



UK Health
Security
Agency

Influenza A(H5N1) 2.3.4.4b B3.13: US cattle outbreak

Human health risk assessment ratified 13
May

UKHSA, APHA, FSA and Defra

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Overview

The UK Health Security Agency (UKHSA) is working with the Animal and Plant Health Agency (APHA), the Department for Environment, Food and Rural Affairs (Defra), Food Standards Agency (FSA), and the public health agencies of the 4 nations to monitor the risk to human health from emerging influenza viruses. This document contains assessments on current and future human health risk in England from the influenza A(H5N1) outbreak in US cattle. It takes account of all situational and technical data available to UKHSA. This document contains the assessment ratified on 13 May 2024 by NERVTAG.

Summary

1. UKHSA monitors the risk posed by emerging influenza viruses to human health and has previously published situational assessments of the global epizootic of influenza A(H5N1) clade 2.3.4.4b. UKHSA, APHA, Defra and UK academic partners work closely through a technical group to monitor, and where appropriate generate, human and animal health data, genomics and phenotypic virological data.
2. There is an ongoing outbreak of influenza A(H5N1) in cattle in the US. UKHSA together with Defra, APHA and FSA have considered 4 potential risks to the UK public, as related to this outbreak:
 - i. The risk of importation of contaminated food.
 - ii. The risk of infection of UK cattle.
 - iii. The risk of direct zoonotic infections (infections acquired by humans from animals).
 - iv. The risk of the virus evolving to become human to human transmissible.
3. The current risk assessment for these has been issued by [FSA for \(i\)](#) and [Defra for \(ii\)](#). The multi-agency group [HAIRS assesses risk \(iii\)](#) and has currently assessed this risk as very low.
4. UKHSA assesses (iv) via a structured situational assessment framework which provides indicators used to identify increasing human health threat from zoonotic influenza, either because the opportunities for it to evolve are increasing or because there is evidence that it has already begun to evolve. This framework has been updated to take account of experiences with mammalian transmission of influenza A(H5N1) in the past year, including in cats, mink, pinnipeds and cattle (section 1).

5. In response to the current outbreak in US dairy cattle, UKHSA together with the technical group has updated the situational assessment and finds that the outbreak is now at level 3 (with high confidence) and may have risen to level 4 (low confidence).

6. In addition, UKHSA with Defra, APHA and FSA have developed a structured 6-month forward look for the 4 risks (section 2). These risk statements provide a common framework in which risks related to human health can be compared and monitored over time.

7. The assessments in this document have been produced by the zoonotic influenza technical group (incorporating members from UKHSA, APHA, Defra, FSA and academic partners) and were ratified by NERVTAG on 13 May 2024.

Part 1. Current situational assessment

Levels are indicators that a zoonotic influenza virus outbreak may be an increasing human health threat, either because the opportunities for it to evolve are increasing or because there is evidence that it has already begun to evolve. All levels are pre-pandemic events.

Since the previous publication of the [risk levels](#), the descriptions have been updated by the zoonotic influenza technical group. These adjusted levels synthesise epidemiological, genomic and virology indicators at every stage and take into account recent experience with mammalian outbreaks.

The current situational assessment is shown in Table 1 alongside accompanying evidence. Since the date this assessment was performed, a further human case has been identified in the US, bringing the total to 2 human cases. This does not change the assessment presented here.

Situational assessment: the outbreak is currently at level 3 (with high confidence) and may have risen to level 4 (low confidence).

Confidence levels for this assessment are set using modalities of data supporting the assessment.

If one of epidemiology, genomic, or virological data supports: Low confidence
 If 2 of 3 categories of data support: Moderate confidence
 If all 3 categories of data support: High confidence

Table 1. Situational assessment framework and evidence supporting the assessment. Cells highlighted in blue indicate the current level and evidence available

Level	Level description	Epidemiology supporting evidence	Genomics supporting evidence	Virology supporting evidence
0	Avian influenza circulating in birds, epidemiology within seasonal norms.			
1	Avian influenza circulating in birds, epidemiology outside seasonal norms.			
2	Evidence of propensity to infect humans and/or other mammals (individual cases without onwards transmission).			
3	Limited or facilitated mammalian transmission (facilitated indicating outbreaks that are driven by, for example, intensive farming or close contact settings but would not otherwise be sustained).	Level 3 or 4: Multistate US outbreak with high proportion of US milk testing PCR positive. Transmission between herds due to cattle transport. Transmission within herds likely to involve direct contact/fomite/milk but respiratory has not been excluded. This could be consistent with spread facilitated by farming practices rather than non-facilitated sustained transmission. One human case with no onwards transmission detected, in the context of very limited human testing overall [note 1].	Level 3: Polymerase mutations are present but have also been seen in limited outbreaks such as mink farms. Haemagglutinin (HA) is not static and requires continued assessment. Genomic data is limited and unlikely to represent the whole outbreak.	Level 3: In vitro data show the polymerase mutations present improve ability to replicate in mammalian cell lines.
4	Sustained and/or multispecies mammalian outbreaks; increasing human zoonotic cases or limited person-to-person spread, linked to zoonotic exposures.			
5	Human outbreaks (larger or without identified zoonotic links).			
6	Sustained human to human transmission.			

Note 1: Since the date of this assessment, one further human case reported, which does not change the level of the assessment.

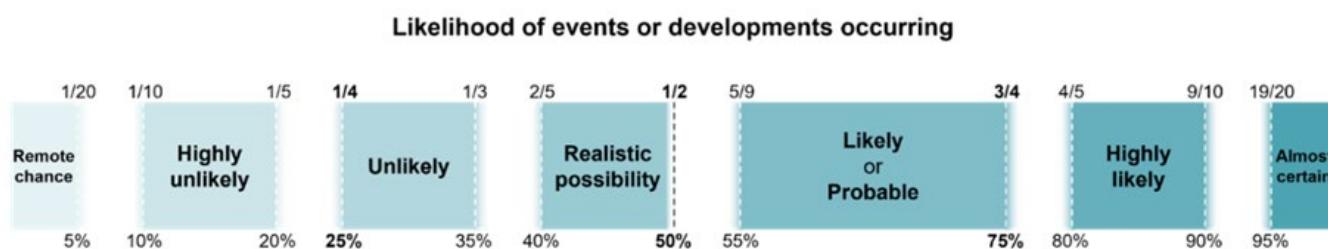
Part 2. Statements on future risk

2.1 Methodology

The statements in Part 2.2 provide assessments of the ranges of probability of 4 different risks manifesting in the next 6 months, assuming that the UK does not take any action over and above its current posture as of 8 May 2024 and that the cattle outbreak and risk is specific to genotype B3.13. These assessments use the [PHIA probability yardstick](#) (Figure 1) and PHIA's analytical confidence ratings.

Use of the probability yardstick is intended to accurately communicate the level of uncertainty associated with judgements made in this report. Probability reflects an estimate of the chances that a given statement is true. The methodology and use of language described here applies only to the future risk statements.

Figure 1. Probability yardstick: the likelihood of events developing or occurring



Analytical confidence is the extent to which there is a sound and stable basis for assessing probability, taking into account the complexity and volatility of the environment being analysed and assessed, and the information base and analytical rigour that underpin that analysis and assessment.

Analytical confidence ratings do assess the strength of analytical judgement and how sensitive that judgement is to change. They do not express the likelihood of an event or outcome, nor do they reduce or eliminate real-world uncertainty conveyed in assessment. The confidence ratings and their definitions are:

High confidence: uncertainties remaining should have negligible or no effect on key judgements.

Moderate confidence: uncertainties remain that could expose the key judgements to change.

Low confidence: critical uncertainties remain that could invalidate the key judgements.

2.2 Statements on future risk

These statements provide assessment of the ranges of probability of 4 different risks manifesting in the next 6 months, as described in the methodology in Part 2.1. Additional risk

assessments have been undertaken across government and links are provided to those assessments where available.

1. UK cattle are **highly unlikely** (10-20%) to be infected with influenza A(H5N1) clade 2.3.4.4b genotype B3.13 **in the next 6 months**. This risk is included as it underpins some human health risks in the UK.

Moderate confidence to current assessment horizon of 6 months.

The most likely route by which infection could spread to UK cattle in this assessment horizon is through exposure to birds that have migrated from North America or that have been in contact with birds recently in North America. Although some birds migrate directly from North America to Europe via the East Atlantic Flyway, this is primarily used by birds that breed in high latitude areas, for example, Canada and Greenland in the American Atlantic Flyway. Migratory birds travelling directly from North America will not reach Northern Europe until late autumn or later (that is, outside of the time horizon of this assessment), and even then, the number of species is limited. Although it would not be expected for influenza viruses to spread in this direction based on the findings of animal health surveillance over the past few years, the current global spread of clade 2.3.4.4b is already highly unusual and it may not follow expected patterns.

If the current outbreak persists, even if confined to cattle in the US, the likelihood of this virus reaching the UK will increase: more birds using the East Atlantic Flyway will arrive in Europe in late autumn 2024, and the potential that outbreaks will travel east from the US due to mingling of bird populations will increase. There is currently no evidence of infected cattle in Canada; if there is evidence of spread outside the US to the north, the probability of this virus reaching the UK would increase further. Spread to the south would increase the uncertainty but would not necessarily change our overall assessment within this time horizon.

Additional assessments associated with this statement have been performed by [Defra and APHA](#). Defra has ruled out other routes for incursion from the USA to UK cattle (live animals, live poultry, captive birds, products of animal origin and animal by-products).

2. There is a **remote chance** (0-5%) that human infection in the UK with this virus will result from exposure to via legal importation of dairy products **in the next 6 months**.

Medium confidence to current assessment horizon.

Importation of unpasteurised dairy products into the UK from the US is subject to voluntary restrictions. The US has reported that pasteurisation is effective at inactivating this virus in several products. The effectiveness of a range of different pasteurisation techniques of dairy products is also subject to current study in the UK. Avian influenza is relatively heat-sensitive compared to other organisms that milk pasteurisation is intended to kill, but it cannot be ruled out that pasteurisation would not fully inactivate very high levels of virus in contaminated milk products. It is a realistic possibility that H5N1 RNA fragments would be detected in even pasteurised imported dairy products by RT-PCR. This would not necessarily mean that such a

product would itself pose an infection risk. Dilution of bulk milk is also likely to further reduce risk to humans. The small relative amount of dairy product that the UK imports from the US is more heavily processed, reducing the risk that infectious viral material is present. Similarly, only very small amounts of meat are imported from the US and Canada due to regulations on the use of hormonal growth promoters. We also know that dairy products are occasionally brought into the UK against the regulations by passengers from overseas in small amounts relative to legitimate imports.

The likelihood of infection being imported via meat or dairy imports will remain remote chance (0-5%) outside the time horizon of this assessment if the current outbreak remains confined to North America. While we know that meat and dairy products – including unpasteurised milk products - may be brought into the UK by passengers (against the regulations), we cannot assess the likelihood of this as a route of infection. As the UK imports large quantities of meat and dairy products from Europe, the risk of this as a potential route of infection reaching the UK will increase if outbreaks spread outside of North America.

Additional risk assessment has been performed and [published by the FSA](#).

3. If cattle are infected in the UK with this (or a similar) genotype the next 6 months it is a **realistic possibility** (40-50%) that this will result in one or more zoonotic human infections.

It is almost certain (95-100%) that more zoonotic infections have occurred in the US than have been detected, given the mild clinical symptoms of the one identified case and the limited human testing conducted.

Moderate confidence to current assessment horizon of 6 months.

It is not possible to assess the likelihood of zoonotic infections outside of the assessment window as this will be dependent on the efficacy of interventions that would be applied, including animal health outbreak control and enhanced protection of farm workers against occupational exposures.

Additional risk assessment has been performed by the [Human Animal Infections and Risk Surveillance \(HAIRS\)](#) group.

4. **The baseline risk** of influenza A(H5N1) evolving to cause human transmission before the current cattle outbreak was previously considered to be remote chance (0-5%). There is consensus that this risk has now increased. However, with current limited information we cannot resolve the risk further and it may fall at **highly unlikely** (10-20%) or **unlikely** (25-35%).

Rapid phenotypic investigation of the current virus and ongoing genomic assessment is underway and may help to further clarify this.

Low confidence to current assessment horizon of 6 months.

Influenza A(H5N1) clade 2.3.4.4b has already shown potential to transmit successfully between mammals such as mink and sealions, although likely transmitting predominantly through close contact in these species rather than by the respiratory route. The current outbreak in cows is an unprecedented event, increasing risk due to the potential for adaptation to be driven by replication in cows (extent uncertain due to limited data on bovine receptors) and opportunities to adapt or reassort in other mammals and humans infected by cows. Transmission in cows is ongoing, with expanding opportunities for interaction between humans and infected cows.

Acknowledgments

UKHSA zoonotic influenza technical group

The zoonotic influenza technical group includes expert members from UKHSA, Defra, APHA, FSA, and academic partners with relevant expertise who are willing to share and jointly assess data. The group includes epidemiology, virology, genomics and human and animal health clinical specialists.

Technical group members

Technical group members undertaking risk assessment of 8 May 2024:

Ashley Banyard, Wendy Barclay, Ian Brown, Alex Byrne, Meera Chand (chair), John Edmunds, Eileen Gallagher, Daniel Goldhill, Natalie Groves, Yper Hall, Bassam Hallis, Susan Hopkins, Robert Jordan, Rowland Kao, Angie Lackenby, Nicola Lewis, Nicholas Loman, Sophia Makki, Kimberly Marsh, Paul Millar, Catherine Moore, Richard Myers, Massimo Palmarini, Tom Peacock, Richard Pebody, Richard Puleston, Oliver Pybus, Andrew Rambaut, Helen Roberts, Sakib Rokadiya, Deborah Williamson, Anthony Wilson, James Wood, Maria Zambon

Contributing organisations

- UKHSA
- Animal and Plant Health Agency
- Department for Environment, Food and Rural Affairs
- Food Standards Agency
- Health and Social Care Northern Ireland
- Public Health Scotland
- Public Health Wales
- Imperial College London
- Royal Veterinary College
- The London School of Hygiene and Tropical Medicine
- The Pirbright Institute
- University of Edinburgh
- University of Glasgow
- University of Birmingham
- University of Cambridge
- Worldwide Influenza Centre, Francis Crick Institute

About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

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