

Risk Assessment for public health related to outbreaks caused by Highly Pathogenic Avian Influenza (HPAI) A(H5N1), clade 2.3.4.4b, in animal species in the Region of the Americas

20 September 2023

Risk assessment date: 20 September 2023¹

Overall risk
Regional
Low

Confidence in available information
Regional
Moderate

Criteria		Assessment		Risk	Rationale
		Likelihood	Consequences		
Potential risk to human health related to animal exposure	Regional	Unlikely	Minor	Low	<ul style="list-style-type: none"> Globally, sporadic detections of influenza A(H5N1) clade 2.3.4.4b virus have been reported in humans, but remain very rare, with 8 cases reported since December 2021. Infections in humans can cause severe illness with a high mortality rate. So far, human cases detected are mostly related to close contact with infected birds and contaminated environments.² In the Region of the Americas, to date and since the detection of the avian influenza A(H5N1) virus in the Americas in 2014, 3 cases have been reported in humans, all related to the current outbreak of HPAI A(H5N1) – Clade 2.3.4.4b in birds and mammals. Clinical symptoms have ranged from mild to severe and no deaths have been reported. Although the Highly Pathogenic Avian Influenza (HPAI) A(H5N1) - Clade 2.3.4.4b, has mainly affected wild and poultry birds, the recent increase of cases in mammals could suggest more exposure for humans. To date, there have been no known cases of transmission from mammals to humans. Cases of human infection with this virus have occurred after exposure to infected birds. Although there were some cases of human infection during past outbreaks of A(H5N1) in poultry worldwide, human infections have occasionally been reported to WHO since 1997 (see hazard assessment). There has been no known sustained person-to-person transmission of the HPAI A(H5N1) in any country in the region or globally. Six countries in the Region of the Americas have reported confirmed cases of HPAI (H5N1) in mammals (Argentina, Canada, Chile, the United States of America, Peru, and Uruguay). In the United States, more than 200 cases have been confirmed in 19 species, while red foxes and skunks are the most frequently affected in North America, and sea lions in South America. Sporadic infection in domestic cats with the other clades of A(H5N1) virus was confirmed in 2004 in Thailand; in 2006 in Iraq, Austria, and Germany; in 2012 in Israel; in December 2022 in France; in April 2023 in the United States; and in July 2023 in Italy. However, these cats likely became infected through close contact with infected poultry or infected poultry meat. The infection was also detected in dogs in Canada in April 2023³.

¹ This assessment includes the information available as of 20 September 2023.

² FAO, WHO, and WHOA declaration, Ongoing outbreaks of avian influenza in animals pose a risk to humans. July 12, 2023. Geneva: WHO; 2023. Available from: <https://www.who.int/news/item/12-07-2023-ongoing-avian-influenza-outbreaks-in-animals-pose-risk-to-humans>.

³ World Organisation for Animal Health. Avian influenza. Informes de situación, Influenza Aviar. Paris: WOA; 2023 (Cited on 20 September 2023). Disponible en: <https://www.woah.org/es/enfermedad/influenza-aviar/#ui-id-2>

					<ul style="list-style-type: none"> In June 2023, Poland reported unusual cat deaths to the World Organisation for Animal Health (WOAH). A total of 29 positive cases of influenza A (H5N1) were detected. There were 14 cats euthanized and 11 natural deaths. No associated human cases were reported.⁴ Additionally, cases have been reported in pets in North America (see exposure assessment section).
Risk of spreading among humans	Regional	Unlikely	Minor	Low	<ul style="list-style-type: none"> There is lack of evidence of mammal to mammal spread although there have been mass mortality events. Spread of the virus in birds and mammals may continue to increase according to the migratory pattern of birds from North America to South America. The spread is expected to be lowest in September, while beginning to increase in October, and peaking in February⁵.
Risk of insufficient control capacities with available resources for public health	Regional	Extremely Unlikely	Major	High	<ul style="list-style-type: none"> If the virus spreads among humans and sustained human to human transmission occurs the resources will be stretched. In a sustained human to human transmission scenario, some countries may be challenged to respond in a timely manner, including implementation of isolation measure, contact tracing, and clinical management. There is no approved vaccine to prevent human infection of influenza A(H5) virus. Candidate vaccines have been developed to prevent human infection with influenza A(H5) virus authorized for pandemic preparedness purposes only.

Background information

Hazard assessment

Highly pathogenic avian influenza (H5N1)
<p>Avian influenza (AI) is a highly contagious viral disease that affects both domestic and wild birds. Birds are the natural hosts of avian influenza viruses, however less commonly, avian influenza viruses have also been isolated from mammalian species as well as humans.</p> <p>Avian influenza is caused by influenza A viruses of the Orthomyxoviridae family, which are divided into multiple subtypes (i.e., H5N1, H5N3, H5N8, etc.), whose genetic characteristics evolve very rapidly. The disease occurs worldwide, but different subtypes are more prevalent in certain regions (1). Influenza viruses have two main surface antigens: hemagglutinin (H) and neuraminidase (N). There are many subtypes of H and N for poultry and birds, but historically Highly Pathogenic Avian Influenza viruses have been limited to H5 or H7 subtypes (2).</p> <p>In general, the multiple strains of avian influenza virus can be classified into two categories based on the severity of the disease in birds (particularly chickens): Low pathogenic avian influenza (LPAI), which typically causes few or no clinical signs and Highly Pathogenic Avian Influenza (HPAI) which can cause severe clinical signs and potentially high mortality rates (3).</p> <p>Animal influenza viruses are distinct from human seasonal influenza viruses and are not easily transmitted between humans. However, zoonotic influenza viruses (animal influenza viruses that can occasionally infect humans through direct or indirect contact) can cause illness in humans ranging from a mild upper respiratory tract infection (fever and cough) to rapid progression to severe pneumonia, acute respiratory distress syndrome, shock, and even death. Gastrointestinal symptoms such as nausea, vomiting, and diarrhea have been reported more frequently in A(H5N1) infection. Disease characteristics, such as incubation period, severity of symptoms, and</p>

⁴World Health Organization. Influenza A(H5N1) in cats – Poland [Internet]. Geneva: WHO; 2023. [cited 10 August 2023]. Available from: <https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON476>

⁵World Organisation for Animal Health. Global dynamics of highly pathogenic avian influenza outbreaks in poultry between 2005 and 2016. Paris: WOAH; 2023 (Cited 3 August 2023). Available from: <https://www.woah.org/app/uploads/2022/03/awada-et-al-2018-transboundary-and-emerging-diseases-2.pdf>

clinical outcome, vary depending on the virus causing the infection, but primarily manifest with respiratory symptoms (3).

Following an outbreak of the A(H5N1) virus in 1997 in poultry in the Hong Kong Special Administrative Region (SAR), China (People's Republic of), since 2003, this avian influenza virus has spread from Asia, Africa, Europe, and the Americas. Since its identification in China (People's Republic of) in 1996, there have been multiple waves of intercontinental transmission of the H5Nx Gs/GD lineage virus (4).

Avian influenza, which typically spreads among birds, has raised concerns due to an increase in cases of avian influenza A(H5N1) in mammals, which are genetically closer to humans than birds. Since 2020, a variant of the A(H5N1) virus belonging to the H5 2.3.4.4b clade has caused a significant number of deaths in birds, both wild and free-range, in Africa, Asia and Europe. This situation raises concerns about a possible adaptation of the virus to infect humans more effectively, since some mammals can act as reservoirs for the flu, which could lead to the emergence of new viruses that are more harmful to both animals and humans (5).

This variant expanded to North America in 2021 and then to Central and South America in 2022. During 2023, several countries, mostly in the Americas, reported outbreaks. Several episodes of mass deaths have been reported in wild birds due to the A(H5N1) clade 2.3.4.4b virus (3).

In the current epidemic season of HPAI, subtype A(H5N1)- clade 2.3.4.4b has been the most predominant, causing outbreaks in poultry, wild birds and mammals in Europe and America, as well as the appearance of some cases in humans.

Exposure assessment

On 12 July 2023, the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO) and the World Organization for Animal Health (WOAH) issued a joint statement in which they mentioned that the current outbreaks of avian flu have wreaked havoc on animal populations, particularly poultry, wild birds and some mammals, undermining farmers livelihoods as well as the food trade. Although these outbreaks mainly affect animals, they pose a constant risk to humans (5).

Whenever avian influenza viruses circulate in bird populations, particularly farmed birds, there is potential for occasional human infections due to contact with infected birds or contaminated environments. From 2003 to 14 July 2023, a total of 878 cases of influenza A(H5N1) infection in humans have been reported to the World Health Organization (WHO), with a record of 458 deaths (which represents a mortality rate of 52%) in 23 countries around the world (6).

The detection of outbreaks of Highly Pathogenic Avian Influenza (HPAI) in 15 countries in Latin America and the Caribbean region is an unprecedented situation. The foci of contagion identified are mostly in areas corresponding to the Pacific migratory route. To date and since the introduction of the avian influenza A(H5N1) – clade 2.3.4.4b virus in the Americas in 2014, three cases of human infection have been documented: the first occurred in the United States of America and was reported on 29 April 2022 (7); the second occurred in Ecuador and was reported on 9 January 2023 (8); finally, the third case was registered in Chile and was reported on 29 March 2023 (9).

Of the three confirmed human cases in the Region of the Americas, two of them had close contact with infected birds. In the United States case, the case participated in the slaughter of birds at a commercial poultry facility in Colorado, where the influenza A(H5N1) virus was detected in birds and no additional associated cases were reported (5). In Ecuador, the individual's case had been in contact with backyard birds acquired a week prior to the onset of symptoms. These birds subsequently died without any apparent cause, and there were no recorded associated cases (8).

Regarding the confirmed case in Chile, the epidemiological investigation indicated that the most plausible transmission was through environmental exposure, given the large number of dead wild birds and marine mammals infected with the HPAI A virus (H5N1) found in the area near the patient's home. The case's close contacts remained asymptomatic and tested negative for influenza viruses. This suggests that no human-to-human transmission has been documented (9).

In the Region of the Americas until epidemiological week (EW) 31 of 2023, the agricultural authorities of Argentina, Bolivia⁶, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Ecuador, Guatemala, Honduras, Mexico, Panama, Peru, the United States of America, Uruguay and Venezuela⁷ have detected HPAI A(H5N1) virus outbreaks in domestic birds, poultry and/or wild birds, and mammals (Table 1 and Table 2). Among the mammals identified, red foxes and skunks were the most frequently affected in North America, and sea lions in South America. Six countries in the Region have identified cases in mammals: Argentina, Canada, Chile, United States of America, Peru and Uruguay (10-82).

Table 1. Avian influenza outbreaks by infected animal type. Region of the Americas, up to EW 31 of 2023

Country	Wild birds	Poultry farm	Backyard poultry	Mammals
Argentina	Yes	Yes	Yes	Yes
Bolivia (Plurinational State of)	Yes	Yes	Yes	
Brazil	Yes		Yes	
Canada	Yes	Yes	Yes	Yes
Chile	Yes	Yes	Yes	Yes
Colombia	Yes		Yes	
Costa Rica	Yes			
Cuba	Yes			
Ecuador	Yes	Yes		
Guatemala	Yes			
Honduras	Yes			
Mexico	Yes	Yes		
Panama	Yes		Yes	
Peru	Yes	Yes	Yes	Yes
United States	Yes	Yes	Yes	Yes
Uruguay	Yes		Yes	Yes
Venezuela (Bolivarian Republic of)	Yes			

Source: Adapted from: Data reports to PAHO by the International Health Regulations (IHR) National Focal Points (NFP) or available from on the websites of the Ministries and Institutes of Health of the countries and territories of the Region.

Table 2. Mammals infected with avian influenza. Region of the Americas, up to EW 31 of 2023

Mammals	Canada	Chile	Peru	United States of America	Uruguay
<i>Canis latrans</i> (Coyote)				Yes	
<i>Canis lupus familiaris</i> (Domestic dog)	Yes				
<i>Cephalorhynchus eutropia</i> (Chilean dolphin)		Yes			
<i>Didelphis virginiana</i> (Virginia opossum)				Yes	
<i>Enhydra lutris</i> (Sea otter)		Yes			
<i>Felis silvestris catus</i> (Domestic cat)				Yes	
<i>Felis silvestris catus</i> (Feral cat)	Yes			Yes	
<i>Lontra felina</i> (Marine otter)		Yes		Yes	
<i>Lynx rufus</i> (Bobcat)				Yes	
<i>Martes americana</i> (Marten)				Yes	
<i>Mephitis mephitis</i> (Skunk)	Yes			Yes	
<i>Nasua nasua</i> (South American coati)					Yes
<i>Neovison vison</i> (Mink)	Yes				
<i>Otaria flavescens</i> (South American sea lion)		Yes	Yes		
<i>Panthera leo</i> (Lion)			Yes		
<i>Panthera pardus</i> (Leopard)				Yes	
<i>Panthera tigris</i> (Tiger)				Yes	
<i>Pekania pennanti</i> (Fisher)				Yes	
<i>Phoca vitulina</i> / <i>Halichoerus grypus</i> (Seal)	Yes			Yes	
<i>Phocaena spinipinnis</i> (Burmester's porpoise)		Yes			
<i>Procyon lotor</i> (Raccoon)	Yes			Yes	
<i>Puma concolor</i> (Cougar)				Yes	
<i>Tursiops truncatus</i> (Dolphin)			Yes	Yes	
<i>Ursus americanus</i> / <i>U. arctos horribilis</i> (Bear)	Yes			Yes	
<i>Vulpes vulpes</i> (Fox)	Yes			Yes	

Source: Adapted from: World Organisation for Animal Health (WOAH). Avian influenza. Paris: WOA; 2023 [Cited 20 September 2023]. Available from: <https://www.woah.org/en/disease/avian-influenza/#ui-id-2>

⁶ Plurinational State of Bolivia

⁷ Bolivarian Republic of Venezuela

In Europe, on 27 June 2023, Poland reported to WHO unusual cat deaths. Out of 47 samples taken from cats, 29 tested positive for influenza A (H5N1). Some cats were euthanized, and some died, but it is still unknown how they became infected. As of 12 July 2023, no human contact of infected cats reported symptoms. Based on the risk assessment carried out by the WHO, the risk of human infections following exposure to infected cats at the national level was assessed as low for the general population, and low to moderate for cat owners and those occupationally exposed to H5N1 infected cats (such as veterinarians) without the appropriate use of personal protective equipment (82).

Context assessment

Throughout the Region of the Americas, four main migratory routes of wild water birds have been described, crossing the entire continent from north to south (2): the Mississippi, Pacific, Western Atlantic and East Atlantic. These migration routes of waterbirds represent the greatest risk of spread of the AI virus, since in areas where these wild waterbirds congregate and where poultry are not kept in poultry houses with adequate biosecurity measures that isolate them from them, or prevent the contamination of their water or food, transmission of the virus can occur through contact with contaminated water or through direct contact between wild birds and poultry. HPAI A(H5N1) outbreaks follow the historical seasonal pattern of the virus, which shows that the spread is less intense in September but increases in October to reach its peak in February (3, 4, 5). This pattern may change, considering the new epidemiological scenario.

Currently, the countries of the Region of the Americas produce 20.4% of the poultry meat and 10% of the eggs consumed worldwide⁸. It is a sector of great development in the Region and of importance for the livelihood of millions of small and medium-sized agricultural producers and a source of protein for families in several countries of the Region (6). Brazil is the second largest producer of chicken meat in the world. In 2023 it would export almost 5 million tons of poultry meat, out of a global trade estimated at 14 million tons, which means that 35% of the export market belongs to it (83).

The current influenza A(H5N1) epidemic has resulted in high morbidity and mortality in backyard birds, such as hens, chickens and wild birds, which represents a real threat to animals and a potential threat to humans. According to the information included in the most recent epidemiological update of the Region of the Americas published by the Pan American Health Organization (PAHO), as of 20 September 2023, 17 countries in the Americas have registered cases of A(H5N1) in animals. The occurrence of influenza A (H5N1) outbreaks of this magnitude in Latin American countries is a situation that had previously not occurred in the region; although there have been cases of highly pathogenic avian influenza in previous years, mainly in North America, it had never had this degree of impact or spread in the rest of the region.⁹

Since the publication of the 19 November 2022 [epidemiological alert](#)¹⁰ by PAHO/WHO, which alerted on the increase in outbreaks of highly pathogenic avian influenza in poultry farms, backyard farms and in wild birds in countries of the Region of the Americas, only three detections of the A(H5N1) virus have been recorded in samples from people exposed or presumed directly exposed to infected birds or contaminated environments despite the high number of poultry outbreaks and potential human exposures to the virus at the human-animal-environment interface (84).

Three human cases were reported in the Region, in the United States, Ecuador and Chile, one each. All three cases presented moderate to severe symptoms, two of them (Ecuador and Chile) have been hospitalized. All recovered completely, and antiviral treatment was administered as part of the clinical management.

⁸ Food and Agriculture Organization of the United Nations - FAO launches Avian Influenza Emergency Preparedness Course. Rome: FAO; 2023 [Cited 20 September 2023]. Available from: <https://www.fao.org/americas/noticias/ver/en/c/1638378/>

⁹ Pan American Health Organization Epidemiological Update - Outbreaks of avian influenza caused by influenza A(H5N1) in the Region of the Americas - August 2023. Available from: <https://www.paho.org/en/documents/epidemiological-update-outbreaks-avian-influenza-caused-influenza-ah5n1-region-americas-0>

¹⁰ Epidemiological Update Outbreaks of avian influenza and public health implications in the Region of the Americas - 14 December 2022: <https://www.paho.org/en/documents/epidemiological-update-outbreaks-avian-influenza-and-public-health-implications-region>

Recently, there has been an increase in reports of transmission of the virus from wild birds to some mammal species in various countries in the American region. This suggests a high prevalence of the virus in bird populations in these regions. Nevertheless, there is still limited evidence of mutations associated with adaptation to mammals and humans, even when transmission in mammals has been documented. Increased detection of avian influenza A(H5N1) among mammals, which are biologically closer to humans than birds, is raising concerns that the virus may adapt to infect humans more easily. However, as of today, the risk of infection in humans remains low and sustained human-to-human transmission has not been reported.

Table 3: Strengths and vulnerabilities of the countries and territories of the Region of the Americas related to Highly Pathogenic Avian Influenza (HPAI) A(H5N1), August 2023.

Strengths	Vulnerabilities
<ul style="list-style-type: none"> • To enhance the early detection of unusual respiratory events, Member States have made concerted efforts to strengthen surveillance systems for influenza in both animals and humans. • Given the identification of HPAI foci in birds and mammals, animal and agricultural sector authorities have coordinated with the human health sector authorities for the exchange of information and the implementation of control actions. • Improved information systems in place to monitor the behavior of HPAI outbreaks in birds and other mammalian species. • Dissemination of regional epidemiological alerts and updates on a regular basis by PAHO. • Many Member States have robust public health systems that enable them to quickly detect and respond to disease outbreaks, including avian influenza. • Several countries in the region have advanced laboratories capacities to diagnose and characterize viral strains, which is crucial to identify the presence of HPAI. • Most Member States have epidemiological surveillance systems in place that monitor diseases in humans and animals, aimed to detect any unusual changes in disease patterns. • At the animal laboratory level, many countries have participated in interlaboratory performance rounds, generally obtaining good results. • High degree of collaboration among countries of the Region through organizations such as the Pan American Health Organization, facilitating the exchange of information and coordination in the event of outbreaks. • Some Member States have faced similar disease outbreaks in the past, giving them valuable experience in responding quickly and effectively to such situations. • Many countries have animal health authorities, training and resources to monitor animal health, which are 	<ul style="list-style-type: none"> • Wildlife surveillance in some countries is not well structured, which reduces sensitivity and early detection. • Difficulty in detecting HPAI outbreaks in a timely manner in territories with high geographic area or with low sensitivity and low capacity for early detection in backyards poultry owners. • Lack of a compensation policy for poultry slaughter in the event of avian influenza detection in many countries makes it difficult for poultry producers and keepers to notify its occurrence, harming sensitivity, and early detection. • Outbreaks in commercial and backyard poultry flocks, as well as infections in wild birds and certain mammals, may put some groups of people at higher risk of infection due to exposure to birds for work or recreation. • Limited laboratory diagnostic capacity in some countries to test suspected human cases and send samples to the WHO Collaborating Centre. • Although veterinary laboratories generally have a capacity to test samples, during emergency response the capacity can be compromised as there is a need to test large volumes of samples, with a potential of shortage of reagents and tests, and lack of human resources. • Lack of personnel in the official veterinary services of some countries which can compromise the emergency response capacity by causing saturation peaks at times of response to different tasks (manage of suspected cases contact monitoring at farms, control activities, quarantine, depopulation, disposal of dead animal, cleaning, and disinfection). • The contingency plans and capacity of many countries are not updated in accordance with the new methodologies for depopulation, which are more efficient and considerate of animal welfare;

<p>essential to prevent and control the spread of the disease at its source.</p> <ul style="list-style-type: none"> • Member States have improved their risk communication capacities over the years, which is essential to inform the public and take appropriate action in emergency situations. • Member States are updating their pandemic influenza response plans based on lessons from COVID-19 and the current A(H5N1) outbreak. • Support and strengthening activities by PAHO/WHO, mainly by the team of the Pan American Center for Foot-and-Mouth Disease and Veterinary Public Health (PANAFTOSA) and the Influenza teams, aimed at member countries: <ul style="list-style-type: none"> ○ Workshop on “Management of High Mortality in Animals in Avian Influenza Emergencies”, provided by the Pan American Center for Foot-and-Mouth Disease and Veterinary Public Health (PANAFTOSA). (85) ○ Regional consultation to strengthen intersectoral work in the human-animal influenza interface, representatives of the ministries of Health and Agriculture of Argentina, Brazil, Canada, Chile, Colombia, Ecuador, the United States, Guatemala, and Mexico, as well as PAHO and partners, developed a series of guidelines to mitigate the risk of transmission of avian influenza, which will be added to the PAHO’s recommendations and may be adopted by the countries of the region. (86) ○ Specifically in the animal component, PAHO has worked to strengthen surveillance by reviewing the strategies and training of personnel, supporting in decision-making in the response to the emergency, epidemiological monitoring, the characterization of the risk, and by creating diagnostic capacity in veterinary laboratories together with the regional WHOA reference laboratory in Campinas, Brazil. 	<p>and disposal of dead animals in a way that optimizes the inactivation of the pathogen while respecting the environment, such as through composting.</p> <ul style="list-style-type: none"> • Generally, managing real-time emergency information poses a challenge, impeding context-based decision-making. • Limited biosecurity measures in poultry farms, which can lead to the spread of the virus if outbreaks occur in these locations. This is particularly concern for small farms and backyard owners. • Lack of community engagement in prevention and control activities. • Limited capacity in some Member States to conduct joint risk assessments across sectors involved in the response. • Lack of integration in surveillance systems between different sectors for monitoring the situation in animals and cases in humans.
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