Risk Assessment

H5N1 Scenario-Based Human Health Risk Assessment

Summary: H5N1 Scenario-Based Human Health Risk Assessment for the United States as of August 5, 2024

Due to recent events, the Center for Outbreak Response Innovation (CORI) judges that the ongoing H5N1 outbreak in cattle, poultry, and other animals is now within Scenario 3, *meaning the virus is infecting multiple animal species that facilitate the mixing and spreading of influenza viruses, increasing the likelihood that the virus reassorts with other influenza viruses and adapts to humans.*

This judgment is based on the widespread occurrence of H5N1 infections among cattle herds in more than one-fifth of US states since March 2024, continued reports of human H5 avian flu infections among dairy workers and poultry workers, and continued reports from the US Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS) of H5N1 in other mammalian species (domestic cats, racoons, foxes, mice, and others). In addition new information from USDA and early access articles in *Nature* regarding the potential for cow-to-cow and cross-species transmission, provide mounting evidence indicating potential for airborne transmission, and evidence of potentially undetected H5 human cases among farmworkers which have contributed to this risk analysis. *See a detailed risk assessment analysis beginning on the next page.*

	Risk to farm workers	Risk to other people in contact with affected workers and animal populations	Risk to healthcare workers	Risk to the US general public
Scenario 3 – Increased potential for reassortment and human adaptation, still no human-to-human transmission	Moderate-High	Moderate	Low	Low

Our **confidence** in these risk scores remains low, as the level of testing conducted in cattle, and other animals, and humans is limited, and several key studies remain as either preprint or early access, meaning peer review and/or final edits have not been completed. To decrease the risk to human health in the current situation we recommend:

- Farm workers diligently use personal protective equipment (PPE) when working directly with or closely to cattle, poultry, infected animals, and potentially infected environments.
- Increased diagnostic testing in cattle and other farm animals, continued genomic surveillance of human and cattle cases, separation of infected cattle from other animals, and stringent control of potentially infected food products.
- Information sharing between the agricultural and public health sectors to increase transparency and monitor for increases in human transmission.
- Increased diagnostic testing and serosurveillance of animal farm workers and broadened public health surveillance for H5N1 cases in surrounding communities.

- Enhanced communication with the public about the situation and the measures being taken to address it.

HPAI A(H5N1) Scenario-Based Human Health Risk Assessment for the United States Center for Outbreak Response Innovation (CORI) Updated as of August 5, 2024

Since the last update on July 22, 2024:

- ***Due to continued, widespread transmission of H5N1 among cattle, continued reports of H5 avian flu human cases among dairy cattle and poultry workers, mounting evidence for cross-species and cow-to-cow transmission, and new evidence indicating potential for airborne transmission,*** CORI judges that the H5N1 outbreak in cattle is now within Scenario 3, meaning that the risk to the general public and healthcare workers is low, but the risk to farm workers is moderate to high and the risk to other people in contact with affected workers and animal populations is moderate. Overall opportunity for adaptation of H5N1 to efficiently spread among humans appears to be increasing.
- On July 25, 2024, CDC reported 3 new human cases of H5 bird flu in Colorado workers involved in a poultry egg operation at a second Colorado farm, bringing the total to 13 human cases of H5N1 (four from affected cows and nine from affected poultry) since April 2024. The states reporting human cases associated with the current H5N1 outbreak in US poultry and dairy farms include Texas, Michigan, and Colorado.
- The US Department of Agriculture Animal Plant Health Inspection Service (USDA APHIS) is now reporting a total of 179 confirmed cases in dairy cattle across 13 states, 37 of which have occurred across 7 states in the last 30 days.
- A new early access article in *Nature* reports genomic and epidemiologic evidence of cow-to-cow and cross-species transmission of H5N1 between birds, domestic cats, and racoons on a dairy farm, adding to the weight of evidence indicating broader potential for future viral adaptation, potentially to facilitate human infection and transmission.
- New information from USDA and an early access article in *Nature* indicate that airborne transmission between mammals is possible and may include airborne transmission to humans, although this is not believed to be the primary source of transmission.
- A seroprevalence study completed by the University of Texas and published as an early access article indicates previously ill farm workers on two farms affected by H5N1 may have been infected with H5N1 without detection by existing testing and surveillance system, lending credence to concerns about underreporting due to minimal surveillance measures. Initial findings from a CDC seroprevalence study completed in Michigan, which showed no evidence of prior H5N1 infection among farm workers at affected farms. CDC continues to support seroprevalence studies in Michigan and Colorado.
- To align with other risk assessments developed by CORI, the risk scores for this assessment has been updated to a five-level scale, assessing the risk to populations as either low, low-moderate, moderate, moderate-high, or high. Due to this change, the risk

level "very low" has been removed and the risk to healthcare workers and the general public for the scenarios 1 and 2 have changed from "very low" to "low". Please note, this change does not reflect a change in actual risk.

Highly pathogenic avian influenza (HPAI) A(H5N1) clade 2.3.4.4b viruses began circulating in Europe, Africa, and Asia in 2020, leading to an unprecedented number of deaths in wild birds and poultry. In 2021 and 2022, the virus spread across the globe, reaching North, South, and Central America. In 2023, the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO), and the World Organization for Animal Health (WOAH) released a joint report regarding the increasing cases of land and sea mammals infected with A(H5N1) clade 2.3.4.4b, including outbreaks with high mortality. The US Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS) began tracking the ongoing panzootic in wild birds and poultry in the US in 2022, and now reports detections in nearly 10,000 wild birds and over 100 million poultry. In March 2024, A(H5N1) clade 2.3.4.4b was detected for the first time in dairy cattle in the US. Since then, the virus has been detected in nearly 200 cattle herds across more than one-fifth of US states and more than a dozen farm workers have tested positive for H5N1. To date, all human cases in the US have been mild, with conjunctivitis (eye redness/pink eye) and mild respiratory symptoms being most common, and there has been no documented human-to-human transmission. Based on sequenced human samples, CDC currently reports there are no markers of antiviral resistance and candidate vaccine viruses (CVVs) are expected to provide protection.

Notably, however, the risks to human health from this outbreak are highly uncertain because of a current lack of surveillance data and other basic scientific and epidemiological information. The situation is complex and may change rapidly. Risk assessment can be very helpful in times of significant uncertainty because it enables structured consideration of complex scenarios, likelihoods, and consequences to inform decisions around policy and operational action, as well as implementation of protective measures and future planning for worst-case scenarios. It is important not to wait for perfect information to estimate potential risk, because decisions must be made even in the absence of plentiful data.

Therefore, the Center for Outbreak Response Innovation (CORI) conducted a scenario-based risk assessment to consider human health risks both now and in potential future scenarios. We will update this assessment as additional data become available.

*__Please note:__ We are evaluating the risks to human health should each scenario occur, **not** the relative risk of any one scenario occurring.

Features that would characterize each scenario include:

Scenario 1 – Minimal spread in cattle: The virus is predominantly infecting cattle and there is minimal spread within herds and to other animals. Likelihood of widespread

human infections is low. Population health consequences are low. Overall risk to human health in this scenario is low.

Scenario 2 – Widespread transmission in cattle, few human infections, no human-to-human transmission: The virus is predominantly infecting cattle but spreads widely within herds. There is also occasional cow-to-human transmission but no human-to-human transmission. Likelihood of widespread human infections is low. Population health consequences are low. Overall risk is low, but population-specific risk is increased for farm workers.

Scenario 3 – Increased potential for reassortment and human adaptation, still no, or very limited, human-to-human transmission: The virus begins to infect swine or other animal species that could facilitate the mixing and spreading of influenza viruses. This increases the likelihood that the virus reassorts with other influenza viruses and adapts to humans. In this scenario, we expect that some limited human-to-human transmission could be reported but only among farm workers or close contacts of those workers, and not among healthcare workers. Likelihood of widespread human infections is low. Population health consequences are low. Overall risk of widespread transmission in humans is low, but risk is increased for farm workers and close contacts of those workers. The relative risk of a future pandemic has increased, but the absolute risk remains low.

Scenario 4 – Increasing reports of human infections, limited human-to-human transmission between close contacts: There are more reports of human infections due to contact with infected animals like cattle, swine, and/or poultry. Limited human-to-human transmission is reported among close contacts of infected individuals, including healthcare workers, but there is no efficient human-to-human transmission. Likelihood of widespread human infections is moderate. Population health consequences are low. Overall risk of widespread transmission is low, but population-specific risk is increased for farm workers, close contacts of farm workers, and healthcare workers. The likelihood of a future pandemic is increased.

Scenario 5 – Efficient human-to-human transmission: There are reports of efficient human-to-human transmission. Likelihood of human infections is high because the virus now transmits efficiently and will be very difficult to contain. Population health consequences are high. Overall risk is high for all populations. The likelihood of a pandemic is very high.

Due to recent events, CORI judges that the ongoing H5N1 outbreak in cattle and poultry is now within Scenario 3, *meaning the virus is infecting multiple animal species that facilitate the mixing and spreading of influenza viruses, increasing the likelihood that the virus reassorts with other influenza viruses and adapts to humans.*

This judgment is based on the widespread occurrence of H5N1 infections in cattle herds across more than one-fifth of US states since March 2024, continued reports of human H5 among dairy

workers and poultry workers, continued reports from USDA APHIS of H5N1 in other species (domestic cats, racoons, foxes, mice, and others), and new information from USDA and early access articles in *Nature* regarding the potential for cow-to-cow and cross-species transmission and the potential for H5N1 to bind with sialic acids expressed in human respiratory upper airways. This assessment also builds on the previous judgment regarding the detection of H5 in wastewater in multiple states, high mortality among H5N1-infected cats that live on affected farms, and remaining concern from a preprint article that cows may serve as mixing vessels for influenza reassortment because of the existence of both avian and human influenza receptors in cows.

Although all studies regarding the potential for cows as mixing vessels and cow-to-cow and cross-species transmission are preprint and early access, respectively, meaning they have not been either peer-reviewed, finalized, or replicated, the continued transmission of H5N1 from poultry and cattle to humans in combination with the recent preliminary findings from epidemiologic studies raise concern for increased reassortment potential. To date, no human-to-human transmission has been reported in the current outbreak, however, recent events may increase the potential for transmission to close contacts of affected farm workers and animal populations.

At this time, CORI judges that the likelihood of widespread human infections is low and the population health consequences are low. Furthermore, the overall risk of widespread transmission in humans remains low, but risk is increased for farm workers and close contacts of farm workers. The relative risk of a future pandemic has increased compared to the previous months, but the absolute risk remains low.

CORI are continuing to monitor and adapt this risk assessment to the evolving changes of the H5N1 outbreak in the US. Factors that may contribute to a change in this assessment include increased reports of H5N1 human infections among farm workers, reports of human-to-human transmission, evidence of H5N1 clade 2.3.4.4b adapting for human-to-human transmission, or detection of H5N1 among individuals in the US without a known exposure to infected animals.

H5N1 Human Health Risk Assessment Scenario Table

	Risk to farm workers	Risk to other people in contact with affected workers and animal populations	Risk to healthcare workers	Risk to the US general public
Scenario 1 – Minimal spread in cattle	Low	Low	Low	Low
Scenario 2 – Widespread transmission in cattle, few human infections, no	Moderate	Low	Low	Low

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human-to-human transmission				
Scenario 3 – Increased potential for reassortment and human adaptation, still no, or very limited, human-to-human transmission	Moderate-High	Moderate	Low	Low
Scenario 4 – Increasing reports of human infections, limited human-to-human transmission between close contacts	High	Moderate-High	Moderate	Low-Moderate
Scenario 5 – Efficient human-to-human transmission	High	High	High	High

Methods: The purpose of this document is to consider possible future developments in this outbreak and describe corresponding risks to human populations should a given scenario occur. A risk score is determined for each key population across multiple possible scenarios. Risk scores are evaluated on a five-point scale, with scores including low, low-moderate, moderate, moderate-high, and high. The confidence in each of these risk level assignments are based on the breadth, depth, and the quality of information available. The overall confidence of each risk score determination is based on a three-point scale, which includes low, moderate, and high. Each risk score and the confidence in the score is discussed in the Appendix.

In each scenario regarding H5N1, we consider the risk to four distinct populations: farm workers on affected farms, other people in the vicinity of affected animal populations and farm workers (eg, household contacts of workers, people living near affected facilities with potential contact with infected animals or farm workers, healthcare providers treating infected individuals), US healthcare workers, and the US general public.

In determining these risks, we consider several factors, including cow-to-cow transmission pathways (eg, respiratory transmission, drinking contaminated water and feeding on contaminated grasslands, aerosolization of the virus through the milking process, etc.), cross-species transmission (eg, cow to domestic cat, bird, racoon, etc.), cow-to-human transmission pathways (eg, unprotected and close contact with infected animals, consumption of unpasteurized dairy products, etc.), and human-to-human transmission pathways (eg, aerosol, oral, direct contact). We also consider disease morbidity and mortality, instances of

transmission, the level of testing conducted in cattle and other farm animals, the level of testing conducted in humans, existing processes to limit spread from infected animals, genomic surveillance capabilities, and any new mutations showing greater potential for sustained human-to-human transmission. Other factors include events that could increase human-to-human transmission (eg, mass gatherings, seasonal trends, school terms, etc.), treatments available to humans (eg, antivirals), preventative measures against animal-to-worker transmission (eg, use of N95 mask or equivalent, goggles, gloves, gown, head cover, and boot covers), preventative medical countermeasures (eg, vaccines), preventative nonpharmaceutical interventions for human-to-human transmission (eg, isolation of infected people, mask wearing), and ongoing response operations to address the outbreak.

Appendix

Scenario 1: H5N1 outbreak stays predominantly in cattle and has minimal spread within herds and to other animals.

In the first scenario, we considered the risk to human health if the H5N1 virus stays in cattle and has minimal spread within herds and to other animals. We determined the health risk to **farm workers** to be **low**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **low**, the risk to **healthcare workers to be low**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **low**,.

Our **confidence** in these risk scores is high given the current level of information known for each of these factors and the fact that the virus is not actively spreading to humans or within human populations in this scenario. To minimize the spread of H5N1 in animals, USDA recommends:

- Increased diagnostic testing in cattle.
- Separation of infected cattle during convalescence.
- Enforced cattle import restrictions to limit the movement of infected cattle across state borders.
- Stringent control of potentially infected food products (removal of milk or other infected products).

To minimize the potential for cow-to-human transmission, USDA recommends:

- Farm workers and other individuals in close contact with infected cattle or environments use adequate protective equipment and hygienic/sanitation measures.

Scenario 2: H5N1 virus stays predominantly in cattle but spreads widely within herds. There is low incidence of cow-to-human transmission but no human-to-human transmission.

In the second scenario, we considered the risk to human health if the H5N1 virus spreads widely within cattle herds but has minimal spread to other animal species. We determined the health risk to **farm workers** in this scenario to be **moderate**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **low**, the risk to **healthcare workers to be low**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **low**.

Our **confidence** in these risk scores is low, as the level of testing conducted in cattle and other farm animals is low. Based on available USDA data, there is considerable cow-to-cow transmission occurring. We do not know the level or types of exposure farm workers have to infected cattle, but it is likely sufficient to enable transmission. Furthermore, we do not have details on the transmission routes to humans, making it difficult to determine the exact risk to workers who have contact with infected animals. Though we determined the risk of widespread human infection to be low given the low incidence of documented cow-to-human transmission, that could change. As the number of infected cattle increases, so does the risk to farm workers. To reduce risk, USDA recommends:

- Farm workers diligently use appropriate personal protective equipment (PPE; including masks, goggles, gloves, gowns, head covers, and boot covers) when working directly with or closely to cattle and poultry, other infected or potentially animals, and potentially infected environments.
- Increased diagnostic testing in cattle.
- Separation of infected cattle during convalescence.
- Enforced cattle import restrictions to limit the movement of infected cattle across state borders.
- Stringent control of potentially infected food products (removal of milk or other infected products).
- Information sharing between the agricultural and public health sectors to increase transparency and monitor for increases in animal-to-human transmission.

Scenario 3: H5N1 virus begins to infect swine or other animal species that could facilitate the mixing and spreading of influenza viruses. This increases the likelihood that the virus reassorts with other influenza viruses and adapts to humans. Some limited human-to-human transmission is reported, but only among close contacts of human cases. Healthcare workers have not reported infections.

In the third scenario, we considered the risk to human health if the H5N1 virus begins spreading widely in pigs or other potential mixing vessel hosts, creating greater opportunity for reassortment with human influenza viruses. To date, naturally occurring H5N1 outbreaks have

been reported in several of the potential mixing vessels, such as minks, seals, cats, dogs, and many different kinds of birds. In this scenario, we expect some very limited human-to-human transmission would be reported among close contacts of cases. We determined the health risk to **farm workers** to be **moderate-high**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **moderate** the health risk to **healthcare workers** to be **low**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **low**.

Our **confidence** in these risk scores is low, as the level of testing conducted among farm animals and people in contact with potentially infected animals is low. The jump from cattle to swine poses an increased risk for new mutations that could have a greater potential for sustained transmission within human populations, particularly for farm workers and local communities. To decrease risk to human health, we recommend:

- Farm workers diligently use personal protective equipment (PPE; including masks goggles, gloves, gowns, head covers, and boot covers) when working directly with or closely to cattle and poultry, other infected or potentially animals, and potentially infected environments.
- Increased diagnostic testing and genomic surveillance in cattle.
- Separation of infected cattle during convalescence.
- Enforced cattle import restrictions to limit the movement of infected cattle across state borders.
- Stringent control of potentially infected food products (removal of milk or other infected products).
- Information sharing between the agricultural and public health sectors to increase transparency and monitor for increases in animal-to-human or human-to-human transmission.
- Increased public health surveillance for H5N1 cases in local communities.
- Enhanced communication with the public about the situation and the measures being taken to address it.

Scenario 4: There are more reports of human infections due to contact with infected animals. Limited human-to-human transmission is reported among close contacts of infected individuals, including healthcare workers, but there is no efficient human-to-human transmission.

In the fourth scenario, we considered the risk to human health if the H5N1 virus begins spreading more readily among close human contacts, including healthcare workers. In this scenario, increased, but still limited, human-to-human transmission is reported among close contacts of infected individuals. Transmission between people is still not efficient. We determined the health risk to **farm workers** to be **high**, the health risk to **other people in the**

vicinity of affected workers and animal populations to be **moderate-high**, the health risk to **healthcare workers** to be **moderate**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **low-moderate**.

Our **confidence** in these risks scores is low, as the level of testing conducted among farm animals and humans is generally low. Increased incidence of human-to-human transmission may indicate increased transmission efficiency, but it may also be due to greater prevalence of the virus in communities. There is still significant uncertainty about whether the virus will spread efficiently among people. To reduce risk to human health, we recommend actions including but not limited to:

- Implementation of and support for recommended isolation of human cases and quarantine of close contacts of cases through escalated case finding and contact tracing, antiviral (eg, Tamiflu) prophylaxis for those exposed, compensation for individuals who are isolated/quarantined and cannot report to work, and social support to provide for essential needs of those in isolation/quarantine.
- Increased focus on sentinel surveillance, wastewater surveillance, and education of clinicians to consider H5N1 as a possible diagnosis for people who present with new respiratory illness.
- Continued development and widespread implementation of antigen and molecular testing in both hospital and outpatient healthcare settings.
- Policy preparation for the possibility of a pandemic, including congressional deliberations about emergency funding and emergency planning by healthcare institutions, workplaces, and federal, state, territorial, local, and tribal public health agencies.
- Increased investment and urgent development, testing, and production of vaccines and treatment options.
- Enhanced communication with the public about the situation and the measures being taken to address it, as well as efforts to mitigate the spread of rumors and disinformation.

Scenario 5: There are reports of efficient human-to-human transmission in addition to animal-to-human transmission. The likelihood of human infections is high because the virus now transmits efficiently and will be very difficult to contain.

In the fifth scenario, we considered the risk to human health if H5N1 continues to spread from animals to humans and develops the ability to transmit efficiently between humans. We determined the health risk to **farm workers** to be **high**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **high**, the health risk to **healthcare workers** to be **high**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **high**.

Our **confidence** in these risks scores is high. The level of H5N1 testing in humans is minimal, and we have limited information or evidence available to determine the exact human-to-human transmission pathways. Preventative medical countermeasures to address human-to-human transmission, such as vaccines, are available, but their effectiveness is unclear. Nonpharmaceutical interventions are not currently in use, and there are no human public health response operations in place. The risk is therefore high for farm workers and the local and global communities. To decrease the risk of human-to-human transmission, we recommend actions including but not limited to:

- Increased diagnostic and surveillance testing in humans, including increased genomic surveillance.
- Implementation of and support for recommended isolation of cases and quarantine of close contacts of cases through escalated case finding and contact tracing, antiviral (eg, Tamiflu) prophylaxis for those exposed, compensation for individuals who are isolated/quarantined and cannot report to work, and social support to provide for essential needs of those in isolation/quarantine.
- Increasing sentinel surveillance, wastewater surveillance, and education of clinicians about how to recognize and treat H5N1 infection.
- Widespread implementation of antigen and molecular testing in both hospital and outpatient healthcare settings.
- Congressional approval of supplemental appropriations to fund public health response activities.
- Urgent development, testing, and production of vaccines and additional treatment options.
- Adoption and implementation of medical countermeasures and nonpharmaceutical interventions.
- Increased risk communication to the public to provide regular epidemiologic updates, discuss recommended and potential interventions, recommend measures that individuals and organizations can take to protect personal and public health, and address rumors and disinformation.
- Monitoring and mitigation of transmission at mass gathering events.

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