

Influenza at the human-animal interface

Summary and risk assessment, from 22 December 2023 to 26 February 2024¹

- New infections²: From 22 December 2023 to 26 February 2024, five human cases of infection with influenza A(H5N1) viruses, one human case of infection with an A(H5N6) influenza virus, one human infection with an A(H9N2) virus, one human case of infection with an A(H10N5) virus, and two human cases of infection with influenza A(H1N1) variant viruses were reported officially. Additionally, one human case of infection with an influenza A(H9N2) variant virus was detected.
- **Risk assessment:** The overall public health risk from currently known influenza viruses at the human-animal interface has not changed, and sustained human-to-human transmission of the viruses from these cases is currently considered unlikely. Although human infections with viruses of animal origin are unusual, they are not unexpected at the human-animal interface wherever these viruses circulate in animals.
- **Risk management:** New candidate vaccine viruses (CVVs) for zoonotic influenza viruses for pandemic preparedness purposes were selected through a recent WHO consultation.³
- IHR compliance: All human infections caused by a new influenza subtype are required to be reported under the International Health Regulations (IHR, 2005). This includes any influenza A virus that has demonstrated the capacity to infect a human and its haemagglutinin gene (or protein) is not a mutated form of those, i.e. A(H1) or A(H3), circulating widely in the human population. Information from these notifications is critical to inform risk assessments for influenza at the human-animal interface.

Avian Influenza Viruses

Current situation:

Avian influenza A(H5) viruses

A(H5N1), Cambodia

Since the last risk assessment of 21 December 2023, five human cases of infection with A(H5N1) influenza viruses were notified to WHO from Cambodia (see Table 1).

¹ This summary and assessment covers information confirmed during this period and may include information received outside of this period.

² For epidemiological and virological features of human infections with animal influenza viruses not reported in this assessment, see the reports on human cases of influenza at the human-animal interface published in the Weekly Epidemiological Record here.

³ World Health Organization. Genetic and antigenic characteristics of zoonotic influenza A viruses and development of candidate vaccine viruses for pandemic preparedness, February 2024. Available at: https://cdn.who.int/media/docs/default-source/influenza/who-influenza-recommendations/vcm-northern-hemisphere-recommendation-2024-2025/202402 zoonotic vaccinvirusupdate.pdf?sfvrsn=70150120 4

³ World Health Organization. Case definitions for the 4 diseases requiring notification to WHO in all circumstances under the International Health Regulations (2005). <u>Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005).</u>

The A(H5N1) viruses from the first four cases belong to the H5 haemagglutinin (HA) clade 2.3.2.1c. Viruses belonging to this clade have been detected in poultry since 2014 in Cambodia in longitudinal surveillance done in the animal health sector. Clade information on the virus from the last case reported in Kampot province has not yet been determined. Based on the phylogenetic patterns, the third and fourth cases were likely exposed to the same source, although the possibility of human-to-human transmission cannot be excluded. No further cases or evidence of sustained human-to-human transmission were reported.

Table 1. Human cases of influenza A(H5N1) reported to WHO from Cambodia from 26 January 2024 to 26 February 2024.

Onset date	WHO notification date	Reporting province	Age (years)	Hospitalization date	Outcome	Poultry exposure
13 January 2024	26 January 2024	Prey Veng	3	16 January 2024	Recovered	Contact with dead backyard chickens ⁵
21 January 2024	28 January 2024	Siem Reap	69	23 January 2024	Recovered	Raised domestic poultry and fighting cocks; three chickens were found to be A(H5N1)- positive ⁵
31 January 2024	9 February 2024	Kratie	10	8 February 2024	Deceased 8 February 2024	Contact with sick and dead backyard chickens
Asymptomatic; tested 10 February 2024	12 February 2024	Kratie	16	NR	NA	Contact with sick and dead backyard chickens; contact of 10- year-old case above
15 February 2024	21 February 2024	Kampot	17	17 February 2024	NR	Contact with dead backyard chickens

NA=not applicable; NR=not reported

A(H5N6), China

Since the risk assessment of 21 December 2023, one human case of infection with an A(H5N6) influenza virus was notified to WHO from China on 3 January 2024. A 59-year-old woman, with underlying comorbidities, from Sichuan province developed illness on 25 November 2023 and was hospitalized with severe pneumonia on 29 November. As of 9 January 2024, she was improving. She had exposure to a live poultry market. Environment samples from the market tested positive for influenza A(H5). No further cases were detected among her contacts.

According to reports received by the World Organisation for Animal Health (WOAH), various influenza A(H5) subtypes continue to be detected in wild and domestic birds in Africa, Asia, Europe and the Americas. Infections in non-human mammals are also reported.

⁵ World Health Organization. Disease Outbreak News. Influenza A(H5N1) – Cambodia, 8 February 2024. Available at: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON501

Risk Assessment:

1. What is the risk of additional sporadic human cases of infection with avian influenza A(H5) viruses?

Most human cases so far were sporadic infections in people exposed to A(H5) viruses through contact with infected poultry or contaminated environments, including live poultry markets. While the viruses continue to be detected in animals and related environments, further human cases among exposed individuals are expected but unusual. The impact for public health if additional sporadic cases are detected is minimal. The overall risk is low.

- 2. What is the likelihood of human-to-human transmission of avian influenza A(H5) viruses? No sustained human-to-human transmission was identified associated with the event described above. In the past, small clusters of A(H5) virus infections were reported, including those involving health care workers, but without evidence of sustained human-to-human transmission. Current epidemiological and virological evidence suggests that contemporary influenza A(H5) viruses have not acquired the ability of sustained transmission among humans. Human-to-human transmission is thus currently considered unlikely.
- **3.** What is the likelihood of international spread of avian influenza A(H5) viruses by travellers? Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely as current evidence suggests these viruses have not acquired the ability to transmit easily among humans.

Avian influenza A(H9) viruses

A(H9N2), China

Since the last risk assessment of 21 December 2023, two human cases of infection with A(H9N2) influenza viruses were notified to WHO from China.

On 22 February 2024, the International Health Regulations (IHR) Contact Point of Hong Kong SAR, China notified WHO of one human infection with avian influenza A(H9N2). A two-year-old girl had an onset of influenza-like illness (ILI) symptoms on 15 February 2024. She went to hospital on 16 February where a sample was collected, and she was not hospitalized at that time. She was admitted to the isolation ward of a public hospital and was in in stable condition at the time of reporting. According to the initial investigation, the patient visited Guangdong province during the incubation period. The patient has no known poultry exposure or consumption of undercooked poultry. One of her home contacts developed a sore throat on 17 February, but the symptoms subsided, and the contact was not sampled. Other home contacts remain asymptomatic. The epidemiological investigations are ongoing.

Additionally, one human case of infection with an influenza A(H9N2) virus was detected in China according to information received during the WHO Consultation and Information Meeting on the Composition of Influenza Virus Vaccines for Use in the 2024-2025 Northern Hemisphere Influenza Season held in February 2024.³ A six-year-old boy from Anhui province developed illness on 3 January 2024.

Avian influenza A(H9N2) viruses are enzootic in poultry in Asia and increasingly reported in poultry in Africa.

Risk Assessment:

1. What is the risk of additional sporadic human cases of infection with avian influenza A(H9N2) viruses?

Most human cases follow exposure to the A(H9N2) virus through contact with infected poultry or contaminated environments. Human infection tends to result in mild clinical illness in most cases. Since the virus continues to be detected in poultry populations, further human cases can be expected but remain unusual. The impact to public health if additional sporadic cases are detected is minimal. The overall risk is low.

- 2. What is the likelihood of human-to-human transmission of avian influenza A(H9N2) viruses? Prior to the event described above, only sporadic cases have been reported. Limited human-to-human transmission cannot be excluded. No sustained human-to-human transmission has been identified associated with the event described above. Current epidemiologic and virologic evidence suggests that contemporary influenza A(H9N2) viruses assessed by GISRS have not acquired the ability of sustained transmission among humans. Human-to-human transmission is thus currently considered unlikely.
- **3.** What is the likelihood of international spread of avian influenza A(H9N2) virus by travellers? Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely as current evidence suggests the A(H9N2) virus subtype has not acquired the ability to transmit easily among humans.

Avian influenza A(H10N5) viruses

A(H10N5), China

Since the last risk assessment on 21 December 2023, one human case of infection with an influenza A(H10N5) virus was reported from China. A 63-year-old female, with chronic comorbidities, from Anhui province developed fever, a cough and sore throat on 30 November 2023. She was admitted to hospital on 2 December, was transferred to a medical institution in Zhejiang province on 7 December and passed away on 16 December. Zhejiang Province health officials isolated seasonal influenza A(H3N2) subtype and avian influenza A(H10N5) subtype viruses from the patient's samples on 22 January after nucleic acid testing, viral culture and gene sequencing conducted by local health care facilities.

The patient had exposure to live poultry through the purchase of a duck on 26 November. From the duck meat stored in the fridge, seven samples tested positive for influenza A(H10N5), and two samples were positive for N5 (no result for haemagglutinin). The agricultural authority has conducted culling and hazard management of the ducks which tested positive for A(H10N5) in a traceback investigation and has carried out disinfection of affected areas. The patient had no contact with pigs or other mammals. Environmental samples collected from her home tested negative for influenza viruses. Monitoring of close contacts did not identify any further cases.

This is the first case of human A(H10N5) infection detected in China and globally.

Risk Assessment:

1. What is the likelihood that additional human cases of infection with avian influenza A(H10N5) viruses will occur?

This is the first human infection with avian influenza A(H10N5) to be detected. Human infections with avian influenza A(H10) viruses have been detected and reported previously. The extent of circulation and epidemiology of these viruses in birds is unclear. Avian influenza A(H10) viruses with

different genetic characteristics have been detected previously in migratory and other wild birds since the 1970s. While the viruses continue to be detected in animals and related environments, further human cases among exposed individuals are expected but unusual. The impact for public health if additional sporadic cases are detected is minimal. The overall risk is low.

- 2. What is the likelihood of human-to-human transmission of avian influenza A(H10N5) viruses? No human-to-human transmission was identified associated with the event described above. Current epidemiological and virological evidence suggests that contemporary influenza A(H10) viruses have not acquired the ability of sustained transmission among humans. Human-to-human transmission is thus currently considered unlikely.
- **3.** What is the likelihood of international spread of avian influenza A(H10N5) virus by travellers? Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely based on current limited evidence.

Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely based on current limited evidence.

Swine Influenza Viruses

Current situation:

Since the risk assessment of 21 December 2023, one human infection with an influenza A(H1N1) variant virus [A(H1N1)v] was reported from Brazil and one was reported from Spain.

A(H1N1)v, Brazil

On 16 January 2024, Brazil notified WHO of a laboratory-confirmed human infection with swine-origin influenza A(H1N1)v virus, in the State of Paraná. The patient, an adult male who had underlying medical conditions, developed ILI symptoms on 12 December 2023 and was hospitalized on 16 December. He had no history of exposure to pigs. He did not receive antiviral treatment but fully recovered on 18 December, when he was discharged from the hospital. From the epidemiological investigation, no close contacts were identified.

A sample was sent on 19 December to the Central Public Health Laboratory of the State of Paraná for analysis of influenza and SARS-CoV-2. The sample was subtyped as influenza A/H1 virus by real-time polymerase chain reaction (RT-PCR). On 11 January 2024, the sample was sent for confirmation to the National Influenza Center (NIC), National Reference Laboratory for respiratory viruses of FIOCRUZ, Rio de Janeiro, where on 15 January 2024, influenza A (H1N1) variant virus was confirmed.

According to the sequencing results, the virus shares 99% similarity with the A/Paraná/ 20675/2022 (A/H1N1pdm09-like) virus previously detected in a human case from Paraná in October 2022. On 1 February, the NIC sent the sample to the US Centers for Disease Control and Prevention (US CDC) Influenza Division – a WHO Collaborating Centre (CC) for Surveillance, Epidemiology, and Control of Influenza – for further characterization.

This is the first human infection caused by an influenza A(H1N1)v virus reported in Brazil in 2024, and the ninth case of a human infection with a swine variant virus reported in the state of Paraná, Brazil, since 2015.⁶

⁶ World Health Organization. Disease Outbreak News. Influenza A (H1N1) variant virus – Brazil, 7 February 2024. Available at: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON502.

A(H1N1)v, Spain

On 29 January 2024, the Spanish health authorities notified WHO of a laboratory confirmed human case of infection with swine-origin influenza A(H1N1)v virus, in the province of Lleida (Cataluña autonomous community). An adult male adult male, who worked on a pig farm in the province of Lleida, developed ILI symptoms on 25 November 2023. He sought medical care at an outpatient clinic on 29 November and was seen again twice in December 2023, where he was diagnosed with bronchitis. He did not receive antiviral treatment and has completely recovered.

A sample collected on 12 December tested positive for an influenza A virus at the laboratory of the regional hospital on 14 December 2023 but could not be subtyped. The sample was subsequently sent to a national surveillance network lab for sequencing, where swine influenza A(H1N1) virus was identified and notified to the General Sub-Directorate for Surveillance and Response to Public Health Emergencies of Catalonia on 10 January 2024. The sample was sent for confirmation to the National Institute of Microbiology on 19 January and the virus isolate will also be shared with the WHO Collaborating Centre for Reference and Research on Influenza at the Francis Crick Institute in London, United Kingdom. Including the current case, three cases of human infection with influenza A(H1N1)v virus have been reported in Spain.⁷

Risk Assessment:

- 1. What is the risk of additional sporadic human cases of infection with swine influenza viruses? Swine influenza viruses circulate in swine populations in many regions of the world. Depending on geographic location, the genetic characteristics of these viruses differ. Most human cases are exposed to swine influenza viruses through contact with infected animals or contaminated environments. Human infection tends to result in mild clinical illness in most cases. Since these viruses continue to be detected in swine populations, further human cases can be expected but remain unusual. The impact to public health if additional sporadic cases are detected is minimal. The overall risk is low.
- 2. What is the likelihood of human-to-human transmission of swine influenza viruses? No human-to-human transmission was identified associated with the event described above. Current evidence suggests that contemporary swine influenza viruses have not acquired the ability of sustained transmission among humans. Human-to-human transmission is thus currently considered unlikely.
- **3.** What is the likelihood of international spread of swine influenza viruses by travelers? Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely as current evidence suggest that these viruses have not acquired the ability to transmit easily among humans.

For more information on A(H5), A(H9N2), A(H10) and A(H1)v viruses, see the report from the WHO Consultation on the Composition of Influenza Virus Vaccines for Use in the 2024-2025 Northern Hemisphere Influenza Season held on 19-22 February 2024 at the following link: Genetic and antigenic characteristics of zoonotic influenza A viruses and development of candidate vaccine viruses for pandemic preparedness, February 2024.

Overall Risk Management Recommendations:

⁷ World Health Organization. Disease Outbreak News. Influenza A(H1N1) variant virus – Spain, 9 February 2024. Available at https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON503.

- WHO does not advise special traveller screening at points of entry or restrictions with regards to
 the current situation of influenza viruses at the human-animal interface. For recommendations
 on safe trade in animals and related products from countries affected by these influenza viruses,
 refer to WOAH guidance.
- Given the observed extent and frequency of avian influenza in poultry, wild birds and some wild
 mammals, the public should avoid contact with animals that are sick or dead from unknown
 causes, including wild animals, and should report dead birds and mammals or request their
 removal by contacting local wildlife or veterinary authorities. Eggs, poultry meat and other
 poultry food products should be properly cooked and properly handled during food preparation.
- WHO advises that travellers to countries with known outbreaks of animal influenza should avoid farms, contact with animals in live animal markets, entering areas where animals may be slaughtered, or contact with any surfaces that appear to be contaminated with animal excreta. Travelers should also wash their hands often with soap and water. All individuals should follow good food safety and hygiene practices.
- Due to the constantly evolving nature of influenza viruses, WHO continues to stress the importance of global surveillance to detect virologic, epidemiologic and clinical changes associated with circulating influenza viruses that may affect human (or animal) health. Continued vigilance is needed within affected and neighbouring areas to detect infections in animals and humans. Collaboration between the animal and human health sectors is essential. As the extent of influenza viruses circulation in animals is not clear, epidemiologic and virologic surveillance and the follow-up of suspected human cases should continue systematically. Guidance on investigation of non-seasonal influenza and other emerging acute respiratory diseases has been published on the WHO website here: https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2018.2.
- Vigilance for the emergence of novel influenza viruses of pandemic potential should be
 maintained at all times including during a non-influenza emergency. In the context of the cocirculation of SARS-CoV-2 and influenza viruses, WHO has developed practical guidance for
 integrated surveillance. The guidance is available here:
 https://www.who.int/publications/i/item/WHO-2019-nCoV-Integrated sentinel surveillance-2022.1
- All human infections caused by a new subtype of influenza virus are notifiable under the International Health Regulations (IHR, 2005). State Parties to the IHR (2005) are required to immediately notify WHO of any laboratory-confirmed case of a recent human infection caused by an influenza A virus with the potential to cause a pandemic Evidence of illness is not required for this report.
- It is critical that these influenza viruses from animals or from people are fully characterized in appropriate animal or human health influenza reference laboratories. Under WHO's Pandemic Influenza Preparedness (PIP) Framework, Member States are expected to share influenza viruses with pandemic potential on a **timely basis**¹¹ with the Global Influenza Surveillance and Response System (GISRS), a WHO-coordinated network of public health laboratories. The viruses are used

⁸ World Health Organization. <u>Case definitions for the four diseases requiring notification in all</u> circumstances under the International Health Regulations (2005).

⁹ World Health Organization. Manual for the laboratory diagnosis and virological surveillance of influenza (2011). Available at: https://apps.who.int/iris/handle/10665/44518

¹⁰ World Health Organization. Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits, 2nd edition. Available at: https://iris.who.int/handle/10665/341850

¹¹ World Health Organization. Operational guidance on sharing influenza viruses with human pandemic potential (IVPP) under the Pandemic Influenza Preparedness (PIP) Framework (2017). Available at: https://apps.who.int/iris/handle/10665/25940

- by the public health laboratories to assess the risk of pandemic influenza and to develop candidate vaccine viruses.
- When there has been human exposure to a known outbreak of an influenza A virus in domestic poultry, wild birds or other animals or when there has been an identified human case of infection with such a virus enhanced surveillance in potentially exposed human populations becomes necessary. Enhanced surveillance should consider the health care seeking behaviour of the population, and could include a range of active and passive health care and/or community-based approaches, including: enhanced surveillance in local influenza-like illness (ILI)/severe acute respiratory infection (SARI) systems, active screening in hospitals and of groups that may be at higher occupational risk of exposure, and inclusion of other sources such as traditional healers, private practitioners and private diagnostic laboratories.
- The Tool for Influenza Pandemic Risk Assessment (TIPRA) provides an in-depth assessment of risk associated with some zoonotic influenza viruses notably the likelihood of the virus gaining human-to-human transmissibility, and the impact should the virus gain such transmissibility. TIPRA maps relative risk amongst viruses assessed using multiple elements. The results of TIPRA complement those of the risk assessment provided here, and those of prior TIPRA analyses will be published at http://www.who.int/teams/global-influenza-programme/avian-influenza/tool-for-influenza-pandemic-risk-assessment-(tipra).

Links:

WHO Human-Animal Interface web page

https://www.who.int/teams/global-influenza-programme/avian-influenza

WHO Influenza (Avian and other zoonotic) fact sheet

https://www.who.int/news-room/fact-sheets/detail/influenza-(avian-and-other-zoonotic)

WHO Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2018.2

WHO Public health resource pack for countries experiencing outbreaks of influenza in animals:

https://www.who.int/publications/i/item/9789240076884

Cumulative Number of Confirmed Human Cases of Avian Influenza A(H5N1) Reported to WHO

https://www.who.int/teams/global-influenza-programme/avian-influenza

Avian Influenza A(H7N9) Information

https://www.who.int/teams/global-influenza-programme/avian-influenza/avian-influenza-a-(h7n9)-virus

World Organisation of Animal Health (WOAH) web page: Avian Influenza

https://www.woah.org/en/home/

Food and Agriculture Organization of the United Nations (FAO) webpage: Avian Influenza

https://www.fao.org/animal-health/avian-flu-qa/en/

OFFLU

http://www.offlu.org/