

5 June 2024

The Pan American Health Organization / World Health Organization (PAHO/WHO) calls on Member States to work in a collaborative and intersectoral manner to preserve animal health and protect public health. PAHO/WHO urges Member States to implement protocols for the timely detection, notification and rapid response to outbreaks in animals and/or human infections. PAHO/WHO encourages Member States to review and test their pandemic influenza preparedness and readiness plans. In addition, virus sharing with Collaborating Centers in both sectors is encouraged to strengthen risk analysis and to have candidate vaccine viruses.

### Global Context

The detection of avian influenza virus infection, which is usually transmitted among birds, has increased increasingly in mammals. This increase in mammalian cases is attributed to changes in the ecology and epidemiology of the virus (1). Indeed, influenza A(H5N1) viruses, especially clade 2.3.4.4b, continue to diversify genetically and spread geographically. Since 2020, the clade 2.3.4.4b variant has caused an unprecedented number of deaths in wild birds and poultry in numerous countries in Africa, Asia, and Europe (1). In 2021, the virus spread to North America and, in 2022, to Central and South America (1). That same year, outbreaks of highly pathogenic avian influenza (HPAI)<sup>1</sup> H5N1 in poultry and wild birds were reported to the World Organization for Animal Health (WOAH) from 67 countries on all continents. By 2023, epidemic outbreaks in animals were reported by 14 countries and territories, mainly in the Americas (1, 2).

Whenever birds infected with avian influenza virus are detected, there is a risk of sporadic infections in mammals and humans due to exposure to infected animals or contaminated environments (2). Since 2022, ten countries on three continents have reported outbreaks in mammals to WOAH, with both marine and terrestrial mammals affected, including cattle, dogs, cats, farmed mink, seals, and sea lions (3). Regarding clade 2.3.4.4b, in October 2022, an outbreak of HPAI H5N1 of clade 2.3.4.4b was reported in farmed mink in Spain, with evidence of mink-to-mink transmission, but the mode of transmission was not identified (4). In July 2023, an outbreak by the same clade affected a mink breeding farm for commercial fur production in Finland. Infection was confirmed in foxes, American mink, and raccoon dogs

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<sup>1</sup> Broadly speaking, the multiple strains of avian influenza virus can be classified into two categories according to the severity of disease presentation in poultry: low pathogenic avian influenza viruses (LPAI) and highly pathogenic avian influenza viruses (HPAI) (3).

from 20 farms. Genetic analysis suggested the introduction from wild birds foraging in agricultural areas. Investigations pointed to direct animal-to-animal transmission (5).

Since 2003 and up to 3 May 2024, there had been 889 human cases and 463 deaths (52% case fatality) caused by influenza A(H5N1) virus reported to WHO, affecting 23 countries globally (1, 2, 6).

## Summary of the situation in the Region of the Americas

The HPAI A(H5N1) virus currently circulating in the Americas belongs to the HPAI genotype, product of a recombination that occurred in wild birds in Europe and strains of low pathogenicity in wild and domestic birds during its global dissemination (7). This new genotype has spread rapidly from Europe to North America, Africa, and West Asia through waterfowl migratory routes. Following the detection of the influenza A(H5N1) virus in the Americas in 2021, it has been detected throughout the continent (7, 8, 9).

Since 2022 as of epidemiological week (EW) 20 of 2024, a total of 19 countries and territories in the Region of the Americas reported 5,261 outbreaks of avian influenza in domestic and wild birds to WOA: Argentina, the Plurinational State of Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Ecuador, the Falkland Islands, Guatemala, Honduras, Mexico, Panama, Paraguay, Peru, the United States of America, Uruguay, and the Bolivarian Republic of Venezuela (**Table 1**) (3). During this period, 457 outbreaks of HPAI A(H5N1) have been reported in mammals in Argentina, Brazil, Canada, Chile, Mexico, Peru, the United States, and Uruguay (**Table 2**) (3). Between EW 1 and EW 20 of 2024, six countries in the Region of the Americas have identified 210 avian influenza outbreaks in birds and 78 outbreaks in mammals (**Table 3**) (**Figure 1, Figure 2, Figure 3, Figure 4, and Figure 5**) (3).

Six human infections caused by avian influenza A(H5N1) have been reported since 2022 in the Americas. Four were reported in the United States of America, on 29 April 2022 (10), 1 April 2024 (2), 22 May 2024, and 30 May 2024 (11); one in Ecuador, reported on 9 January 2023 (12); and one in Chile, reported on 29 March 2023 (13).

The following is a summary of the situation in countries and territories in the Region of the Americas that reported outbreaks of avian influenza A(H5N1) in birds and mammals during 2024.

In **Brazil**, between EW 1 and EW 20 of 2024, 14 outbreaks of avian influenza A(H5) have been confirmed in wild birds in the states of Espírito Santo, Rio de Janeiro, Rio Grande do Sul, and São Paulo. To date, no outbreaks in production birds or human cases of avian influenza (H5N1) infection have been detected (3).

In **Canada**, between EW 1 and EW 20 of 2024, multiple outbreaks of HPAI A(H5N1) in poultry and wild birds have been reported to WOA in nine provinces of Canada. The provinces of Alberta, Nova Scotia, Prince Edward Island and Quebec have reported ten outbreaks in wild mammals. No human cases of avian influenza (H5N1) infection have been reported in the outbreaks identified to date (3).

In **Ecuador**, between EW 1 and EW 20 of 2024, an outbreak of H5N1 avian influenza in backyard domestic poultry was reported to WOA. The outbreak was identified in the province of Pastaza (3).

In the **United States of America**, since the beginning of 2024, detections of HPAI A(H5) virus in wild birds, commercial poultry, and/or backyard poultry have been reported in 28 states<sup>2</sup> to WOAHA (3). On 25 March 2024, the first detection of HPAI H5N1 was reported in dairy cattle and in samples of unpasteurized milk obtained from dairy cattle (1, 2). Since then and as of 31 May, detections of A(H5N1) have been reported in dairy cattle and other animals, affecting 69 dairy herds and one site with Alpacas in nine states: Colorado, Idaho, Kansas, Michigan, New Mexico, North Carolina, Ohio, South Dakota, and Texas (11, 14, 15, 16). Deaths have also been observed among wild cats and birds within some affected farms (17).

Since 1 April 2024, there have been three confirmed human cases of influenza A(H5N1): one in Texas, and two unrelated cases in Michigan that are related to the dairy cattle event in the United States (16). These cases represent the first instance of probable transmission of HPAI A(H5N1) avian influenza virus from mammals to humans. The three cases are in workers who had direct contact with sick animals: the first two presented mild symptoms particularly with conjunctivitis, and the third presented with upper respiratory tract symptoms, including cough without fever (16).

Between March and May 2024, local, state, and national authorities in the United States of America have monitored persons exposed to infected livestock for a period of ten days post-exposure; at least 390 individuals were monitored, with 44 samples collected and three confirmed human cases of influenza A(H5N1) (11). Studies to date indicate that pasteurization is effective in inactivating the virus in milk (18). The U.S. authorities are working in a multisectoral manner through a One Health based approach to respond to this situation (16, 19).

In the **Falkland Islands**, between EW 1 and EW 20 of 2024, seven incidences of avian influenza were reported through the Falkland Islands Department of Agriculture website, all involving wild birds (20).

In **Mexico**, between EW 1 and EW 20 of 2024, three outbreaks of avian influenza in birds were reported to WOAHA. The outbreaks occurred in the states of Chihuahua, with an outbreak in wild birds; and in Jalisco and Michoacán, with an outbreak affecting domestic birds, respectively (3).

In **Peru**, between EW 1 and EW 20 of 2024, WOAHA was notified of an outbreak of HPAI A(H5) in backyard domestic poultry. The outbreak occurred in the department of La Libertad (3).

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<sup>2</sup> California, Colorado, Florida, Idaho, Indiana, Kansas, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nebraska, New York, New Mexico, North Carolina, Ohio, Oregon, Pennsylvania, South Carolina, South Dakota, Texas, Vermont, West Virginia, Washington, and Wisconsin.

**Table 1.** Number of outbreaks in birds and mammals in the Americas between 2022 and EW 20 of 2024.

<b>Country/Territory</b>	<b>Birds</b>	<b>Mammals</b>
<b>Argentina</b>	148	40
<b>Bolivia</b>	40	
<b>Brazil</b>	195	12
<b>Canada</b>	1,708	100
<b>Chile</b>	464	34
<b>Colombia</b>	73	
<b>Costa Rica</b>	10	
<b>Cuba</b>	11	
<b>Ecuador</b>	43	
<b>Falkland Islands</b>	7	
<b>Guatemala</b>	1	
<b>Honduras</b>	9	
<b>Mexico</b>	180	1
<b>Panama</b>	14	
<b>Paraguay</b>	7	
<b>Peru</b>	384	3
<b>United States of America</b>	1,946	253
<b>Uruguay</b>	19	14
<b>Venezuela</b>	2	
<b>Total</b>	<b>5,261</b>	<b>457</b>

**Source:** Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOA; 2024 [cited 23 May 2024]. Available from: <https://wahis.woah.org/#/event-management>; and Falkland Islands Department of Agriculture. Avian Influenza Information. 2024 [cited 29 May 2024]. Available from: <https://falklands.gov.fk/agriculture/avian-influenza>

**Table 2.** Record of outbreaks in mammals in the Americas from 2022 to EW 20 of 2024.

Mammals	Argentina	Brazil	Canada	Chile	Mexico	Peru	United States	Uruguay
<i>Arctocephalus australis</i> (two-hair fur seal)	Yes	Yes						Yes
<i>Canis latrans</i> (Coyote)							Yes	
<i>Canis lupus familiaris</i> (domestic dog)			Yes					
<i>Capra hircus</i> (domestic goat)							Yes	
<i>Didelphis virginiana</i> (Virginia opossum)							Yes	
<i>Felis silvestris catus</i> (domestic cat)			Yes				Yes	
Dairy cattle							Yes	
<i>Halichoerus grypus</i> (gray seal)							Yes	
<i>Lontra canadensis</i> (northern river otter)							Yes	
<i>Lontra felina</i> (sea otter)				Yes				
<i>Lontra provocax</i> (huillin)				Yes				
<i>Lynx rufus</i> (Red lynx or bobcat)							Yes	
American Tuesday (Marta)							Yes	
<i>Mephitis mephitis</i> (Skunk)			Yes				Yes	
<i>Mirounga leonina</i> (Southern Elephant Seal)	Yes							
<i>Nasua nasua</i> (Cochi or South American coati)								Yes
<i>Neogale vison</i> (American mink)			Yes				Yes	
<i>Otaria flavescens</i> (South American fur seal)	Yes	Yes		Yes		Yes		Yes
<i>Panthera leo</i> (Lion)						Yes		
<i>Panthera pardus orientalis</i> (Amur Leopard)							Yes	
<i>Panthera tigris</i> (Tiger)							Yes	
<i>Pekania pennanti</i> (Fisherman)							Yes	
<i>Phoca vitulina</i> / <i>Halichoerus grypus</i> (Seal)			Yes				Yes	
<i>Procyon lotor</i> (Raccoon)			Yes				Yes	
<i>Puma concolor</i> (Puma)							Yes	
<i>Sciurus aberti</i> (Squirrel)							Yes	
<i>Tursiops truncatus</i> (Bottlenose dolphin)							Yes	
<i>Ursus americanus</i> / <i>U. arctos horribilis</i> (Bear)			Yes				Yes	
<i>Ursus arctos</i> (Brown bear)							Yes	
<i>Ursus maritimus</i> (Polar bear)							Yes	
<i>Vulpes vulpes</i> (Fox)			Yes				Yes	

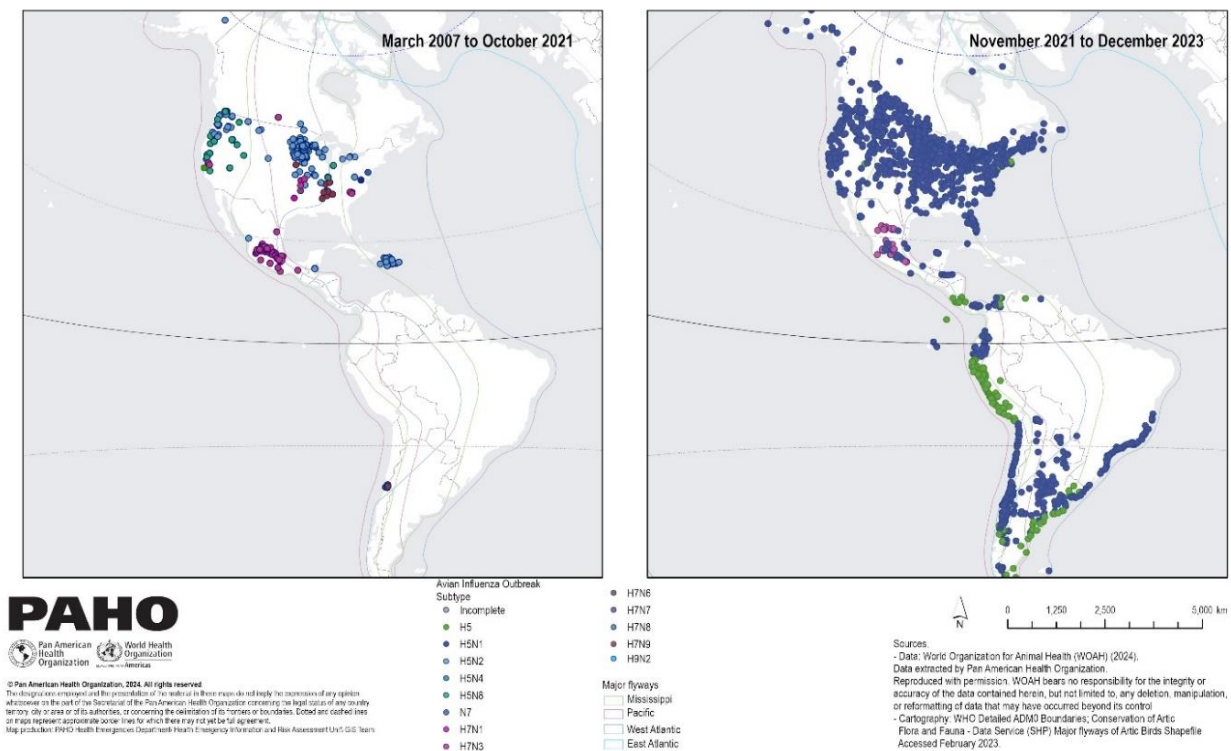
**Source:** Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOA; 2024 [cited 23 May 2024]. Available from: <https://wahis.woah.org/#/event-management>

**Table 3.** Avian influenza outbreaks in the Region of the Americas as of EW 20 of 2024.

Country	Outbreaks in birds	Outbreaks in mammals
Brazil	14	
Canada	99	11
Ecuador	1	
Falkland Islands	7	
Mexico	3	
Peru	1	
United States	92	67
<b>Total</b>	<b>217</b>	<b>78</b>

**Source:** Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOA; 2024 [cited 23 May 2024]. Available from: <https://wahis.woah.org/#/event-management> and Falkland Islands Department of Agriculture. Avian Influenza Information, 2024 [cited 29 May 2024]. Available from: <https://falklands.gov.fk/agriculture/avian-influenza>

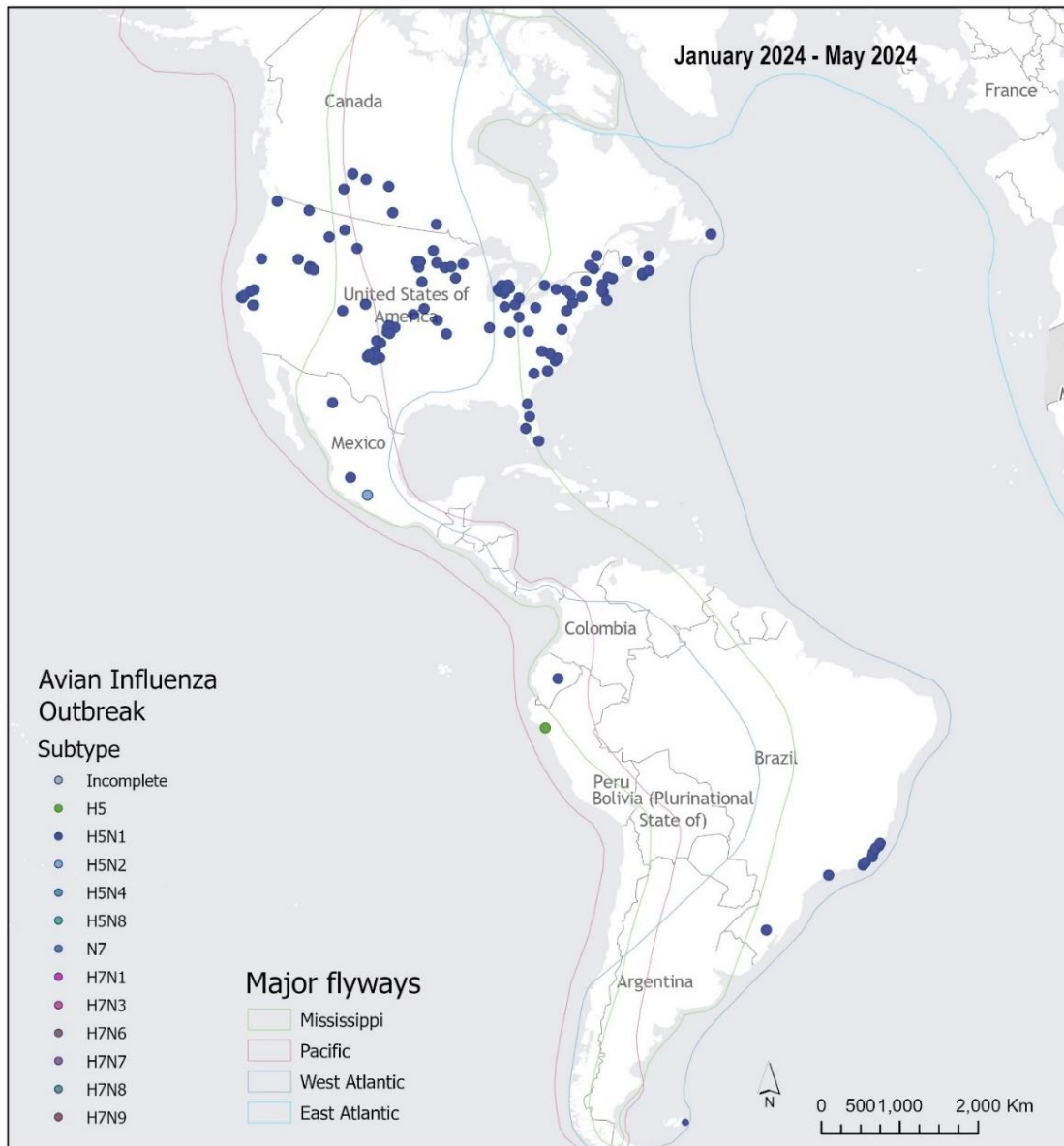
**Figure 1.** History of avian influenza outbreaks by subtype and main migratory routes of wild birds from March 2007 to October 2021 and November 2021 to December 2023 in the Region of the Americas.



**Source:** Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOA; 2024 [cited 23 May 2024]. Available from: <https://wahis.woah.org/#/event-management>



**Figure 2.** History of avian influenza outbreaks in 2024 up to EW 20 by subtype and major flyways in the Region of the Americas.

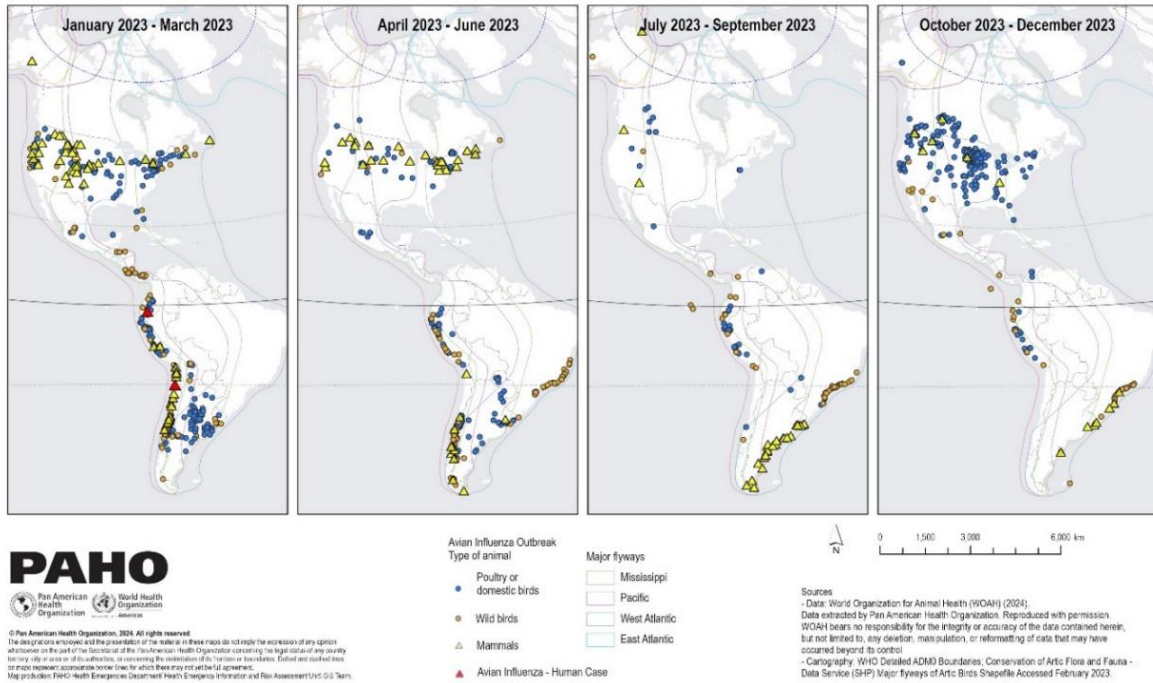


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 Map production: PAHO Health Emergencies Department/ Health Emergency Information and Risk Assessment Unit\ GIS Team.

Sources:  
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 - Falkland Islands Department of Agriculture  
 - Cartography: WHO Detailed ADMO Boundaries; Conservation of Arctic Flora and Fauna - Data Service (SHP) Major flyways of Arctic Birds Shapefile Accessed February 2023.

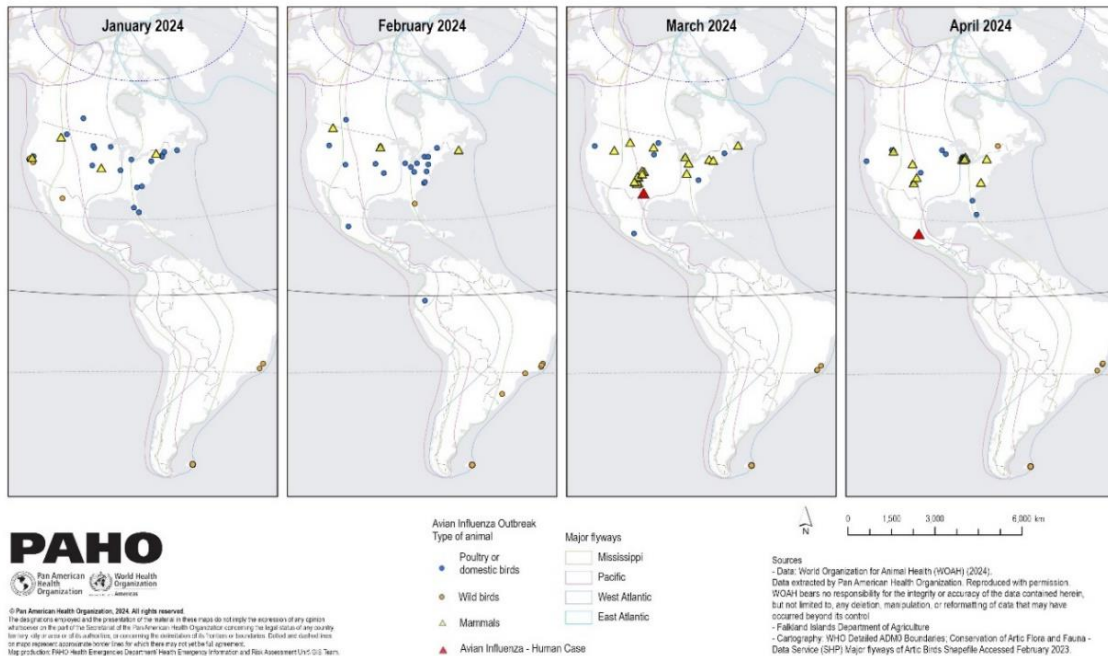
**Source:** Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOA; 2024 [cited 23 May 2024]. Available from: <https://wahis.woah.org/#/event-management>; and Falkland Islands Department of Agriculture. Avian Influenza Information. 2024 [cited 29 May 2024]. Available from: <https://falklands.gov.fk/agriculture/avian-influenza>

**Figure 3.** History of avian influenza outbreaks and major flyways by type of animal during 2023 in the Region of the Americas.



**Source:** Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOA; 2024 [cited 23 May 2024]. Available from: <https://wahis.woah.org/#/event-management>; and Falkland Islands Department of Agriculture. Avian Influenza Information. 2024 [cited 29 May 2024]. Available from: <https://falklands.gov.fk/agriculture/avian-influenza>

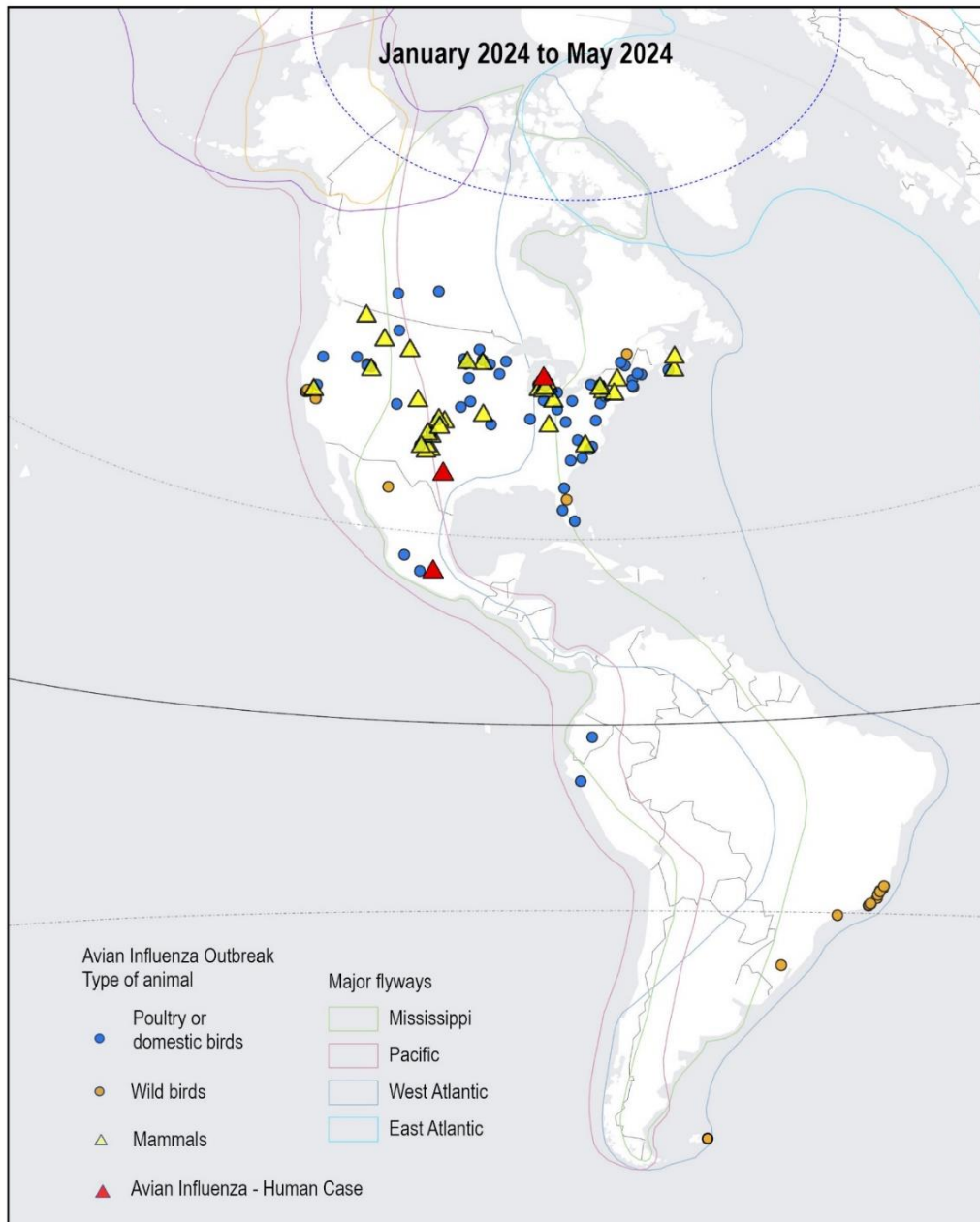
**Figure 4.** Monthly history of avian influenza outbreaks and major flyways by type of animal during 2024 up to EW 20 in the Region of the Americas.



**Sources:** Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOA; 2024 [cited 23 May 2024]. Available from: <https://wahis.woah.org/#/event-management>; and Falkland Islands Department of Agriculture. Avian Influenza Information. 2024 [cited 29 May 2024]. Available from: <https://falklands.gov.fk/agriculture/avian-influenza>



**Figure 5.** History of avian influenza outbreaks and major flyways by type of animal clusters during 2024 up to EW 20 in the Region of the Americas.



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0 500 1,000 2,000 Km



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**Source:** Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOA; 2024 [cited 23 May 2024]. Available from: <https://wahis.woah.org/#/event-management>; and Falkland Islands Department of Agriculture. Avian Influenza Information. 2024 [cited 29 May 2024]. Available from: <https://falklands.gov.fk/agriculture/avian-influenza>

## Recommendations for Member States

While largely affecting animals, avian influenza outbreaks pose continuing risks to public health. Together, the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO), and the World Organization for Animal Health (WOAH) urge Member States to work in a collaborative and intersectoral manner to preserve animal health and protect human health (1, 2).

Detected sporadic cases of H5 clade 2.3.4.4b virus in humans are mostly associated with direct contact with infected animals and contaminated environments. Current evidence reflects that the virus does not appear to be easily transmitted from one person to another. However, surveillance should be strengthened to detect any possible changes in this situation (2).

WOAH has specific recommendations on the avian influenza situation and mammals. These recommendations advise countries to maintain intensified surveillance for the disease in domestic and wild birds, preventing the spread of the disease by implementing biosecurity measures (21). WOAHA recommends controlling the movement of susceptible domestic animals and their products and protecting people in close contact with sick animals. Monitoring of susceptible domestic and wild animals, investigating increases in mortality in wild animals, is crucial. In addition, timely reporting and sharing of avian influenza virus genetic sequences are essential for understanding the dynamics of the disease (21).

The Pan American Health Organization / World Health Organization (PAHO / WHO) calls for action for Member States to work in a collaborative and intersectoral manner to preserve animal health and protect public health. It is essential to implement avian influenza preventive measures at the source, to establish protocols for detection, notification and rapid response to outbreaks in animals, to strengthen surveillance for both animal and human influenza, to carry out epidemiological and virological investigations in relation to animal outbreaks and human infections, to share genetic information about viruses, fostering collaboration between animal and human health settings, with effective risk communication, and ensuring preparedness at all levels for a potential influenza pandemic (22, 23).

The following are the main lines of recommendation for Member States with a One Health based approach, which include coordination for multisectoral surveillance and response, as well as prevention measures and risk communication.

### Multi-sector coordination

Preparedness for detection and response to public health emergencies requires the adoption of a holistic multisectoral and multidisciplinary approach. Multisectoral actions such as the establishment of standardized protocols that are inclusive of all relevant sectors, with well-established roles that facilitate information sharing and analysis, the development of a One Health based response strategy that includes both human and/or animal risk, and the training of human resources. A viable, culture-driven coordination and systemic approach to emergency preparedness and health systems strengthening is essential before it is necessary to respond to an event. Integration of the One Health perspective and stakeholder roles is essential and should be promoted (24).

High-level political commitment, stakeholder mapping and analysis, joint needs assessment, and the establishment of communication channels are key elements of multisectoral

coordination for health emergency preparedness. These pillars should be implemented through a transparent, reliable, and accountable framework (24).

## **Surveillance of human cases (23)**

In order to identify cases or transmission events at the human-animal interface early, surveillance and follow-up of exposed persons and their contacts is recommended. Due to the constantly evolving nature of influenza viruses, PAHO/WHO continues to emphasize the importance of strengthening indicator-based surveillance, i.e., severe acute respiratory infection (SARI) and influenza syndrome (ILI) surveillance, as well as strengthening event-based surveillance.

This allows the detection of virological, epidemiological, and clinical changes associated with circulating influenza viruses, which may impact human health. In addition to the active case-finding, contact identification and follow-up activities carried out during the epidemiological investigation of zoonotic events, it is advisable to alert and sensitize clinicians to consider the diagnosis of avian influenza and to strengthen existing surveillance systems in areas near poultry farms, areas where human cases and animal outbreaks have been reported, or where the source of infection is suspected. To complement surveillance for SARI and ILI, PAHO/WHO recommends establishing early warning systems to detect unusual events and to have a more complete picture of the situation and to conduct a timely and coordinated joint risk assessment between the human, animal, and environmental sectors.

PAHO/WHO reiterates to Member States the need to maintain and strengthen seasonal and zoonotic influenza virus surveillance, including the immediate submission of human influenza samples caused by avian influenza to the WHO Collaborating Center, the U.S. Centers for Disease Control and Prevention (U.S. CDC).

Because information on the circulation of avian influenza A(H5N1) viruses is important for human influenza vaccine composition and to generate 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 posed to humans by zoonotic influenza viruses.

## **Laboratory diagnosis of human cases**

### **Sample collection in humans**

Samples should be collected by trained personnel in compliance with all biosafety standards, including the use of personal protective equipment (PPE) appropriate for respiratory viruses.

The recommended specimens are the same type of specimens used for routine influenza surveillance. Nasopharyngeal swabbing is the optimal specimen collection method for influenza testing. However, a combined nasal and pharyngeal swab or aspirate specimen may be collected.

In the context of influenza A(H5) infection in humans recently described in the United States, it has been observed that it is possible to have a negative result on a nasopharyngeal swab but a positive result on a conjunctival swab (25, 26). Therefore, in suspected cases or in individuals exposed to influenza A(H5) with symptoms of conjunctivitis, it is suggested, in addition to the nasopharyngeal swab, to consider taking a conjunctival swab. It is essential to follow established protocols and collect both nasopharyngeal and ocular samples in patients with conjunctivitis for a comprehensive evaluation of possible infection by the A(H5N1) virus (27, 28, 29, 30, 31).

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

Collection of specimens within four days of symptom onset is recommended for highest yield of influenza virus and best detection. Sampling of asymptomatic contacts is not recommended unless deemed necessary according to national guidelines.

Specimens should be kept refrigerated (4-8°C) and sent to the laboratory (central, national or reference laboratory) where they should be processed within 24-72 hours of collection. If samples cannot be shipped within this period, it is recommended to freeze at -70°C (or below) until samples are shipped (ensuring that the cold chain is maintained).

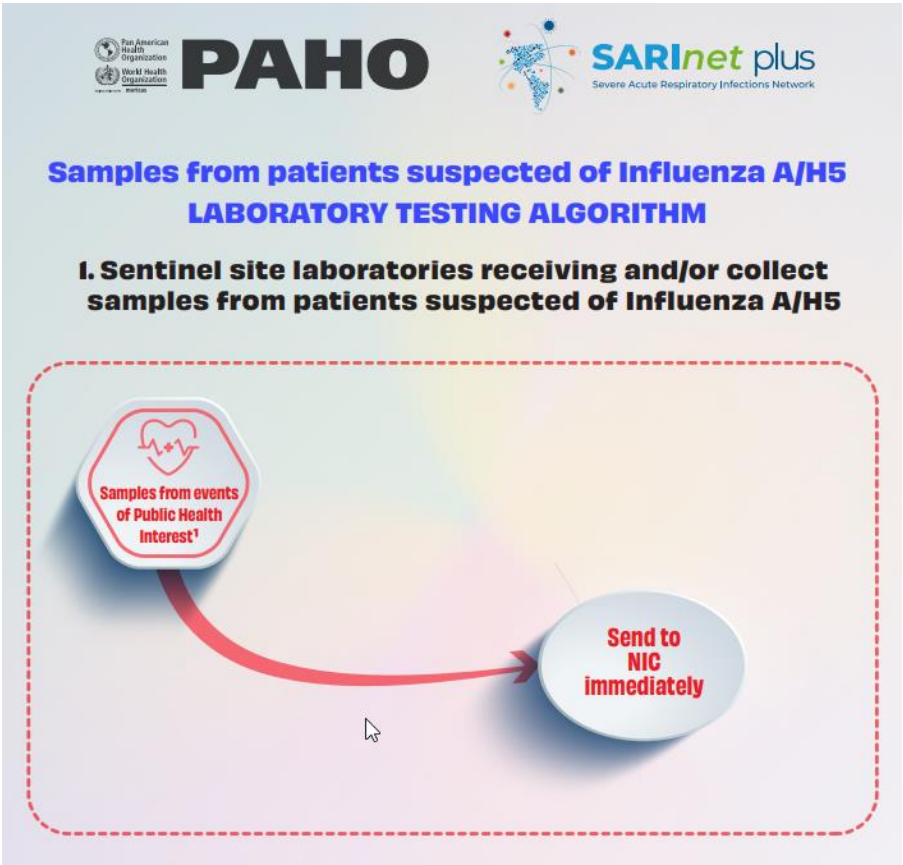
### **Sample flow and laboratory testing algorithm**

In the Region of the Americas, all National Influenza Centers (NICs) and National Reference Laboratories (NRLs) for human influenza, as part of the WHO Global Influenza Surveillance and Response System (GISRS), use molecular diagnostic protocols and reagents developed and validated by the WHO Collaborating Center at the U.S. CDC.

Upon identification of suspected cases of human infection with avian influenza A(H5), a respiratory specimen should be collected and submitted to the NIC or LNR for analysis (**Figure 6**) (32).

Specimens collected from suspected human cases exposed to birds or humans infected with avian influenza A(H5) should be tested for influenza. Influenza A positive specimens should be further subtyped for H5 (**Figure 7**) (32, 33).

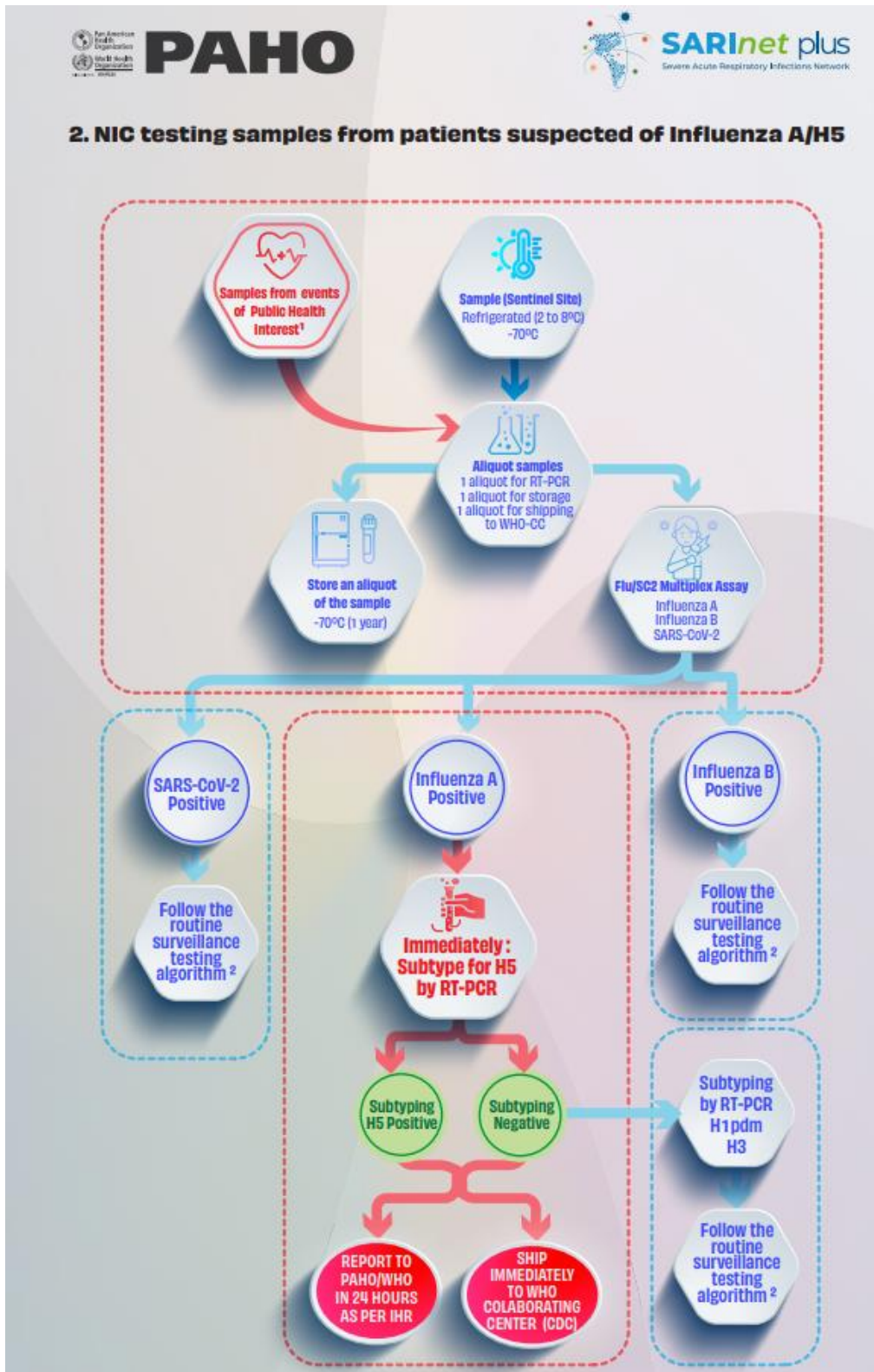
**Figure 6.** Sample flow for samples of influenza A(H5) suspected cases at sentinel sites and/or decentralized laboratories.



**Source:** Pan American Health Organization. Samples from patients suspected of Influenza A(H5) - Laboratory testing algorithm. 2 December 2022. Washington, DC: PAHO; 2022. Available from: <https://www.paho.org/en/documents/samples-patients-suspected-influenza-ah5-laboratory-testing-algorithm>.



**Figure 7.** NIC testing samples from suspected cases of influenza A(H5)



**Source:** Pan American Health Organization. Samples from patients suspected of Influenza A(H5) - Laboratory testing algorithm. 2 December 2022. Washington, DC: PAHO; 2022. Available from: <https://www.paho.org/en/documents/samples-patients-suspected-influenza-ah5-laboratory-testing-algorithm>

## Laboratory Reagents

The U.S. CDC kits for real-time reverse transcriptase polymerase chain reaction (qRT-PCR) detection of influenza viruses are available through the International Reagent Resource (IRR).

For influenza detection and influenza A(H5) subtyping, the following molecular detection kits and controls are available:

- 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)

## Interpretation of results

The U.S. CDC kit markers (targets) for detection of influenza A(H5) subtype are as follows: INFA (M), H5a (HA), H5b (HA) and RP.

When using the U.S. CDC A(H5) influenza subtyping kit:

- Samples positive for INFA, H5a and H5b markers are considered **positive for influenza A(H5)**.
- Samples positive for a single H5 marker are considered **presumptive for influenza A(H5)**.

In both cases, specimens should be submitted to a WHO Collaborating Center for further characterization or confirmation (in the case of presumptive results). However, a positive specimen for influenza A(H5) (both marker positive) should be reported immediately.

PAHO is currently working to support Member States in preparing for and responding to influenza A(H5). For additional assistance, contact [flu@paho.org](mailto:flu@paho.org).

## Shipment of samples

The U.S. CDC is the designated WHO Collaborating Center in the Region of the Americas to receive human specimens positive for avian influenza A(H5). International air shipment of human specimens to the U.S. CDC WHO Collaborating Center must meet all international standards in accordance with the International Air Transport Association (IATA), with special documents required for transport to the United States that are different from the documents for routine shipment of seasonal influenza specimens. It is important to note that specimens should not be submitted to the U.S. CDC as routine influenza specimens.

## Response to human cases

Upon detection of human infection, early notification is essential for investigation and implementation of appropriate measures, including isolation and early treatment of the case, active search for other cases associated with the outbreak, as well as identification of close contacts for appropriate management and follow-up (34).

It is recommended that the animal and human health sectors work together in risk analysis at the human-animal interface so that health personnel can be alerted to areas where avian influenza transmission (HPAI or LPAI) is occurring in birds, and where there is a higher probability of infection in people exposed to these viruses (22).

### Case Investigation

In the presence of a confirmed or suspected human infection caused by an influenza virus with pandemic potential, including an avian virus, it is recommended:

- A thorough epidemiological investigation of the history of animal exposure, travel, and ill contacts should be carried out. The investigation should not be delayed, even if confirmatory laboratory results are awaited.
- The epidemiological investigation should include early identification of unusual respiratory events, which could signal person-to-person transmission of the new virus.
- Clinical specimens collected at the time and place where the case occurred should be tested and sent to the WHO collaborating center for characterization within one week of detection.
- Standard infection prevention and control (IPC) procedures and standard precautions should always be applied and appropriate personal protective equipment (PPE) should be used according to risk (according to the most likely modes of transmission) to protect the health of investigators. PPE should be used when in contact with symptomatic persons and in situations where person-to-person transmission is suspected.
- The epidemiological investigation should include information from official veterinary services and the private sector (animal production) on the origin of animals and records of movements on and off the premises. This information will help define the scope (location) of investigations in humans exposed to infected animals.
- Information from official veterinary services could provide guidance on possible influenza events (both notifiable and non-notifiable) occurring in the area and farms related to the event.
- For more information regarding the investigation of non-seasonal influenza cases, the World Health Organization's "Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases" is available from: <https://iris.who.int/handle/10665/275657>.

## Notification of a human case

- A **confirmed case** of human infection with avian influenza should be reported **immediately** through two channels: to the WHO International Health Regulations (IHR) Regional Contact Point via the IHR National Focal Point (NFP), and to the WHO Global Influenza Surveillance and Response System (GISRS) administered by PAHO and WHO ([flu@paho.org](mailto:flu@paho.org)). The report should include all available results of the epidemiological investigation of the case and the virological characteristics of the virus.
- A suspected case of human infection with avian influenza should be reported **immediately** to the GISRS ([flu@paho.org](mailto:flu@paho.org)), and information on the suspected case may be shared with the WHO IHR Regional Contact Point, given that it is an unusual event. The report should include all available results of the epidemiological investigation of the case and the characteristics of the virus.

## Animal surveillance, diagnosis and response

FAO, WHO and WOAHA urge countries to prevent avian influenza at its source to facilitate a rapid response. The implementation of a comprehensive surveillance program, including wild birds and poultry, both backyard and commercial, is essential for early detection. Targeted risk-based surveillance strategies should be combined with a strengthening of general surveillance. In this aspect, awareness-raising among trained actors and the community in general, particularly in rural areas, is key to promote prevention and health surveillance. The information collected can allow the modeling of spread and strengthen risk analyses to increase their accuracy (2, 22, 23).

Avian influenza is included in the WOAHA list of notifiable diseases by the competent authorities. This includes notification of infections with HPAI viruses, infections in birds other than poultry with highly pathogenic influenza A viruses, and infections in domestic and captive wild birds with low pathogenic avian influenza viruses, provided that natural transmission has been demonstrated in humans and is associated with severe consequences (35).

At the regional level, there are veterinary laboratories with the capacity to detect and type the virus in both serological and molecular samples. A recent round of proficiency testing carried out by the WOAHA regional reference laboratory in Campinas, São Paulo, Brazil conducted in 2021 with the support of PANAFTOSA-PAHO/WHO proved a good aptitude of the participating laboratories to perform serological (ELISA, HI, and AGID), and molecular (RT-qPCR) diagnostic tests for the purpose of reaching a final diagnosis of avian influenza. This round included Argentina, Bolivia, Chile, Colombia, Costa Rica, the Dominican Republic, Ecuador, Paraguay, Peru, and Uruguay, in addition to Brazil as the coordinating laboratory. Other veterinary services laboratories participated in other proficiency tests in 2022 with excellent results, for example, those developed by the WOAHA reference laboratory of the U.S. Department of Agriculture (USDA) Ames, Iowa, United States, in which the Vesicular Disease Diagnostic Laboratory of Panama participated, or coordinated by GD Laboratory as in the case of the National Service of Health, Safety and Agrifood Quality of Mexico.

Surveillance strategies combine serological and molecular techniques to detect both previous exposure to the virus and the current presence of the virus, which is crucial for early detection. In poultry, virus subtyping in birds focuses primarily on identifying Influenza A virus subtypes H5 or H7. These analyses, which allow differentiating the presence of highly pathogenic avian influenza, are sufficient to support field actions. The collection of nerve tissue samples from wild birds during the investigation of suspicious outbreaks is highlighted to optimize pathogen detection.

The regional reference laboratory in Campinas, Brazil, is collaborating in the diagnostic confirmation and subtyping of South American countries. Full virus sequencing is being conducted with the support of other laboratories including the USDA WOAHA reference laboratory in Ames, Iowa, USA.

### Shipment of samples

It is recommended to send samples from animals detected with the virus for analysis and assessment, for their inclusion in the preparation of seasonal human vaccines. To do this, animal samples should be sent to the WHO Collaborating Center at St. Jude Children's Hospital. Special documents are required 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 through [flu@paho.org](mailto:flu@paho.org).

## Genome sequencing and surveillance

### Sequencing

Submission of a positive sample for influenza A(H5), animal or human, to the appropriate WHO Collaborating Centre **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.

The publication of sequences in GISAID requires the use of the nomenclature recommended by the WHO (36):

- 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



## Genomic Surveillance

**Human influenza A(H5) virus:** Since the beginning of 2020, the influenza A(H5) viruses reported to WHO as infecting humans have been of the 2.3.4.4b genetic group. Virus sequences from these human cases, when available, showed no markers of mammalian adaptation or resistance to antivirals, including oseltamivir and baloxavir (37). Results of molecular tests available for the human cases in the United States confirmed avian influenza A(H5N1) virus of clade 2.3.4.4b (2) closely related to the B3.13 genotype detected in dairy cattle, suggesting direct animal-to-human transmission. Both the viruses detected in cows and in two human cases maintain mainly avian genetic characteristics and lack (according to information available) changes that would make them more suitable for infecting or transmitting between humans (38). No known markers for antiviral resistance against influenza were found in the virus sequences of the specimen from the first case reported in Michigan (38).

**Animal influenza A(H5) virus:** clade 2.3.4.4b that was introduced in late 2021 into North America by wild birds has spread across the continent throughout 2022 and 2023. Worldwide circulation of the virus has led to opportunities to generate multiple genotypes with varied clinical signs. Through routine monitoring and viral sequencing, few sequences with markers of mammalian adaptation were found. These mutations probably occurred after transmission to the mammalian host and do not appear to be transmitted forward (39). The information currently available for avian influenza cases in dairy cattle in the United States does not show new mutations possibly associated with further transmission to humans (2). Available sequences for the 2.3.4.4b gene cluster of avian and mammalian viruses indicate that markers associated with reduced susceptibility to antivirals are rare (40).

**Vaccine candidate viruses for zoonotic influenza:** WHO's Global Influenza Surveillance and Response System (GISRS), in collaboration with the veterinary and animal health sectors, periodically evaluates candidate vaccine viruses. Candidate influenza A(H5) vaccine viruses from the 2.3.4.4b gene pool have been identified. This includes a candidate A(H5N8) virus, in fact, A/Astrakhan/3212/2020, as well as an A(H5N1) virus, A/chicken/Ghana/AVL-76321VIR7050-39/2021. The A/Astrakhan/3212/2020 vaccine virus is closely related to the recently detected circulating A(H5) influenza strains (39).

## Risk communication and community participation (41, 42)

Risk communication is a fundamental component of preparedness and response to health emergencies, especially those with pandemic or epidemic potential. Early and transparent communication with populations, as well as clear messages about behaviors and preventive measures to be adopted by communities, is vital to reduce transmission. In addition, adequate risk communication will help to reduce rumors, myths and misinformation related to the outbreak and will allow populations to make the right decisions to reduce the risk of contagion.

FAO, WHO and WOAHA urge countries to communicate the risk of avian influenza by alerting and training health care workers and persons occupationally exposed to the virus on how to protect themselves. The general public, and those exposed to sick and/or dead animals, should also be informed to encourage prompt notification of the competent authorities. Guidance should be provided on how to seek medical attention in case of discomfort and to communicate any exposure to animals to their health care provider (2). A differentiated communication strategy should be considered depending on the audience (e.g., livestock

and backyard producers, rural communities, ordinary citizens, wildlife stakeholders, indigenous groups, etc.).

PAHO/WHO recommends that Member States take the following actions among their risk communication preparedness measures for a possible 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 preparations and respond to an eventual outbreak. WHO has guidelines for risk communication plans related to respiratory diseases.
- Gather existing information and/or conduct qualitative assessments and/or rapid quantitative assessments to understand the characteristics of the communities most at risk, communication patterns and channels, language, religion, influencers. This information is vital in order 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 public confidence, 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 the communication processes. Community involvement will contribute to the adoption of preventive behaviors.
- Broadcast messages to the public on symptom identification and prevention, particularly to populations with higher potential for exposure to the virus: rural settings, farmers, farm workers, backyard poultry owners. Messages should be broadcast in the channels and through the platforms consulted by each type of audience.
- Activate social listening for rumors and misinformation through digital platforms and other relevant information exchange channels (hotlines, web portals, etc.), to respond to possible false messages circulating among the public and adapt messages according to the needs detected by this monitoring.

## **Prevention measures for birds and animals**

According to WOAHA, the implementation of strict biosecurity and hygiene measures are essential to prevent outbreaks of avian influenza in animals. These include ensuring that poultry and other domestic animals susceptible to avian influenza infection do not have contact with wild birds, ensuring sanitary conditions in production areas, clothing and personnel, and reporting bird diseases and deaths, and suspicions of avian influenza infection in other domestic animals, to animal health services. If infection in poultry or other domestic animals is detected, the current regulations applied by the animal health authority should be followed to contain, control and rapidly eradicate the disease. These actions result in a significant decrease in environmental viral contamination. WOAHA encourages national authorities to consider developing compensation plans for farm owners and producers whose production are affected by the measures implemented by the authorities (35). According to WOAHA, the use of vaccination in poultry against HPAI is a decision of the national animal

health authorities, in coordination with poultry producers, and should be adapted to the epidemiological and socioeconomic context of the countries (43). Avian influenza vaccination alone should not be considered as a sustainable solution to control avian influenza and should be part of comprehensive disease control strategies (35).

### Prevention measures in humans

Persons at risk of infection are those directly or indirectly exposed to infected domestic poultry and other animals (domestic, wild or captive), for example, individuals who maintain close and regular contact with infected domestic animals, or during slaughter, or during the cleaning and disinfection of affected farms. For this reason, the use of adequate personal protective equipment and other protective measures is recommended to avoid zoonotic transmission in these operators (37).

### Seasonal influenza vaccination in context of avian influenza (44, 45)

Although the seasonal influenza vaccine does not protect against zoonotic influenza in humans, it contributes to reduce the risk of co-infection and genomic recombination of avian and human viruses, which could result in new strains with pandemic potential.

WHO recommends seasonal influenza vaccination in persons at risk of influenza A (H5) virus infection, especially in areas with avian influenza circulation. This recommendation applies to poultry industry workers, veterinary services personnel who are involved in surveillance and disease control, as well as persons who may be in contact with wild birds, workers in wildlife care centers, and those in the field handling wild birds.

Vaccination with seasonal influenza vaccines should be used in combination with other control measures, such as infection prevention and control measures and the use of personal protective equipment, to reduce the risk of avian influenza infection in these populations.

There are some licensed vaccines **for human use** against avian influenza A(H5), but their use is restricted. Since the risk of human infection remains low, WHO does not recommend vaccination of the population with these vaccines in the inter-pandemic period.

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