**Influenza at the human-animal interface**

Summary and risk assessment, from 25 April to 31 May 2023[1]

- **New infections[2]:** From 25 April to 31 May 2023, one human case of infection with an influenza A(H1N2) variant virus, two human cases with positive influenza A(H5N1) detections, one human case of infections 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 the likelihood of sustained human-to-human transmission of these viruses remains low. Human infections with viruses of animal origin are expected 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).[3] 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

In mid-May, the United Kingdom of Great Britain and Northern Ireland reported to the World Health Organization (WHO) the detection of avian influenza A(H5) virus in a poultry worker at a farm in England where poultry was infected with high pathogenicity avian influenza (HPAI) A(H5N1) viruses. Another detection was reported in a second individual performing culling operations on the farm. Both detections were later confirmed by additional testing as A(H5N1). Both cases were asymptomatic and detected as part of an ongoing enhanced surveillance study of asymptomatic workers exposed to poultry infected with avian influenza. Work to determine whether these are infections or not (i.e., could instead be due to transient mucosal contamination of the nose with virus particles) is underway, though it may be difficult to reach a conclusion.

[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).

All the workers at this farm and their contacts have been identified; none of the contacts have reported symptoms, and no other influenza cases have been identified. The United Kingdom Health Security Agency (UKHSA) has not detected evidence of human-to-human transmission.

Based on the available information, WHO considers these as sporadic detections of avian influenza viruses among humans with no evidence of person-to-person transmission to date. More information is available here: https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON468.

On 24 May 2023, China reported a case of human infection with an influenza A(H5N6) virus in a 54-year-old woman from Sichuan province who developed symptoms on 19 May 2023 and was hospitalized the same day with severe pneumonia. She had exposure to backyard poultry. No further cases were suspected among family members 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.

### Risk Assessment:

**1. What is the likelihood that additional human cases of infection with avian influenza A(H5) viruses will occur?**
The overall risk assessment is unchanged. Most human cases were sporadic infections exposed to A(H5) viruses through contact with infected poultry or contaminated environments, including live poultry markets. Since the viruses continue to be detected in animals and related environments, further human cases can be expected. In some cases, the confirmation of infection with influenza A(H5) versus transient contamination of the nasopharynx/oropharynx with virus particles after exposure to infected birds or contaminated environment remains inconclusive.

**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, current epidemiological and virological evidence suggests that influenza A(H5) viruses have not acquired the ability of sustained transmission among humans, thus the likelihood is low.

**3. What is the risk 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.

A preliminary Food and Agriculture Organization of the United Nations (FAO)/WHO/WOAH joint rapid risk assessment on human infections with influenza A(H5N1) viruses in Cambodia was recently published following the report of two human infections.[4]

### Avian influenza A(H9N2) viruses

Since the last risk assessment on 24 April 2023, one human case of influenza A(H9N2) virus infection was reported from China.

[4] World Health Organization. Preliminary FAO/WHO/WOAH Joint Rapid Risk Assessment - Human infection with influenza A(H5N1), Cambodia (2023). https://www.who.int/publications/m/item/human-infection-with-influenza-a(h5n1)-cambodia-(2023).

On 19 May 2023, China notified WHO of one laboratory-confirmed A(H9N2) virus infection in a seven-month-old boy from Jiangxi province. He had onset of mild illness on 1 May 2023, was detected through routine influenza-like illness surveillance and was not hospitalized. He had suspected exposure to backyard poultry. No further cases have been reported among family members. Human cases of infection with avian influenza A(H9N2) viruses were last reported by China in March 2023.

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

### Risk Assessment:

**1. What is the likelihood that additional human cases of infection with avian influenza A(H9N2) viruses will occur?**
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.

**2. What is the likelihood of human-to-human transmission of avian influenza A(H9N2) viruses?**
No case clusters have been reported. Current epidemiologic and virologic evidence suggests that influenza A(H9N2) viruses assessed by GISRS have not acquired the ability of sustained transmission among humans, thus the likelihood is low.

**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:

### Influenza A(H1N2) variant viruses [A(H1N2)v]

Since the last risk assessment on 24 April 2023, information on one human case of infection with an influenza A(H1N2)v virus was received from TCDC on 11 May 2023.

A 16-year-old female student with no recent history of traveling abroad influenza-like illness symptoms 13 March. She visited a paediatric clinic on 14 March and tested positive for influenza A through a rapid test. She was prescribed oseltamivir, and her symptoms subsided on 16 March. This clinic is one of the sentinel clinics for the surveillance of respiratory pathogens in the community. A nasopharyngeal swab was sent to a reference laboratory for additional testing. The respiratory isolate was confirmed to be an influenza A(H1N2)v virus of swine origin on 21 April.

Based on sequence analysis, the haemagglutinin (HA) gene and the neuraminidase (NA) gene showed that this isolate, designated A/Taiwan/1/2023 (H1N2)v, is a novel reassortant virus containing hemagglutinin (HA) and neuraminidase (NA) gene segments derived from swine influenza A(H1N2) viruses, which may have been circulating locally for decades. The other six internal genes are from human influenza A(H1N1)pdm09 viruses. The HA (H1) belongs to influenza clade 1A, Eurasian Avian-like, and shares a similarity of 94% to A/Taiwan/2021 (H1N2)v. No amino acid

mutations in the NA protein were found that are associated with resistance to neuraminidase inhibitors, indicating that the virus is still susceptible to neuraminidase inhibitors.

The case had contact with poultry and pigs at the farm associated with her school. The pigs at the farm tested negative for influenza. No other students developed influenza-like illness symptoms. One contact developed influenza-like illness symptoms but tested negative for influenza and COVID-19. Three family members did not have influenza-like symptoms and tested negative on serological testing.

## Risk Assessment:

**1. What is the likelihood that additional human cases of infection with swine influenza viruses will occur?**
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.

**2. What is the likelihood of human-to-human transmission of swine influenza viruses?**
Current evidence suggests that these viruses have not acquired the ability of sustained transmission among humans, thus the likelihood is low.

**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.
- 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.

- In the current COVID-19 pandemic, vigilance for the emergence of novel influenza viruses of pandemic potential should be maintained. WHO has developed practical guidance for integrated surveillance in the context of the cocirculation of SARS-CoV-2 and influenza viruses. 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).[5] State Parties to the IHR (2005) are required to immediately notify WHO of any laboratory-confirmed[6] case of a recent human infection caused by an influenza A virus with the potential to cause a pandemic[7]. 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 regular and **timely basis**[8] 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
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/

[5] World Health Organization. Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005).
[6] World Health Organization. Manual for the laboratory diagnosis and virological surveillance of influenza (2011). Available at: https://apps.who.int/iris/handle/10665/44518
[7] 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
[8] 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

Food and Agriculture Organization of the UN (FAO) webpage: Avian Influenza
https://www.fao.org/animal-health/avian-flu-qa/en/
OFFLU
http://www.offlu.org/