## Summary: H5N1 Scenario-Based Human Health Risk Assessment for the United States as of May 22, 2024

Currently, the Center for Outbreak Response Innovation (CORI) judges the H5N1 outbreak in cattle to be between Scenario 2 and Scenario 3, meaning the virus is transmitting widely in cattle (Scenario 2), but infections in cattle and other animal species (e.g., cats) may offer opportunity for reassortment (Scenario 3), which would increase the potential for a novel influenza virus that could transmit efficiently between humans.

This judgment is based on the widespread occurrence of H5N1 infections in cattle across the US, the detection of H5 in wastewater in Texas, and high mortality in H5N1-infected cats that live on affected farms. A preprint report released on May 3, 2024, found that cattle may be possible mixing vessels for influenza reassortment because of the existence of both avian and human influenza receptors in cows, which would move the situation into Scenario 3. However, because this study has not yet been peer-reviewed or replicated, we maintain our judgment that we are not yet fully in Scenario 3. If we see additional evidence to support these findings, the study is published in a reputable peer-reviewed journal, or the virus is found in other species such as pigs, we may change our judgment about the risk. To date, no human-to-human transmission has been reported, and we have not seen an increase in human cases.

See the detailed risk assessment analysis beginning on the next page.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Risk to agricultural workers</th>
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<td>Scenario 2 - Widespread transmission in cattle, few human infections, no human-to-human transmission</td>
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<td>Scenario 3 - Increased potential for reassortment and human adaptations, still no human-to-human transmission</td>
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The recent HPAI A(H5N1) virus outbreak in US dairy cattle has drawn significant attention since the USDA reported detections in dairy herds in Texas and Kansas on March 25, 2024. According to the US Centers for Disease Control and Prevention (CDC), as of May 22, 2024, the virus has spread to at least 51 dairy herds in 9 states (Texas, Kansas, New Mexico, Idaho, Michigan, Ohio, North Carolina, South Dakota, and Colorado). There have also been 2 human infections reported in dairy farm workers, the first reported on April 1, 2024, in Texas and the second reported on May 22, 2024, in Michigan, raising concerns about the impact on public health. No human-to-human transmission of the virus has been reported to date.

The risks to human health from this outbreak are complex and may change rapidly. They are also highly uncertain because of a current lack of surveillance data and other basic scientific and epidemiological information. 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 agricultural workers.

Scenario 3 – Increased potential for reassortment and human adaptation, still no human-to-human transmission: The virus begins to infect swine or other animal species that 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 close contacts of agricultural 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 agricultural workers and close contacts of 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 or swine. 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 agricultural workers, close contacts of 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.

Currently, we judge the H5N1 outbreak in cattle to be between Scenario 2 and Scenario 3, meaning the virus is transmitting widely in cattle (Scenario 2), but infections in cattle and other animal species (eg, cats) may offer opportunity for reassortment (Scenario 3), which would increase the potential for a novel influenza virus that could transmit efficiently between humans.

This judgment is based on the widespread occurrence of H5N1 infections in cattle across the US, the detection of H5 in wastewater in Texas, and high mortality in H5N1-infected cats that live on affected farms. A preprint report released on May 3, 2024, found that cattle may be possible mixing vessels for influenza reassortment because of the existence of both avian and human influenza receptors in cows, which would move the situation into Scenario 3. However, because this study has not yet been peer-reviewed or replicated, we maintain our judgment that we are not yet fully in Scenario 3. If we see additional evidence to support these findings, the study is published in a reputable peer-reviewed journal, or the virus is found in other species such as pigs, we may change our judgment about the risk.
To date, no human-to-human transmission has been reported, and we have not seen an increase in human cases.

### H5N1 Human Health Risk Assessment Scenario Table

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<td>Scenario 4 – Increasing reports of human infections, limited human-to-human transmission between close contacts</td>
<td>High</td>
<td>Moderate-High</td>
<td>Moderate</td>
<td>Low-Moderate</td>
</tr>
<tr>
<td>Scenario 5 – Efficient human-to-human transmission</td>
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**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. In each scenario, we consider the risk to 4 distinct populations: agricultural workers on affected farms, other people in the vicinity of affected animal populations and agricultural workers (e.g., 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 (e.g., respiratory transmission, drinking contaminated water and feeding on contaminated grasslands, aerosolization of the virus through the milking process, etc.), cow-to-human transmission pathways (e.g., unprotected and close contact with infected animals, consumption of unpasteurized dairy products, etc.), human-to-human transmission pathways (e.g., aerosol, oral, direct contact), and cow-to-other animal transmission. 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 (e.g., mass gatherings, seasonal trends, school terms, etc.), treatments available to humans (e.g., antivirals), preventative measures for animal-to-worker transmission (e.g., use of N95 mask or equivalent, goggles, gloves, gown, head cover, and boot covers) and transmission to the general public, preventative medical countermeasures, preventative nonpharmaceutical interventions for human-to-human transmission, and ongoing response operations to address the outbreak.
Appendix: Additional Details on Process and Recommendations

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 agricultural 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 very low, and the health risk to the US general public (and the consequent risk of a pandemic) to be very 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.
- Continued separation of infected cattle from the rest of the herd.
- 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:

- Agricultural 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 also a 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 is spreading widely within bovine herds but has minimal spread to other animal species. We determined the health risk to agricultural 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 very low, and the health risk to the US general public (and the consequent risk of a pandemic) to be very 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 precisely how much exposure agricultural workers
have to infected cattle, but it is likely sufficient to enable transmission. Furthermore, we do not have details on the routes of transmission to humans, making it difficult to determine the exact risk to agricultural workers. 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 agricultural workers. To reduce risk, USDA recommends:

- Agricultural workers diligently use appropriate personal protective equipment (such as masks, goggles, gloves, gowns, head covers, and boot covers) when working directly with or closely to cattle and potentially infected environments.
- Increased diagnostic testing in cattle and the continued 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 agriculture and public health sectors to increase transparency and monitor for increases in cow-to-human transmission.

Scenario 3: H5N1 virus begins to infect swine or other animal species that have facilitated 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 animals, creating greater opportunity for reassortment with human influenza viruses. 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 agricultural 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 in cattle and other farm 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 agricultural workers and local communities. To decrease risk to human health, we recommend:
Agricultural workers diligently use personal protective equipment (including masks, goggles, gloves, gowns, head covers, and boot covers) when working directly with or closely to cattle, infected animals, and potentially infected environments.

Increased diagnostic testing in cattle and other farm animals, continued genomic surveillance, the separation of infected cattle and other animals, and stringent control of potentially infected food products.

Information sharing between the agriculture and public health sectors to increase transparency and monitor for increases in 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 like cattle or swine. 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. Transmission between people is still not efficient. We determined the health risk to agricultural 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 in 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:

- Implementing and supporting recommended isolation of human cases and quarantine of close contacts of cases through escalated case finding and contact tracing, 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 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 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.

Increased risk communication to the public to provide regular updates and prevent mis- and disinformation.

Scenario 5: There are reports of efficient human-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 the virus jumps from animals to humans, and we find efficient human-to-human transmission of H5N1. We determined the health risk to agricultural workers to be high, the health risk to non-workers 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 currently 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 it is unclear how effective they would be. Nonpharmaceutical interventions are not currently in use, and there are no human public health response operations in place. The risk is therefore high for agricultural 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).
- Implementing and supporting recommended isolation of cases and quarantine of close contacts of cases through escalated case finding and contact tracing, 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 settings.

Congressional approval of supplemental appropriations to fund public health response activities.

Urgent continued development, testing, and production of vaccines and treatment options.

Adoption of medical countermeasures and nonpharmaceutical interventions.

Increased risk communication to the public to provide regular epidemiologic updates, discuss the interventions that may be used, recommend measures that individuals and organizations can take to protect public health, and address mis- and disinformation.

Monitoring and mitigation of transmission at mass gathering events.

References


7. Kristensen C, Jensen HE, Trebbien R, Webby RJ, Larsen LE. The avian and human influenza A virus receptors sialic acid (SA)-α2,3 and SA-α2,6 are widely expressed in the bovine mammary gland. Published online May 3, 2024:2024.05.03.592326. doi:10.1101/2024.05.03.592326