Epidemiological Update
Outbreaks of avian influenza caused by influenza A(H5N1) in the Region of the Americas

20 March 2024

Global context

Avian influenza is typically spread by birds, however, the increased detection of avian influenza A(H5N1) among mammals, which are biologically closer to humans than birds, raises concerns that the virus may adapt to infect humans more easily. Since 2020, a variant of the avian influenza A(H5N1) virus, belonging to the H5 2.3.4.4b clade, has caused a significant number of deaths in wild birds and poultry in several countries in Africa, Asia, and Europe. In 2021, the virus spread to North America and, in 2022, to Central and South America. In 2023, several countries reported outbreaks, mainly in the Americas. Several mass die-off events have been reported in wild birds caused by virus strain A(H5N1) clade 2.3.4.4b, and an increasing number of cases have been reported in mammals, both terrestrial (including pets) and aquatic, causing morbidity and mortality *(1,2,3)*.

While largely affecting animals, these outbreaks pose ongoing public health risks to humans. The Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO), and the World Organization for Animal Health (WOAH) urge countries to work collaboratively and intersectorally to preserve animal health and protect human health *(1,2,3)*.

In particular, the WOAH recommends that countries maintain and strengthen their animal surveillance systems, on-farm biosecurity measures, and continue timely reporting of avian influenza outbreaks in both poultry and non-poultry species (domestic and/or wild birds). The quality of surveillance is key to the early detection and timely response of potential animal health threats with an impact on human public health *(1,2,3)*.

As long as avian influenza viruses are circulating, there is a risk of sporadic human infections due to exposure to infected animals or contaminated environments. Since 2003 and as of 21 December 2023, a total of 887 human cases of influenza A(H5N1) infection, including 462 deaths (case fatality rate 52%), have been reported to WHO in 23 countries *(4)*.

Situation summary in the Region of the Americas

As of epidemiological week (EW) 52 of 2023, the authorities of Argentina, the Plurinational State of Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Ecuador, Falkland Islands, Guatemala, Honduras, Mexico, Panama, Paraguay, Peru, Uruguay, the United States of America, and the Bolivarian Republic of Venezuela have detected outbreaks of highly pathogenic avian influenza virus (HPAI)[1] A(H5N1) in domestic poultry, poultry farms, and/or wild

[1] Avian influenza viruses are classified into low pathogenic avian influenza viruses (LPAI) and highly pathogenic avian influenza viruses (HPAI) according to their ability to cause disease in birds.

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birds (**Table 1**) *(1)*. HPAI has also been identified in mammals in Argentina, Brazil, Canada, Chile, Peru, the United States, and Uruguay (**Table 2**) *(1)*. Among the mammals identified, red foxes and skunks were the most frequently affected in North America, and sea lions in South America.

With 19 countries and territories reporting outbreaks, indicating a large geographical extension of the virus, as well as the high number of outbreaks recorded in the Region, with more than 2,600 outbreaks in birds and more than 280 outbreaks in mammals, reported to WOAH, as of 31 December 2023, this detection of HPAI outbreaks is a situation that has never before been recorded in the Region *(1)*. The identified outbreaks are located mainly in the Pacific migratory route (**Figure 1, Figure 2, Figure 3**).

Since the introduction of avian influenza A(H5N1) in the Americas in 2014 and as of this update, three human infections caused by avian influenza A(H5N1) have been reported: one in the United States of America, reported on 29 April 2022 *(5)*, one in Ecuador, reported on 9 January 2023 *(6)*, and one in Chile, reported on 29 March 2023 *(7)*. No human infections have been identified and reported so far in 2024.

Table 1. Avian influenza outbreaks by type of animal affected. Region of the Americas, as of epidemiological week (EW) 52 of 2023.

Country/Territory	Wild birds	Poultry farm	Backyard poultry	Mammals
Argentina	Yes	Yes	Yes	Yes
Bolivia	Yes	Yes	Yes	
Brazil	Yes		Yes	Yes
Canada	Yes	Yes	Yes	Yes
Chile	Yes	Yes	Yes	Yes
Colombia	Yes	Yes	Yes	
Costa Rica	Yes			
Cuba	Yes			
Ecuador	Yes	Yes	Yes	
Falkland Islands	Yes			
Guatemala	Yes			
Honduras	Yes			
Mexico	Yes	Yes	Yes	
Panama	Yes			
Paraguay			Yes	
Peru	Yes	Yes	Yes	Yes
United States	Yes	Yes	Yes	Yes
Uruguay	Yes		Yes	Yes
Venezuela	Yes		Yes	

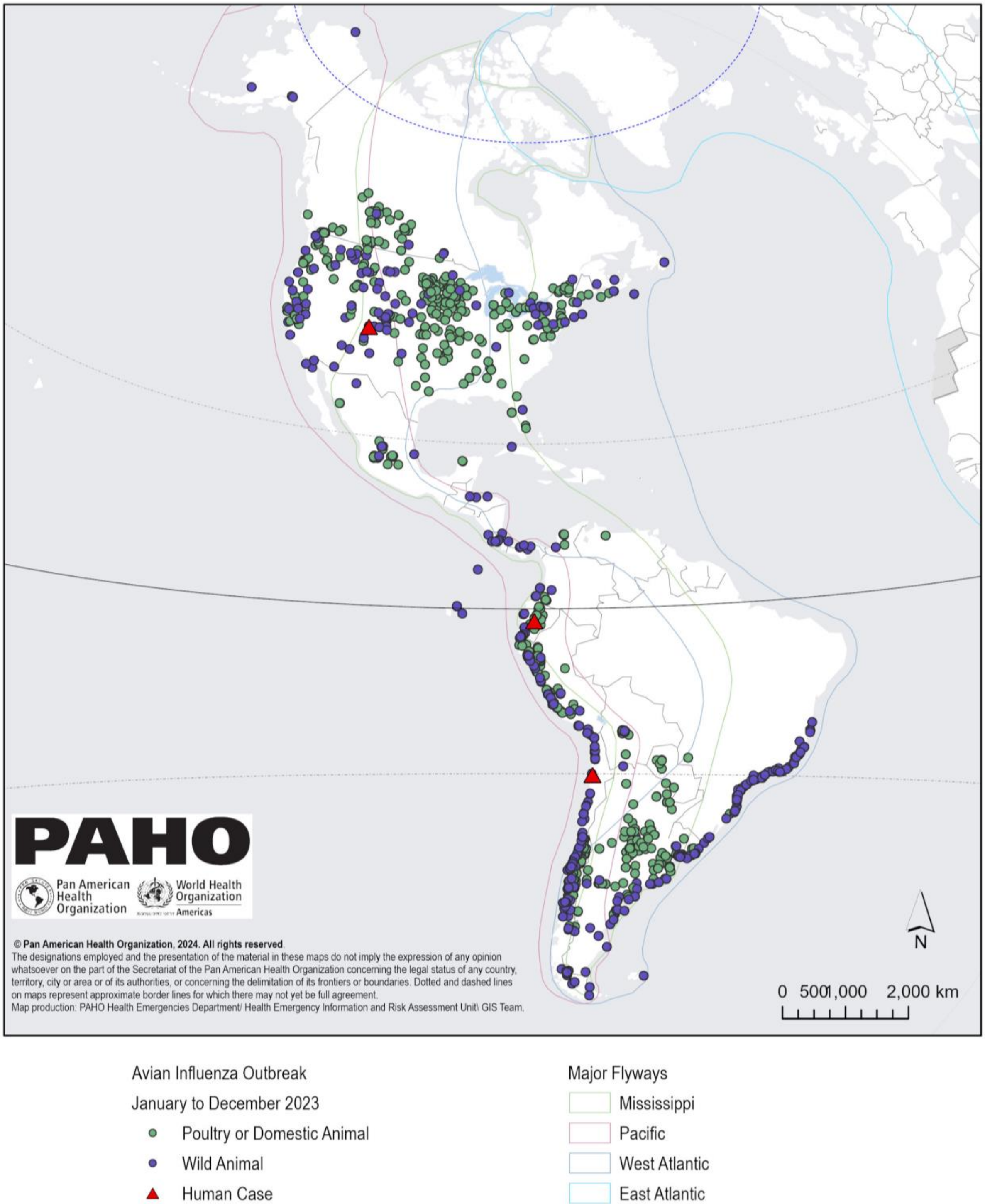
Source: Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOAH; 2024 [cited 18 March 2024]. Available from: https://wahis.woah.org/#/event-management

Table 2. Mammals affected by avian influenza. Region of the Americas, as of EW 52 of 2023

Mammals	Argentina	Brazil	Canada	Chile	Peru	United States	Uruguay
Arctocephalus australis **(South American fur seal)**	Yes	Yes					Yes
Canis latrans **(Coyote)**						Yes	
Canis lupus familiaris **(Domestic dog)**			Yes				
Didelphis virginiana **(Virginia opossum)**						Yes	
Felis silvestris catus **(Domestic cat)**			Yes			Yes	
Lontra canadensis **(Nothern river otter)**						Yes	
Lontra felina **(Marine otter)**				Yes			
Lontra provocax **(Southern river otter)**				Yes			
Lynx rufus **(Bobcat)**						Yes	
Martes americana **(Marten)**						Yes	
Mephitis mephitis **(Skunk)**			Yes			Yes	
Mirounga leonina **(Southern elephant seal)**	Yes						
Nasua nasua **(South American coati)**							Yes
Neovison vison **(Mink)**			Yes				
Otaria flavescens **(South American sea lion)**	Yes	Yes		Yes	Yes		Yes
Panthera leo **(Lion)**					Yes		
Panthera pardus **(Leopard)**						Yes	
Panthera tigris **(Tiger)**						Yes	
Pekania pennanti **(Fisher)**						Yes	
Phoca vitulina / Halichoerus grypus **(Seal)**			Yes			Yes	
Procyon lotor **(Raccoon)**			Yes			Yes	
Puma concolor **(Cougar)**						Yes	
Sciurus aberti **(Squirrel)**						Yes	
Tursiops truncatus **(Dolphin)**						Yes	
Ursus americanus / U. arctos horribilis **(Bear)**			Yes			Yes	
Ursus maritimus **(Polar bear)**						Yes	
Vulpes vulpes **(Red fox)**			Yes			Yes	

Source: Adapted from World Organization for Animal Health. Avian Influenza. Paris: WOAH; 2024 [cited 18 March 2024]. Available from: https://wahis.woah.org/#/event-management

Figure 1. Avian influenza outbreaks and main migratory routes of wild birds. Region of the Americas, 2023.



Sources
- Data: World Organization for Animal Health (WOAH) (2024). Data extracted by Pan American Health Organization. Reproduced with permission.
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- Cartography: WHO Detailed ADM0 Boundaries; Conservation of Artic Flora and Fauna - Data Service (SHP) Major flyways of Artic Birds Shapefile Accessed February 2023.

Figure 2. Avian influenza outbreaks and main migratory routes of wild birds. Region of the Americas, 2023

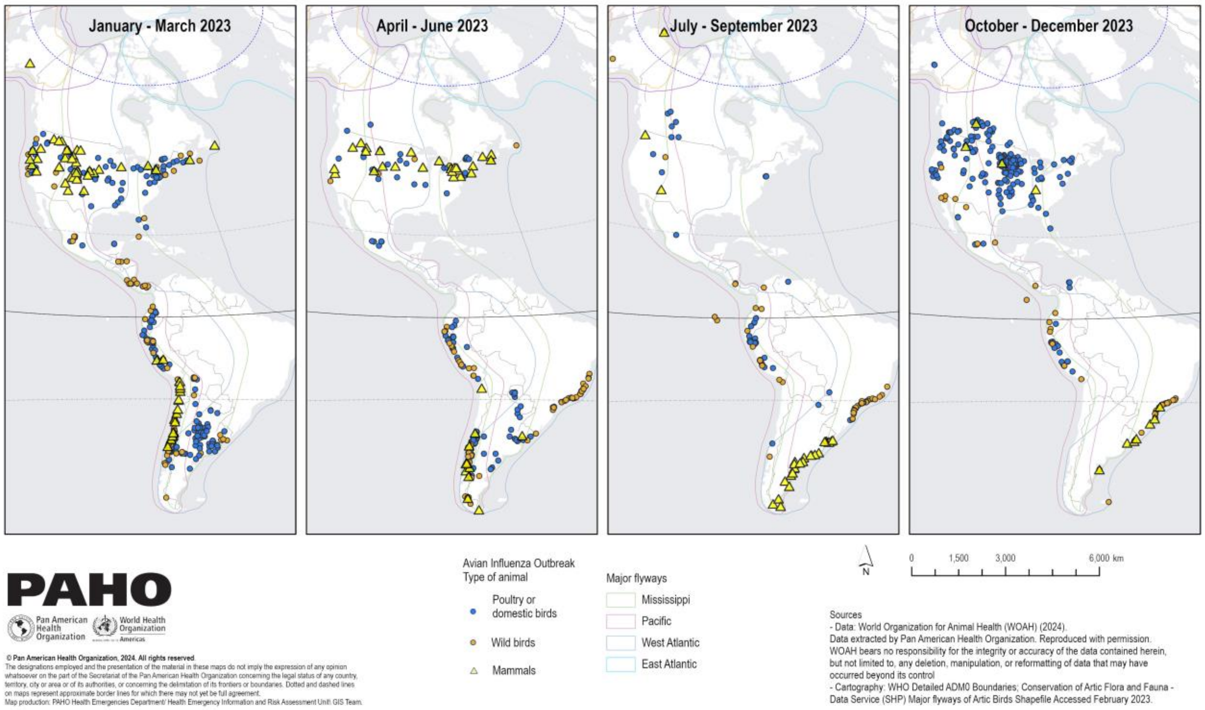
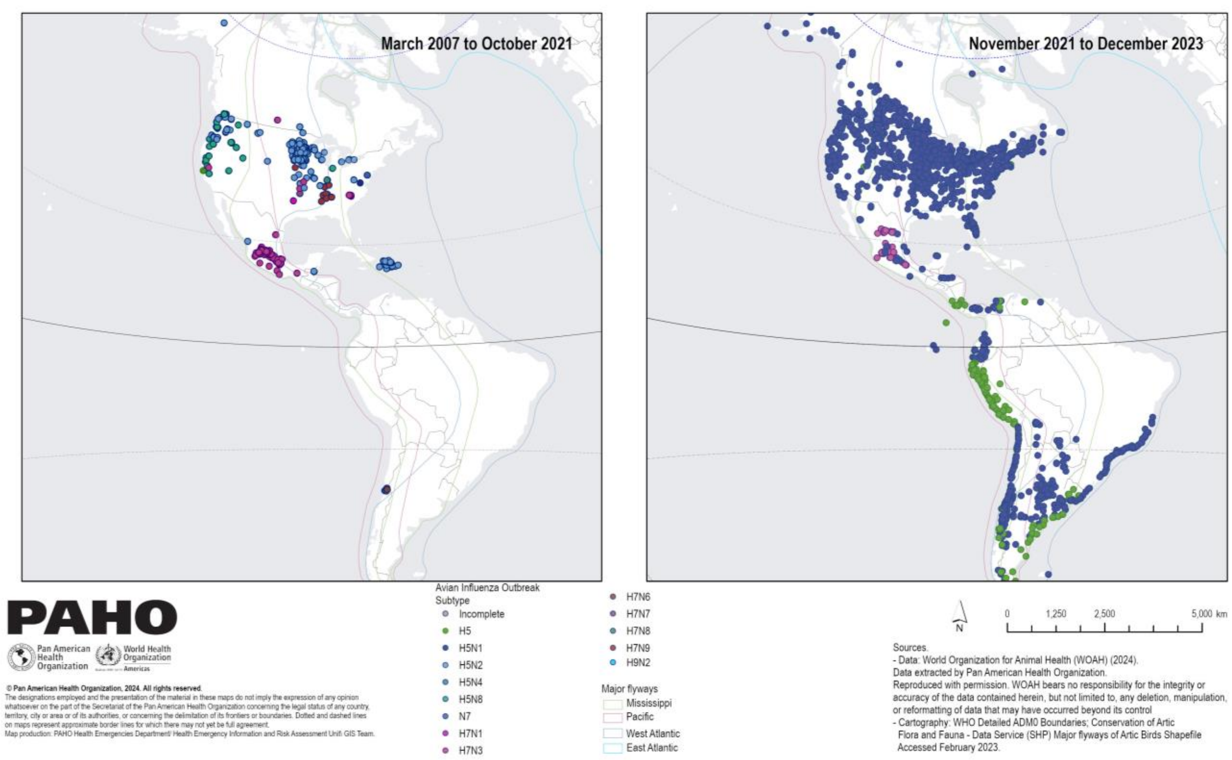


Figure 3. Avian influenza outbreaks and main migratory routes of wild birds. Region of the Americas, March 2007 to October 2021 and November 2021 to December 2023.



The following is a summary of the situation in countries in the Region of the Americas that reported outbreaks of avian influenza during 2024 (**Figure 4**).

In **Brazil**, between 1 January 2024 and 18 March 2024, seven outbreaks of avian influenza A(H5) have been confirmed in wild birds in the States of Espirito Santo, Rio de Janeiro, Rio Grande do Sul, and Sao Paulo. To date, no outbreaks in production birds or human cases of avian influenza infection have been detected *(1)*.

In **Canada**, between 1 January 2024 and 18 March 2024, multiple outbreaks of HPAI A(H5N1) in poultry and wild birds have been reported to WOAH in seven of Canada's ten provinces: Alberta, Manitoba, Nova Scotia, Ontario, Prince Edward Island, Quebec, and Saskatchewan. No human cases of avian influenza infection have been reported in the outbreaks identified to date *(1)*.

In **Ecuador**, between 1 January 2024 and 18 March 2024, an outbreak of H5N1 avian influenza in backyard poultry was reported to WOAH. The outbreak was identified in Pastaza province *(1)*.

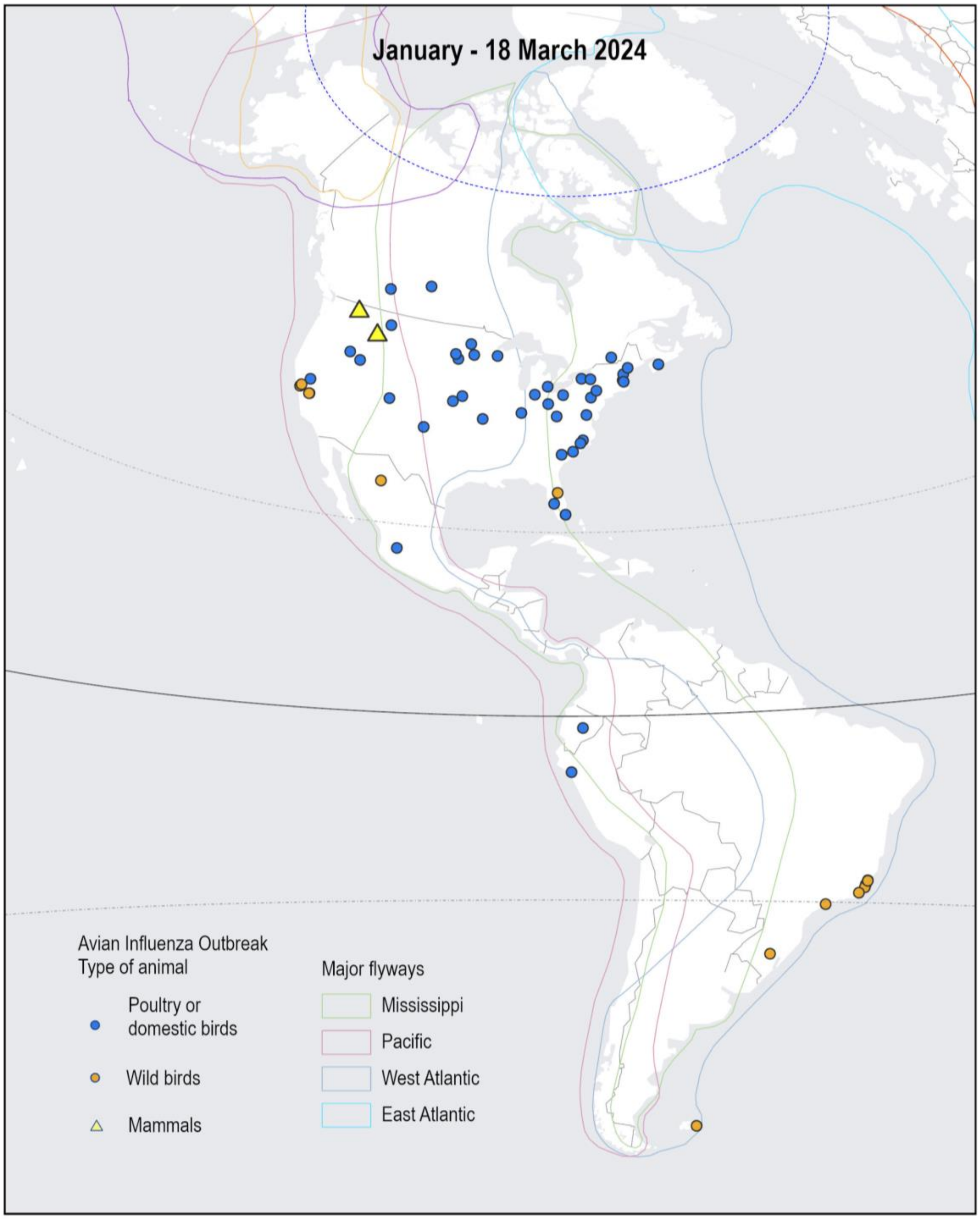
In the **United States**, from early 2024 through 18 March 2024, multiple HPAI A(H5) virus outbreaks in wild birds, commercial poultry, or backyard poultry were reported to WOAH in 23 states in the United States. During the same period, two outbreaks in mammals have been reported in the states of Montana and Washington *(1)*.

In the **Falkland Islands**, between 1 January 2024 and 18 March 2024, the Department of Agriculture reported the occurrence of 6 incidences of avian influenza, all related to wild birds *(8)*.

In **Mexico**, between 1 January 2024 and 18 March 2024, two outbreaks of avian influenza in birds were reported to WOAH. These outbreaks occurred in the states of Chihuahua, with an outbreak in wild birds, and in Jalisco, with an outbreak affecting domestic birds *(1)*.

In **Peru**, an outbreak of HPAI A(H5) in backyard poultry was reported to WOAH during 2024 and as of 18 March. The outbreak occurred in the department of La Libertad *(1)*.

Figure 4. Avian influenza outbreaks and main migratory routes of wild birds. Region of the Americas, 2024



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

Sources
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- Cartography: WHO Detailed ADM0 Boundaries; Conservation of Artic Flora and Fauna - Data Service (SHP) Major flyways of Artic Birds Shapefile Accessed February 2023.

Guidance for Health Authorities in Member States

Both HPAI and LPAI viruses can be rapidly spread among poultry through direct contact with infected wild birds or other poultry, or through direct contact with fomites or surfaces, or water contaminated with the viruses. Infection of poultry with HPAI viruses can cause severe disease with high mortality. LPAI viruses are more associated with subclinical infection. The terms HPAI and LPAI apply only to the symptoms in birds (chickens in particular), and both types of viruses have the potential to cause infections in humans.

Human cases are related to close contact with infected animals and contaminated environments. These cases have been carefully evaluated and, currently, there is no evidence of person-to-person spread. Overall, the risk to human health is low, but vigilance needs to be maintained and strengthened.

PAHO calls for action so that countries work collaboratively and intersectorally to preserve animal health and protect human public health. It is essential to implement avian influenza preventive measures at the source, establish protocols for detection, notification and rapid response to outbreaks in animals, strengthen surveillance for both animal and human influenza, conduct epidemiological and virological investigations in relation to animal outbreaks and human infections, sharing genetic information about viruses, fostering collaboration between animal and human health settings, effective risk communication, and ensuring preparedness for a potential influenza pandemic at all levels *(9,10)*.

Intersectoral coordination *(10,11)*

Control of disease in animals is the first measure to reduce the risk to humans. For this reason, it is important that prevention and control actions, both in the animal and human health sectors, are carried out in a coordinated and concerted manner. Agile mechanisms for the exchange and analysis of information will have to be established and/or strengthened to facilitate coordinated decision-making.

Implementation of a comprehensive surveillance program, including wild birds and both backyard and commercial poultry, is essential. Targeted risk-based surveillance strategies should be combined with a strengthening of general surveillance. In this regard, sensor awareness tasks are key, particularly in the backyard, to encourage the detection and notification of suspicious events. These programs also provide information that enables spread modeling and more accurate risk analysis.

Risk communication and community engagement

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 areas and includes, but is not limited to, institutional communication or communication with the media. So, it is important that the leaders or teams in the health authorities that lead in an integral way the technical aspects related to this component, are clearly established.

The Pan American Health Organization (PAHO) recommends to Member States 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. The WHO risk communication and community engagement (RCE) action plan guidance, COVID-19 preparedness and response, interim guidance, for respiratory diseases can be consulted *(12)*.
- Gather 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, and backyard bird owners. 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.

In the case of avian influenza, an intersectoral communication strategy is essential by addressing key messages that inform about the potential risk and precautions from a public health visit point, including to whom to go to in case of suspicion or contact. And, to raise awareness about animal disease, its clinical presentation, and communication route to veterinary authorizations. Consideration should be given to making a differentiated communication strategy based on the audience (e.g., livestock producers, backyard keepers, ordinary citizens, wildlife stakeholders, etc.).

Surveillance in humans *(9)*

People at risk of contracting infections are those directly or indirectly exposed to infected birds (domestic, wild, or captive), for example, poultry keepers who maintain close and regular contact with infected birds or during slaughter or cleaning and disinfection of affected farms.

For this reason, the use of adequate personal protective equipment (PPE) and other protection measures is recommended to avoid zoonotic transmission in these operators.

In order to identify cases or transmission events at the human-animal interface early, surveillance and monitoring of exposed persons is recommended. Due to the constantly evolving nature of influenza viruses, PAHO/WHO continues to emphasize the importance of strengthening severe acute respiratory infection (SARI) surveillance and influenza syndrome (ILI) surveillance to detect virologic, epidemiologic, and clinical changes associated with circulating influenza viruses that may affect 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 strengthen existing surveillance systems for SARI and ILI where poultry farms are located, where cases reside, where animal outbreaks occur, or where the source of infection is suspected. To complement surveillance for SARI and ILI, PAHO/WHO recommends establishing early warning systems to provide a more complete picture of the situation and to conduct a timely, coordinated joint risk assessment between the human and animal sectors.

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, and identification of close contacts for appropriate management and follow-up *(13)*.

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

PAHO/WHO reiterates to Member States the need to maintain influenza virus surveillance and to immediately ship human influenza samples to the WHO Collaborating Center, the US CDC.

Since information on the circulation of avian influenza A/H5 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.

Case investigation

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

- A thorough epidemiologic investigation of the history of exposure to animals, travel, and ill contacts should be conducted, even while awaiting confirmatory testing.
- The epidemiologic investigation should include early identification of unusual respiratory events 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. Appropriate PPE (according to the most

probable modes of transmission) should be used when in contact with symptomatic persons and in situations where human-to-human transmission is suspected.

- 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 premises. This information will contribute to define the scope (location) of investigations on humans exposed to the infected animals.
- Information from OVS could provide guidance on possible influenza episodes (both notifiable and notifiable) occurring in the area and farms related to the event.
- For more information regarding the investigation of cases of non-seasonal influenza, the World Health Organization protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases, is available from: https://iris.who.int/handle/10665/275657

Notification of cases in humans

- A **confirmed positive case** of human influenza A(H5) infection should be **reported immediately** via two channels—the WHO International Health Regulations (IHR) Regional Contact Point via the IHR National Focal Point, and the WHO Global Influenza Surveillance and Response System (GISRS) managed by PAHO and WHO (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 influenza A(H5) infection should be **reported immediately** to the GISRS (flu@paho.org), and information about the suspected case can be shared with the WHO IHR Regional Contact Point, 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.

Seasonal influenza vaccination in the context of avian influenza *(14,15)*

- Although the seasonal influenza vaccine does not protect against zoonotic influenza A(H5), it contributes to reducing the risk of coinfection 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 infection with influenza A (H5) viruses, especially in areas with influenza circulation in birds. High-risk groups for influenza A(H5) infection include people who are in close contact with animals, including poultry, in areas where avian influenza is known to circulate. This recommendation applies to workers in the poultry industry, veterinary service personnel involved in disease surveillance and control, as well as people who may be in contact with wild birds, such as wild animal care center workers and those in the field preforming tasks involving handling these animals.
- 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 human avian influenza A(H5) vaccines, but their use is restricted. As the risk of human infection remains low, WHO does not recommend vaccination of the population with these vaccines in the inter-pandemic period.

Laboratory diagnosis in humans

Sample collection in humans

Samples should be collected by trained personnel in adherence to all biosafety instructions including the use of appropriate personal protective equipment (PPE) for respiratory viruses.

The recommended samples are the same type(s) of samples used for influenza routine surveillance. A nasopharyngeal swab is the optimal specimen collection method for influenza testing. However, a combined nasal and throat swab specimen or aspirate specimens can be collected. 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).

Sample collection is recommended within 4 days of symptom onset for the highest influenza virus yield and better detection. 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 laboratory (central, national, or reference laboratory) 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 (ensuring the cold chain is maintained).

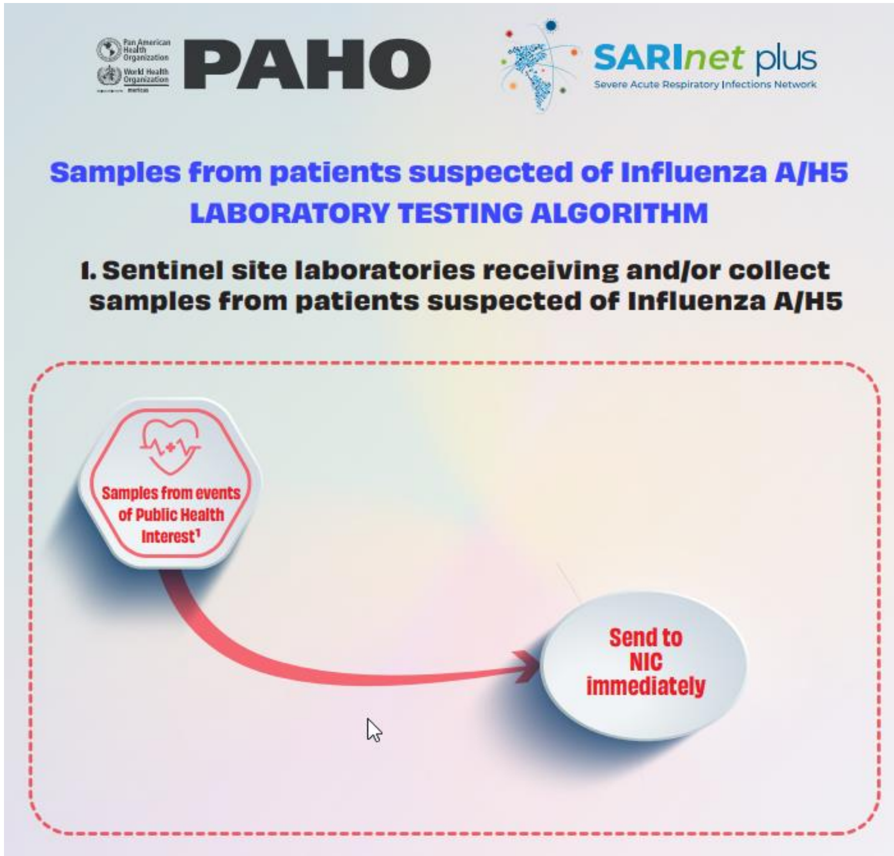
Sample flow and laboratory testing algorithm

In the Americas, all national influenza centers (NICs) and national reference laboratories (NRL) 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 US CDC.

In case of identification of suspected cases of human infection caused by avian influenza A/H5, a respiratory specimen should be taken and refer to the NIC or NRL for testing (**Figure 5**) *(16)*.

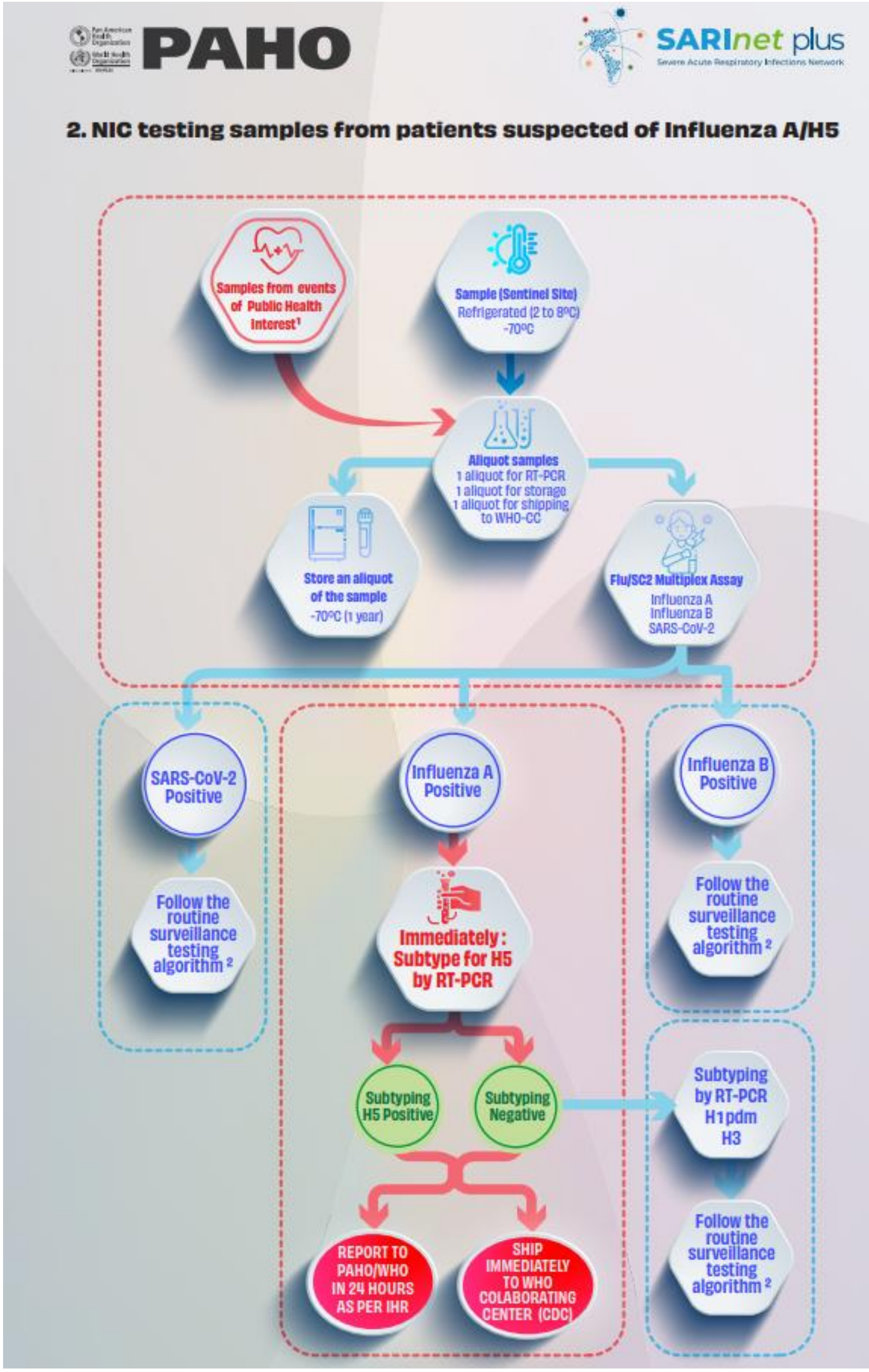
Samples collected from suspected human cases exposed to birds or humans infected with avian influenza A/H5 should be tested for influenza; influenza A-positive samples should be subsequently subtyped for H5 (**Figure 6**) *(16,17)*.

Figure 5. 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 6. 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

US CDC kits for real-time reverse transcription 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 kits and controls for molecular detection 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 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:

- Samples positive for INFA, H5a, and H5b markers are considered **positive for influenza A/H5.**
- Samples positives for only one H5 marker are considered **presumptive for influenza A/H5**.

In both 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 on preparedness and response to Influenza A/H5. For additional support, please contact flu@paho.org.

Shipment of samples

The United States Centers for Disease Control and Prevention (US CDC) is the designated WHO Collaborating Center (CC) in the Region of the Americas for receiving human samples positive for Influenza A/H5. Shipment of human samples to the US CDC WHO Collaborating Center internationally and by air must be in compliance with 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 shipped as routine influenza samples to the US CDC.

Laboratory surveillance and diagnosis in animals

Veterinary laboratories in countries generally have the ability to detect and to some extent type the virus in both serological and molecular samples. A recent round of proficiency tests carried out by the WOAH regional reference laboratory in Campinas, São Paulo, Brazil carried out in 2021 with the support of PANAFTOSA-PAHO/WHO, which verified the capacity of the participating laboratories to perform serological diagnostic tests (ELISA, HI and AGID) and molecular (RT-qPCR) in order to reach a final diagnosis of avian influenza. This round included Argentina, Bolivia, Chile, Colombia, Costa Rica, the Dominican Republic, Ecuador, Paraguay, Peru, and Uruguay, as well as Brazil as the coordinating laboratory. Other veterinary laboratories participated in other competency trials in 2022 with excellent results; such as, those developed by the USDA WOAH reference laboratory, located in Ames, Iowa, USA, in which the LADIVES laboratory of Panama participated, or coordinated by GD laboratory as in the case of SENASICA in Mexico.

Surveillance strategies combine the use of serological and molecular techniques to rule out not only previous exposure to the virus but also the current presence of the virus. This last point is very relevant to achieve early detection. The sub-typing of the virus in birds mainly seeks to rule out/check for the presence of influenza A, H5 or H7 viruses. Of these subtypes, laboratories usually do not have the necessary reagents to continue diagnosis. However, these analyses to differentiate the presence of HPAI are sufficient for support and field actions. The importance of collecting nerve tissue in field samples during the study of suspected cases of wild birds has been noted to optimize pathogen detection.

The regional reference laboratory in Campinas, Brazil, is supporting the confirmation of South American countries diagnoses and sub-typing. Total virus sequencing is being carried out with support from other laboratories including the United States Department of Agriculture (USDA) WOAH reference laboratory in Ames, Iowa, United States.

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 at 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 *(18)*:

- 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 viruses: Since the beginning of 2020, influenza A/H5 viruses reported to WHO detected infecting humans are of genetic group 2.3.4.4b. The virus sequences of these human cases, when available, showed no markers of adaptation in mammals or resistance to antivirals, including oseltamivir and baloxavir *(19)*.

Animal influenza A/H5 virus: Clade 2.3.4.4b, which was introduced in late 2021 in North America by wild birds and has spread throughout Latin America in 2022 and 2023. Avian influenza A(H5N1) viruses, especially those in gene group 2.3.4.4b, continue to diversify genetically and spread geographically. In addition, infection in wild and migratory birds has led to multiple separate incursions into domestic species. This virus circulation 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 *(20)*. Available sequences for the 2.3.4.4b gene cluster of avian and mammalian origin viruses indicate that markers associated with reduced susceptibility to antivirals are rare *(19)*.

Zoonotic influenza vaccine candidate viruses: WHO's Global Influenza Surveillance and Response System (GISRS), in collaboration with veterinary and animal health colleagues, regularly evaluates vaccine candidate viruses. Candidate influenza A/H5 vaccine viruses of genetic group 2.3.4.4b are determined. 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. Vaccine virus A/Astrakhan/3212/2020 is closely related to recently detected circulating influenza A/H5 strains *(19)*.

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Useful Links

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