Influenza at the human-animal interface
Summary and risk assessment, from 15 July to 30 August 2023

- **New infections**: From 15 July to 30 August 2023, one human case of infection with an influenza A(H1N2) variant virus, one human case of infection with an influenza A(H3) variant virus, one human case of infection with an influenza A(H5N6) virus, and one human case of infection with an influenza A(H9N2) virus were reported officially.

- **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.

- **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**

Since the risk assessment of 14 July 2023, one human case of infection with an influenza A(H5N6) virus was reported from China on 23 August 2023. A 27-year-old female farmer from Chongqing had an onset of illness on 16 July 2023 and was hospitalized on 21 July in severe condition with pneumonia. She had exposure to a farmed poultry environment in Sichuan province. Environmental samples collected from the around the case’s residence tested positive for avian influenza A(H5N6) virus. No family members had developed symptoms at the time of reporting.

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. The Food and Agriculture

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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. Case definitions for the 4 diseases requiring notification to WHO in all circumstances under the International Health Regulations (2005). Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005).
Organization of the United Nations (FAO), WHO, and WOAH released a situation analysis on the public health risk of ongoing avian influenza outbreaks in animals.

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 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 and 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?
Even though small clusters of A(H5) virus infections were reported in the past, including those involving health care workers, so far, epidemiological and virological evidence suggests that influenza A(H5) viruses have not acquired the ability of sustained transmission among humans. No human-to-human transmission was reported in the event described above. 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 evidence suggests these viruses have not acquired the ability to transmit easily among humans.

Avian influenza A(H9N2) viruses
Since the last risk assessment on 14 July 2023, one human case of influenza A(H9N2) virus infection was reported from China. On 14 July 2023, China notified WHO of one laboratory-confirmed A(H9N2) virus infection in a 59-year-old man with underlying conditions from Guangxi province. He had onset of illness on 22 June 2023, was detected through routine influenza-like illness surveillance. He was hospitalized with pneumonia on 25 June and has recovered. He had suspected exposure to a backyard poultry although environmental samples tested negative for influenza A(H9) viruses. No further cases have been reported among family members. 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 and 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?
Currently only sporadic cases have been reported. No case clusters have been reported and no human-to-human transmission was reported in the event described above. Current epidemiologic and virologic evidence suggests that 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 the A(H9N2) virus subtype has not been confirmed to have acquired the ability to transmit easily among humans.

Swine Influenza Viruses

Current situation:
Since the last risk assessment on 14 July 2023, two human cases of influenza variant virus infections were reported from the United States of America (USA).

Influenza A(H1N2) variant viruses [A(H1N2)v]
On 4 August 2023, the USA notified WHO of a human infection with an influenza A(H1N2) variant virus identified in the State of Michigan. An individual under 18 years of age developed respiratory illness on 29 July 2023. On 29 July, the case sought medical care at an emergency department, and an upper respiratory tract specimen was collected on 30 July. The specimen tested positive for influenza A virus on the same day.

On 31 July, the specimen was tested at the Michigan Department of Health and Human Services (MDHHS), and RT-PCR results were positive for influenza A virus but lacked reactivity with diagnostic tests for contemporary human influenza viruses representing either (H1) pdm09 or (H3) subtypes. The specimen was then sent to the US Centers for Disease Control and Prevention (CDC) for further testing and RT-PCR analysis of the specimen indicated an influenza A(H1N2) variant (v) virus on 2 August. Sequence analyses identified the virus as belonging to clade 1B.2.1 and confirmed that the virus was closely related to influenza A(H1N2) viruses found in pigs at agricultural fair settings in the USA. The virus was isolated, and antigenic testing demonstrated cross-reactivity of the virus with ferret antisera raised to a recently developed clade 1B.2.1 candidate vaccine virus.

The case was not hospitalized. Investigation by local public health officials identified swine exposure by the patient at an agricultural fair within 10 days prior to illness onset. Additional investigation did not identify respiratory illness in any of the patient’s close contacts or household contacts. No additional cases were identified related to this agriculture fair. No person-to-person transmission of influenza A(H1N2)v virus associated with this case has been identified. No additional cases of human infection with A(H1N2)v virus have been identified as of 10 August 2023.

Influenza A(H3) variant viruses [A(H3)v]
On 1 August 2023, the USA notified WHO of one human case of infection with an influenza A(H3)v virus also identified in the state of Michigan. The case, under 18 years of age, developed mild respiratory illness on 17 July 2023 and sought healthcare on 19 July, when an upper respiratory tract sample was collected. An initial sample was influenza A-positive, and the case was treated with antivirals, was not hospitalized, and has recovered. The case had exposure to swine in the 10 days before illness onset at an agricultural fair where influenza A virus was detected in swine.

A subsequent sample collected on 21 July tested influenza A(H3)v presumptive positive at the Michigan Department of Health and Human Services (MDHHS) but with high Ct values indicating a low level of viral RNA. This sample was submitted to the US CDC for further characterization. On 27
July, results from testing at the CDC were inconclusive. This was, nonetheless, reported as a case of human infection with a variant influenza A virus given the information available.

No further instances of respiratory illness in the case’s contacts were detected and no additional human infections with A(H3)v viruses associated with this case were identified.

**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 and 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 reported in the event described above. Current evidence suggests that these 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 these viruses have not acquired the ability to transmit easily among humans.

**Overall Risk Management Recommendations:**

- **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 cases in 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 wild 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 co-circulation 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).\(^4\) State Parties to the IHR (2005) are required to immediately notify WHO of any laboratory-confirmed\(^5\) case of a recent human infection caused by an influenza A virus with the potential to cause a pandemic\(^6\). 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\(^7\) with the Global Influenza Surveillance and Response System (GISRS), a WHO-coordinated network of public health laboratories. The viruses are used by the public health laboratories to assess the risk of pandemic influenza and to develop candidate vaccine viruses.

- 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 soon 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(HSN1) 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

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\(^4\) World Health Organization. *Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005).*


\(^6\) World Health Organization. Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits. Available at: https://apps.who.int/iris/handle/10665/44796

\(^7\) 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
World Organisation of Animal Health (WOAH) web page: Avian Influenza
https://www.woah.org/en/home/

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

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