Home/eng/Health\\_standards/tahc/2018/en\\_chapitre\\_surveillance\\_general.htm](https://www.woah.org/fileadmin/Home/eng/Health_standards/tahc/2018/en_chapitre_surveillance_general.htm)

**Question: What steps can a Member State take to enhance animal influenza surveillance in preparation for introduction/occurrence of zoonotic influenza viruses in animals?**

**Answer:** For HPAI, early detection primarily relies on passive surveillance, however, to enhance the strategies it is possible to incorporate target risk-based surveillance according to the epidemiological risk scenario. This can be complemented with awareness campaigns particularly targeting the populations at greater risk. Compensation policies in case of depopulation due to HPAI in poultry contributed to promoting the reporting among farmers and bird keepers. Another important strategic action is to guarantee adequate laboratory capacity with sufficient trained staff and reagent stock.

**Question: What are the national level considerations for intra-country reporting of detections of zoonotic influenza viruses in animals?**

**Answer:** As a first step, Sensors such as farmers, animal keepers, local private veterinarians, wildlife actors, etc should notify any suspicions of HPAI to the OVSs. The OVSs should promote and facilitate this reporting, for example via apps, websites, or telephone numbers. The OVS should also have an adequate surveillance information system to manage the data. Any suspicions of HPAI need to be investigated in a timely matter initiating the process with a visit to the establishment by the OVSs to inspect the animals and carry out an epidemiological investigation. This visit should be followed up with laboratory testing if during the visit the AI suspicion is still maintained, to be able to rule it in or rule it out with a diagnostic test.

**Question: What are the national level considerations for international reporting of detections of zoonotic influenza viruses in animals?**

**Answer:** Avian influenza is a notifiable disease listed by the WOA. As detailed by the WOA [Terrestrial Animal Health Code](#), Member Countries must report: all highly pathogenic avian influenza viruses, irrespective of their strain, detected in birds (poultry -defined as all domesticated birds including backyard poultry- and wild); all low pathogenic viruses of subtypes H5 and H7 detected in poultry

[Infection](#) with influenza A viruses of high pathogenicity in birds other than [poultry](#), including [wild](#) birds, should be notified in accordance with Article [1.1.3](#). A sudden and unexpected increase in virulence of low pathogenicity avian influenza viruses in [poultry](#) is notifiable as an [emerging disease](#) in accordance with Article [1.1.4.Infection](#) of domestic and [captive wild](#) birds with low pathogenicity avian influenza viruses having proven natural transmission to humans associated with severe consequences, and [infection](#) of birds other than [poultry](#), including [wild](#) birds, with influenza A viruses of high pathogenicity, are notifiable in accordance with Article [1.3.6](#).



It should be noticed that there is not current requirement at the WOA Terrestrial Animal Health Code to notify occurrence of swine influenza in the countries-

**Question: What steps should be taken by Member States to control an influenza outbreak in animals?**

**Answer:** There are several considerations to be taken into account during the response to an influenza emergency at the animal component, which can be classified as technical, resources and sociopolitical.

Techniques:

- Updated contingency plan and team preparation with drills
- Ability to implement perifocal control actions with quarantines and movement restrictions.
- A strategy for epidemiological monitoring, data management and analysis must be implemented that allows understanding of the situation and making decisions in real-time.
- Laboratory capacity in quality (aptitude) and quantity (many samples to be processed in a short time)
- Ability to handle high morality in case of need for depopulation, destruction of corpses and cleaning and disinfection.
- If the use of vaccination is considered, the recommendations mentioned above should be considered.

Resources

- Sufficient personnel for field tasks, surveillance, control, stamping out, cleaning and disinfection.
- Financing to respond to the emergency (compensation, state of emergency, etc.)
- Acquisition of stock (eg supplies, cars, lab reagents, PPE, )

Socio-political

- Awareness, sensitization and commitment of the sensors (e.g. bird holders) to recognise the disease and to report suspicions
- Adequate legislative framework to respond to the emergency
- Management of risk communication at the livestock, international and citizen level.
- Establish intersectoral work tasks at the human-animal interface.
- Collaboration with other institutions such as law enforcement

**Question: What PPE is needed for farm workers and cullers doing culling and cleaning operations for flocks infected with influenza viruses?**

**Answer:** Standard infection prevention and control (IPC) procedures and standard precautions should always be applied, and personal protective equipment (PPE) used according to risk, to protect their health.



Appropriate PPE (according to the most probable modes of transmission) should be used when in situations where human-to-human transmission is suspected (WHO summary guidance, pp11 for persons in high-risk settings when avian influenza is circulating):

- a. protective clothing, preferably coveralls plus an impermeable apron or surgical gowns with long cuffed sleeves plus an impermeable apron;
- b. heavy duty rubber work gloves that may be disinfected
- c. N95 respirator masks are preferred . Standard well-fitted surgical masks should be used if N95 respirators are not available;
- d. goggles;
- e. rubber or polyurethane boots that can be disinfected or protective foot covers that can be discarded.

NOTE: If PPE is not available locally, there should be plans to contact suppliers or can contact WHO that has a stockpile and PAHO that has a stockpile.

**Question. What steps might be taken by the Member State to enhance animal surveillance and prevent disease transmission along the border with a MS reporting an animal influenza event?**

**Answer:** It is most likely that the main route of entry is through wild birds' migrations and illegal birds' imports. It is important to have an adequate risk evaluation in proximity to the borders and having enhanced animal surveillance focus on live poultry markets, hot spots for the interaction poultry-wildlife such as high-density areas with, with low biosecurity farms and wetlands and at major points of entry.

When we plan to do risk-based surveillance (BMC Health Services Research <http://doi.org/10.1186/1472-6963-6-20>), we need:

- To have a comprehensive knowledge regarding the hazard and risk to study
- To have access to risk information (and the factors that influence it), reliable, exhaustive, complete and updated, good information systems and databases.
- To have a good understanding of the poultry population and how it interacts
- To count on technical capacity for study design and the analyses of the results, maybe in collaboration with an international organization/university.
- To have a well-structured approach of the surveillance strategy to be developed.
- To have a good structure and resources in the veterinary services to implement/execute the study.
- NOTE: Risk-based poultry surveillance is efficient and cost-effective; risk areas can be determined based upon proximity to migratory birds, proximity to wild birds, high poultry density areas, markets/auctions/exhibitions; surveillance can be active or done only if symptomatic (OFFLU, 2013).

Additional steps to strengthening the prevention should include the following:



- a) Review the import risk assessment for legal poultry and poultry products importation.
- b) Strengthen the health border control for poultry and poultry products inspections with the support of the port officers.
- c) If there are no ongoing poultry die-offs consider: active surveillance of avian influenza A viruses in well-appearing birds at regional distribution points; and retrospective surveillance at districts bordering the area of previously collected biological samples
- d) Review current veterinary laboratory capabilities and resources
- e) Ensure that the multi-sectoral RRT is ready
- f) Review reporting mechanisms for human and animal infections
- g) Review procedures for inter-sectoral sharing of information
- h) Consult WOA and neighboring veterinary authorities to understand the avian influenza A virus situation in surrounding countries

## Laboratory considerations for diagnosis and surveillance in humans

### Question: Which samples should be collected from humans to be tested?

**Answer:** Timely collection and testing of appropriate specimens from case patients and symptomatic contacts is the highest priority.

The preferred sample is nasopharyngeal swabs into one viral transport media vial, as well as combined nasal or nasopharyngeal swab with an oropharyngeal swab. Nasal aspirate or wash can also be considered.

A sterile Dacron/nylon swab should be used for sample collection. Cotton tipped and wooded swabs are not recommended as they interfere in the sample processing and inhibit molecular diagnostic reactions. Swabs should be placed in a viral transport media tube containing 3 mL of sterile viral transport medium and transported in the same tube with viral transport medium (VTM).

Further information about specimen collection is available at: [Manual for the laboratory diagnosis and virological surveillance of influenza \(who.int\)](#)

### Question: How should samples be collected in humans?

**Answer:** Samples should be collected by trained personnel in adherence to all biosafety instructions, including appropriate personal protective equipment (PPE) for respiratory viruses.

The specimens should be appropriately labelled with a unique identifier; in this way it will be possible to link the case patient demographic and epidemiological data. Sample collection is recommended within 4 days of symptom onset for the highest influenza virus yield and better detection. A sampling of asymptomatic contacts is not recommended unless considered necessary according to national guidelines.



Samples should be kept refrigerated (4-8°C) and sent to the National Influenza Centers (NICs) or National Reference Laboratories (NRL), where they should be processed within the first 24-72 hours after collection. If samples cannot be sent within this period, freezing at -70 °C (or less) is recommended until samples are shipped. It is important to ensure that all samples are transported to the laboratory maintaining the cold chain.

Further information about specimen collection is available at: [Manual for the laboratory diagnosis and virological surveillance of influenza \(who.int\)](#)

[Technical note: Laboratory Diagnosis of Human Infection with Influenza A/H5 - PAHO/WHO | Pan American Health Organization](#)

Video: [Correct sampling procedure of nasopharyngeal and oropharyngeal swabs - YouTube](#)

**Question: What is the recommended sampling and testing strategy for a human with high risk exposure to avian influenza?**

**Answer:** For avian influenza high risk exposure groups, the recommendation is close monitoring for symptoms onset. And if symptomatic, respiratory specimen should be collected and immediately sent to the NIC or NRL for testing. In case of negative result, a new sample should be collected for retesting, following the recommended testing algorithms.

Please see below for additional recommendations about shipping samples to WHO-CC and algorithm testing.

For additional support, please contact [flu@paho.org](mailto:flu@paho.org).

**Question: What are the recommended laboratory protocols for influenza detection in humans?**

**Answer:** For influenza detection and Influenza A(H5) subtyping, molecular diagnostic protocols and reagents developed and validated by the WHO Collaborating Center at the US CDC should be used. Molecular detection kits and controls are available at the [International Reagent Resource \(IRR\)](#) as follows:

- Influenza SARS-CoV-2 Multiplex Assay (RUO) (500 reactions) (Catalog No. FluSC2PPB-RUO), dried primers and probes
- Influenza SARS-CoV-2 Multiplex Assay Positive Controls Kit (RUO) (500 reactions) (Catalog No. FluSC2PC-RUO)
- CDC Real-Time RT-PCR Influenza Virus A(H5) (Asian Lineage) Subtyping Panel (VER 4) (RUO) (Catalog No. FluRUO-13)
- CDC Influenza A(H5N1) (Asian Lineage) Real-Time RT-PCR Positive Control with Human Cell Material (RUO) (Catalog No. VA2715)



For additional support, please contact [flu@paho.org](mailto:flu@paho.org).

**Question: What are the recommended sample flow and laboratory testing algorithms for suspected avian influenza cases in humans?**

**Answer:** Since samples collected from suspected cases of human infection caused by avian influenza A(H5) needs to be reliably tested and confirmed, all specimens from suspected cases should be referred to the NIC or NRL for testing and assurance of the sample quality for additional required genomic and antigenic characterizations.

Influenza testing for samples collected from suspected cases of human infection caused by avian influenza A(H5) should be done using the WHO-CC protocol (multiplex for influenza A/B and SARS-CoV-2). Influenza A-positive samples should be subsequently subtyped for influenza A(H5).

Positive samples for influenza A(H5) should be sent to WHO-CC for additional genomic and antigenic characterizations.

For countries without capacity to diagnose influenza A(H5) at the NRL, please contact PAHO at [flu@paho.org](mailto:flu@paho.org) for shipping to the WHO-CC.

The influenza A(H5) laboratory testing algorithm is available at: [Samples from patients suspected of Influenza A/H5 LABORATORY TESTING ALGORITHM - PAHO/WHO | Pan American Health Organization](#)

**Question: How should results be interpreted for avian influenza A(H5) detection in humans?**

**Answer:** The markers (targets) of the US CDC kits for influenza A(H5) subtype detection are as follows: INFA (M), H5a (HA), H5b (HA), and RP. When using the US CDC influenza A(H5) subtyping kit:

Target*				Interpretation	Report
INFA (M)	H5a (HA)	H5b (HA)	RP		
+	+	+	+ or -	influenza A(H5) RNA detected	Positive for influenza influenza A(H5)
+	-	-	+ or -	influenza A(H5) RNA detected	Presumptive for influenza influenza A(H5)





# PAHO

-	+	-	+ or -	influenza A(H5) RNA detected	Presumptive for influenza influenza A(H5)
-	-	+	+ or -	influenza A(H5) RNA detected	Presumptive for influenza influenza A(H5)
-	-	-	+	Not detected	Negative
-	-	-	-	Invalid result	Invalid

\*Curves of the real-time RT-PCR assay must present the standard typology with a logarithmic phase and a plateau crossing the threshold line within 38 cycles (Ct<38).

In all cases, samples should be referred to a WHO Collaborating Center for further characterization or for confirmation (in the case of presumptive results). Nevertheless, a positive sample for Influenza A(H5) (both markers positive) should be reported immediately.

Currently, PAHO is working to support Member States in preparedness and response to Influenza A(H5). For additional support, please contact [flu@paho.org](mailto:flu@paho.org).

**Question: If the result is influenza A positive but is not influenza A(H5). How should be the testing algorithms?**

**Answer:** If the sample was tested following the avian influenza A(H5) protocol and the result for subtyping is negative, the laboratory should test the sample with the influenza A subtyping panels, that can indicate unusual influenza A viruses, including potential novel influenza viruses or potential variant influenza viruses.

Even if the sample is not a suspected case from influenza A(H5) and the laboratory is using the seasonal protocol, all markers on each panel from seasonal subtyping should be used while performing molecular diagnostic assays.

Further information available at: [Influenza at the Human-Animal Interface: PAHO Recommendations to Strengthen Intersectoral Work for Surveillance, Early Detection, and Investigation, 9 July 2020](#)

The seasonal influenza laboratory testing algorithm is available at: [Influenza and SARS-CoV-2 integrated surveillance laboratory testing algorithm - PAHO/WHO | Pan American Health Organization](#)

**Question: How should an unusual result in influenza A subtyping be interpretate?**

**Answer:** Using the WHO-CC protocol for influenza detection in human specimens, the detection of the InfA marker with no amplification of any of the subtypes markers or amplification of only one of the influenza A(H1N1)pdmog subtype marker is indicative of a potential novel influenza A virus. The unexpected detection



of the pdmInfA marker together with the detection of the H3 marker is indicative of a potential Influenza A(H3N2)v virus.

Target*					Interpretation	Report
InfaA	H3	pdm InfA	pdm H1	RP		
+	+	-	-	+ or -	influenza A/H3 RNA detected	Positive for influenza A/H3
+	-	+	+	+ or -	influenza A/H1pdm09 RNA detected	Positive for influenza A/H1pdm09
+	-	-	-	+ or -	influenza A RNA detected	Positive for influenza A unsubtypeable <b>Potential novel influenza</b>
+	+	+	-	+ or -	influenza A RNA detected	Positive for influenza A <b>Presumptive positive for influenza A(H3N2) variant virus</b>
-	-	-	-	+	Not detected	Negative
-	-	-	-	-	Invalid result	Invalid

\*Curves of the real-time RT-PCR assay must present the standard typology with a logarithmic phase and a plateau crossing the threshold line within 38 cycles (Ct<38).

**Question:** Could animal specimens be tested and processed in the same laboratory where human specimens are processed?

**Answer:** Due to the segmented genome and the capacity of genomic reassortment. Animal specimens should not be processed in human laboratories to avoid cross contamination with viruses of human origin, such material should preferably be handled in facilities away from those where human specimens and viruses are investigated.

Further information for the NIC requirements is available at: [nic\\_tor\\_en.pdf \(who.int\)](https://www.who.int/nic/en/pdf)



**Question: Which laboratories should test specimens of human suspected avian influenza cases?**

**Answer:** All samples from a suspect case of influenza A(H5) should be tested at the NIC authorized NRL with influenza A(H5) diagnostic capacity.

For additional information, verify the laboratory testing algorithm available at: [Samples from patients suspected of Influenza A/H5 LABORATORY TESTING ALGORITHM - PAHO/WHO | Pan American Health Organization](#)

**Question: How to ship influenza A(H5)-positive human sample to the WHO-CC at US-CDC?**

**Answer:** The US CDC is the designated WHO Collaborating Center in the Americas Region for receiving human samples positive for avian Influenza A(H5).

Shipping to the WHO-CC at US-CDC, internationally and by air, must be following all international standards according to the International Air Transport Association (IATA), being necessary special documents for transportation to the United States other than documents for routine shipment of seasonal influenza sample.

It is important to note that the samples should **not** be sent as routine influenza samples to US CDC.

For logistic and shipping information for human or avian influenza A(H5) samples, PAHO should be contacted at [flu@paho.org](mailto:flu@paho.org).

**Question: How to ship influenza A(H5)-positive animal sample to the WHO CC at St. Jude Children's Hospital?**

**Answer:** Since information on the circulation of avian influenza A(H5N1) viruses is important for the human zoonotic influenza vaccine composition and for generating data for preparedness and response, countries are encouraged to share animal influenza samples with the WHO Collaborating Center, St. Jude Children's Hospital, which focuses exclusively on the threat to humans from zoonotic influenza viruses. The isolate and the phenotypic characterizations are going to be with sorus from the human vaccine. Information from the human part is generated. In addition, the virus may be a potential candidate for a human vaccine.

Animal samples should be sent to the WHO Collaborating Center at St. Jude Children's Hospital. Special documents are necessary for transportation to the United States and must be compliant with all international standards.

For further information regarding logistical and shipment of human or avian Influenza A(H5) samples, PAHO/WHO should be contacted at [flu@paho.org](mailto:flu@paho.org).

Further information is available at: [Operational Guidance on Sharing Influenza Viruses \(who.int\)](#)



## Question: Should the NIC report the situation to the WHO Global Influenza Surveillance and Response System (GISRS)?

**Answer:** All non-seasonal influenza virus detections, including influenza A(H5) laboratory-confirmed cases are requested to be reported to WHO under the International Health Regulations (2005). The National Influenza Center should immediately notify positive results following the in-country IHR official channel.

Further information is available at: [Case definitions for the four diseases requiring notification to WHO in all circumstances under the IHR \(2005\)](#)

## Laboratory considerations for diagnosis and surveillance in animals

### Question: What laboratory findings in animal specimens should be reported to WOAHA by Member States and when it should be reported?

Veterinary laboratories in countries generally have the ability to detect and to some extent type the virus in both serological and molecular samples. In case there is not adequate diagnostic laboratory capacity in the country, the OVS should seek external support by sending samples to the WOAHA/FAO reference laboratories

### Question: What should be reported to WOAHA by MS and when it should be reported?

Avian influenza is a notifiable disease listed by the WOAHA. As detailed by the WOAHA [Terrestrial Animal Health Code](#), Member Countries must report within 24 hours after confirmation of the exceptional epidemiological event (i.e. after the laboratory confirmation) of all highly pathogenic avian influenza viruses, irrespective of their strain, detected in birds.

Other influenza A viruses of avian host origin (i.e. low pathogenicity avian influenza viruses) may have the potential to exert a negative impact on animal and public health. A sudden and unexpected increase in virulence of low pathogenicity avian influenza viruses in [poultry](#) is notifiable as an [emerging disease](#) in accordance with Article [1.1.4.Infection](#) of domestic and [captive wild](#) birds with low pathogenicity avian influenza viruses having proven natural transmission to humans associated with severe consequences,

## Genomic sequencing considerations

### Question: Which genetic group of influenza A(H5) is being recently detected in the Americas region?

**Answer:** Genetic sequence data has shown that all influenza A(H5) viruses circulating in the Americas are influenza A (H5N1). Cases related to the recent outbreaks in the America region belong to the A(H5) genetic group 2.3.4.4b which is the same genetic group of the component for the human zoonotic influenza vaccine.

Further information is available at: [Assessment of risk associated with recent influenza A\(H5N1\) clade 2.3.4.4b viruses \(who.int\)](#)



**Question: Is there a candidate virus available for the human zoonotic influenza A(H5) vaccine?**

**Answer:** Yes. Candidate influenza A(H5) vaccine viruses of genetic group 2.3.4.4b are determined. These include A(H5N1) virus closely related to recently detected circulating influenza A(H5) strains. During the vaccine composition meeting that occurred in February 2023, the antigenic prototype A/American wigeon/South Carolina/22-000345-001/2021-like (clade 2.3.4.4b) was defined as a candidate virus in preparation by CDC.

Further information is available at: [20230224\\_zoonotic\\_recommendations.pdf \(who.int\)](#)

**Question: Do the influenza A(H5) viruses detected in the Americas present resistance to antivirals?**

**Answer:** No. Available sequences of influenza A(H5) from human cases showed no markers of resistance to antivirals, including oseltamivir and baloxavir.

For influenza A(H5) viruses from avian and mammalian origin, genomic sequencing data available indicate that markers associated with reduced susceptibility to antivirals are rare.

Further information is available at: [Assessment of risk associated with recent influenza A\(H5N1\) clade 2.3.4.4b viruses \(who.int\)](#)

**Question: What are the recommendations for sequencing influenza A(H5) viruses? isolated from human samples?**

**Answer:** Shipping of a positive sample for influenza A(H5), animal or human, to the appropriate WHO CC should be prioritized for antigenic and genomic characterization of the sample.

For laboratories that have sequencing capacity, in addition to sending the positive sample to the Collaborating Center, it is encouraged to sequence the sample to generate genomic sequencing data and to upload the sequences in a timely manner to the GISAID global platform.

For further information on human or avian influenza A(H5) sequencing samples, PAHO should be contacted at [flu@paho.org](mailto:flu@paho.org).

**Question: What are the recommendations for the influenza sequences nomenclature?**

**Answer:** For laboratories that have sequencing capacity, in addition to sending the positive sample to the Collaborating Center, it is encouraged to sequence the sample to generate genomic sequencing data and to upload the sequences promptly to the GISAID global platform.

When humans are infected with swine influenza virus, these viruses are called “variant viruses”, and are designated with the letter “v” used after the name of these zoonotic swine viruses, to distinguish these from human viruses of the same subtype (e.g., an A(H3N2)v virus).



The publication of sequences in GISAID, or any other database, requires the use of the proper nomenclature recommended by the WHO:

- The format for humans is:

[Influenza Type]/[Region]/[Internal Reference Number]/[Year of Collection]

Ex: A/Wisconsin/2145/2001

- For all other animal hosts:

[Influenza Type]/[Host]/[Region]/[Internal Reference Number]/[Year of Collection]

Ex: A/chicken/Rostov/864/2007

Further information is available at: [Technical note: Influenza virus nomenclature - PAHO/WHO | Pan American Health Organization](#)

## Considerations on vaccination

**Question: What are the recommendations on the use of human H5N1 influenza vaccines to prevent zoonotic influenza in the interpandemic period?**

**Answer:** In countries affected by HPAI H5N1 influenza, the risk of infection in the general population remains very low. At this stage, vaccination with human H5N1 influenza vaccines is not recommended to immunize the general population against infection with HPAI H5N1 virus. Vaccination with licensed human H5N1 influenza vaccines is only recommended for laboratory staff working with HPAI H5N1 viruses and for workers involved in the front-line response to possible H5N1 outbreaks in animals or humans.

Further information is available at:

SAGE's recommendations on the use of licensed human H5N1 influenza vaccines in the interpandemic period (2009): <https://www.who.int/publications/i/item/WER8424>

SAGE's recommendations on Influenza A (H5N1) Vaccine Stockpile and Inter-Pandemic Vaccine Use (2013): [https://terrance.who.int/mediacentre/data/sage/SAGE\\_Docs\\_Ppt\\_Nov2013/6\\_session\\_influenza/Nov2013\\_session6\\_h5n1\\_vaccine\\_stockpile.pdf](https://terrance.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_Nov2013/6_session_influenza/Nov2013_session6_h5n1_vaccine_stockpile.pdf)

**Question: Can the seasonal influenza vaccine be used to prevent infection from influenza A(H5) virus?**

**Answer:** While seasonal influenza vaccines are not designed to provide protection against avian influenza viruses, they can help to reduce the overall burden of influenza illness and reduce the risk of co-infection with avian influenza viruses in humans.



The use of seasonal influenza vaccine is encouraged in all countries and especially during animal influenza outbreaks for occupational groups at risk of infection from HPAI H5N1 in order to reduce the risk of co-infection and potential reassortant of viruses fostering human-to-human transmissibility of a novel virus.

Groups at high risk of infection with influenza A(H5) include individuals who are in close contact with animals, including poultry, in areas where avian influenza is known to be circulating. This recommendation applies to workers in the poultry industry, as well as individuals who may have contact with wild birds, such as birdwatchers and hunters. Vaccination with seasonal influenza vaccines should be used in combination with other control measures, such as infection prevention and control practices and the use of personal protective equipment, to reduce the risk of avian influenza infection in these populations.

Further information is available at:

Global Influenza Strategy 2019-2030. <https://www.who.int/publications/i/item/9789241515320>

SAGE's recommendations on the use of licensed human H5N1 influenza vaccines in the interpandemic period (2009): <https://www.who.int/publications/i/item/WER8424>

**Question: What are the recommendations on the use of veterinary influenza A(H5) vaccines to prevent against avian influenza in animals?**

**Answer:** Vaccines against H5 influenza viruses can be used in animals to reduce mortality, morbidity and transmission. H5 vaccines can be used in poultry as a preventive measure against avian influenza outbreaks, and in some cases, as a control measure during an outbreak.

Vaccination in animals should be used in combination with other control measures, such as culling, movement restrictions, and biosecurity measures, and that the choice of vaccine and vaccination strategy should be based on the characteristics of the virus, the epidemiological situation, and the local context.

There should be an adequate vaccine matching the field virus and there should be a system in place to monitor deviance of the matching over time.

There must be a risk analysis that justifies the use of the vaccine, as well as defining the strategy to be implemented (e.g. emergency versus preventive vaccination), likewise there must be a strategy and exit criteria.

An adequate selection of the subpopulation to be vaccinated must be made (e.g. long-cycle poultry, breeders) and the necessary requirements for its inclusion must be defined so that it can be monitored and controlled, and implement an active surveillance strategy to detect viral transmission in the vaccinated population.



## Considerations on Risk communication and community engagement

**Question:** What are the main recommendations regarding risk communication messages for preparedness to animal influenza outbreaks?

**Answer:** Risk communication is a fundamental component of preparedness and response to health emergencies, especially those emergencies with pandemic or epidemic potential. Early and transparent communication with populations, as well as issuing clear messages about behaviors and preventive measures to be adopted by communities, are vital to reduce transmission. Additionally, adequate risk communication will contribute to reducing rumors, myths and misinformation related to the outbreak and will allow populations to make comprehensive decisions to reduce the risk of spread. It is worth noting that risk communication in health emergencies is integrated by various aspects and includes, but is not limited to, institutional communication or communication with the media.

**Question:** What are the main recommendations regarding risk communication messages for preparedness and response to animal influenza outbreaks?

**Answer:** The following actions among their preparedness measures for risk communication in the event of an outbreak of avian influenza:

- Delegate a person or team responsible for risk communication to review existing risk communication plans or strategies in pandemic or epidemic contexts and make necessary adjustments or updates to strengthen preparedness and respond to an eventual outbreak. Recent WHO guidance on a risk communication plan for respiratory diseases can be consulted at the following link: <https://bit.ly/3GTSKAr>
- Collect existing information and/or conduct qualitative and/or rapid quantitative assessments to know the characteristics of the communities at highest risk, patterns and communication channels, language, religion, influencers. This information is vital to be able to formulate appropriate preparedness and response actions for risk communication.
- Build trust through early, transparent, timely communication, and dissemination across multiple platforms, methods and channels. To maintain the trust of the population, it is also key to communicate even in the midst of uncertainty, clarifying what is known and what is not.
- Identify communities with whom to work on risk communication actions and allow them to participate in their implementation, to ensure that interventions are collaborative, and that the community takes ownership of communication processes. Community involvement will contribute to the adoption of preventive behaviors.
- Issue messages to the public about symptom identification and prevention, particularly to populations with greater potential for exposure to the virus: rural settings, farmers, farm workers.





# PAHO

The messages must be broadcast on the channels and through the platforms consulted by each type of audience.

- Activate the social listening of rumors and disinformation through digital platforms and other relevant information exchange channels (telephone hotlines, web portals, etc.), to respond to possible false messages circulating among the public and adapt the messages according to the needs detected by this monitoring.

---

PAHO recognizes that all questions will not be answered in this document. Please feel free to reach out for further information to [flu@paho.org](mailto:flu@paho.org).

## References

1. Influenza (Avian and other zoonotic). Available at: [Influenza \(Avian and other zoonotic\) \(who.int\)](#)
2. Assessment of risk associated with recent influenza A(H5N1) clade 2.3.4.4b viruses. Available at: [Assessment of risk associated with recent influenza A\(H5N1\) clade 2.3.4.4b viruses \(who.int\)](#)
3. Influenza at the Human-Animal Interface: PAHO Recommendations to Strengthen Intersectoral Work for Surveillance, Early Detection, and Investigation, 9 July 2020. Available at: [Influenza at the Human-Animal Interface: PAHO Recommendations to Strengthen Intersectoral Work for Surveillance, Early Detection, and Investigation, 9 July 2020](#)
4. International Health Regulations (2005) – Third edition. Available at [International Health Regulations \(2005\) – Third edition \(who.int\)](#)
5. Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005) . Available at: [Case Definitions for the four disease entities \(who.int\)](#)
6. WHO guidance for the use of Annex 2 of the International Health Regulations (2005). Available at: [WHO guidance for the use of Annex 2 of the International Health Regulations \(2005\)](#)
7. Mosaic Respiratory Surveillance Framework. Available at: [WHO Mosaic Respiratory Surveillance Framework](#)
8. Global Influenza Surveillance and Response System (GISRS). Available at: [Global Influenza Surveillance and Response System \(GISRS\) \(who.int\)](#)
9. A guide to establishing event-based surveillance. Available at: [A guide to establishing event-based surveillance \(who.int\)](#)
10. Zoonotic Influenza A Virus outbreak toolbox. Available at: [Zoonotic Influenza A Virus Outbreak Toolbox \(who.int\)](#)
11. Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases. Available at: [Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases \(who.int\)](#)
12. Zoonotic Influenza A Virus outbreak toolbox Case investigation forms. Available at: [generic-respiratory.pdf \(who.int\)](#)
13. WHO rapid advice guidelines on pharmacological management of humans infected with avian influenza A (H5N1) virus. Available at: [WHO rapid advice guidelines on pharmacological management of humans infected with avian influenza A \(H5N1\) virus](#)
14. Guidelines for the clinical management of severe illness from influenza virus infections. Available at: [Guidelines for the clinical management of severe illness from influenza virus infections \(who.int\)](#)
15. Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care. Available at: [Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care \(who.int\)](#)
16. WOAHA Terrestrial Code. Available at: [Terrestrial Code Online Access - WOAHA - World Organisation for Animal Health](#)

17. WAHIS: World Animal Health Information System. Available at: [WAHIS \(woah.org\)](http://WAHIS(woah.org))
18. FAO rapid qualitative risk assessment. Risk of H5 high pathogenicity avian influenza introduction in Central and South America and the Caribbean: <https://www.fao.org/3/cc4720en/cc4720en.pdf>
19. Wild bird highly pathogenic avian influenza surveillance. Sample collection from healthy, sick and dead birds: <https://www.fao.org/documents/card/en/c/de4959ee-b8c2-58c7-b180-907d9d87761d/>
20. Terrestrial Animal Health Code. Chapter 1.4. Animal Health Surveillance. Article 1.4.1: [https://www.woah.org/fileadmin/Home/eng/Health\\_standards/tahc/2018/en\\_chapitre\\_surveillance\\_general.htm](https://www.woah.org/fileadmin/Home/eng/Health_standards/tahc/2018/en_chapitre_surveillance_general.htm)
21. Manual for the laboratory diagnosis and virological surveillance of influenza. Available at [Manual for the laboratory diagnosis and virological surveillance of influenza \(who.int\)](http://Manual%20for%20the%20laboratory%20diagnosis%20and%20virological%20surveillance%20of%20influenza(who.int))
22. Technical note: Laboratory Diagnosis of Human Infection with Influenza A/H5. Available at [Technical note: Laboratory Diagnosis of Human Infection with Influenza A/H5 - PAHO/WHO | Pan American Health Organization](http://Technical%20note:%20Laboratory%20Diagnosis%20of%20Human%20Infection%20with%20Influenza%20A/H5-%20PAHO/WHO|Pan%20American%20Health%20Organization)
23. International Reagent Resource (IRR). Available at [International Reagent Resource \(IRR\)](http://International%20Reagent%20Resource(IRR))
24. Samples from patients suspected of Influenza A/H5 laboratory testing algorithm. Available at [Samples from patients suspected of Influenza A/H5 LABORATORY TESTING ALGORITHM - PAHO/WHO | Pan American Health Organization](http://Samples%20from%20patients%20suspected%20of%20Influenza%20A/H5%20LABORATORY%20TESTING%20ALGORITHM-%20PAHO/WHO|Pan%20American%20Health%20Organization)
25. Terms of Reference for National Influenza Centers of the Global Influenza Surveillance and Response System. Available at [nic\\_tor\\_en.pdf \(who.int\)](http://nic_tor_en.pdf(who.int))
26. Operational Guidance on Sharing Influenza Viruses with Human Pandemic Potential (IVPP) under the Pandemic Influenza Preparedness (PIP) Framework. Available at [Operational Guidance on Sharing Influenza Viruses \(who.int\)](http://Operational%20Guidance%20on%20Sharing%20Influenza%20Viruses(who.int))
27. Genetic and antigenic characteristics of zoonotic influenza A viruses and development of candidate vaccine viruses for pandemic preparedness. Available at: [20230224\\_zoonotic\\_recommendations.pdf \(who.int\)](http://20230224_zoonotic_recommendations.pdf(who.int))
28. Technical note: Influenza virus nomenclature. Available at: [Technical note: Influenza virus nomenclature - PAHO/WHO | Pan American Health Organization](http://Technical%20note:%20Influenza%20virus%20nomenclature-%20PAHO/WHO|Pan%20American%20Health%20Organization)
29. SAGE Working Group on Influenza Vaccines and Immunizations Influenza A (H5N1) Vaccine Stockpile and Inter-Pandemic Vaccine Use. Available at: [Nov2013\\_session6\\_h5n1\\_vaccine\\_stockpile.pdf \(who.int\)](http://Nov2013_session6_h5n1_vaccine_stockpile.pdf(who.int))
30. Summary of key information practical to countries experiencing outbreaks of a(H5N1) and other subtypes of avian influenza. Available at [WHO-OHE-PED-GIP-EPI-2016.1-eng.pdf](http://WHO-OHE-PED-GIP-EPI-2016.1-eng.pdf)
31. Risk Communication and Community Engagement (RCCE) Action Plan Guidance COVID-19 Preparedness and Response. Available at <https://bit.ly/3GTSKAr>