

APPROVED: 3 July 2024

doi: 10.2903/j.efsa.2024.8930

# Avian influenza overview March–June 2024

European Food Safety Authority,  
European Centre for Disease Prevention and Control,  
European Union Reference Laboratory for Avian Influenza, Leonidas Alexakis, Alice Fusaro, Thijs Kuiken, Gražina Mirinavičiūtė, Karl Ståhl, Christoph Staubach, Olov Svartström, Calogero Terregino, Katriina Willgert, Roxane Delacourt, Sonagnon Martin Goudjihounde, Malin Grant, Stefania Tampach and Lisa Kohnle

## Abstract

Between 16 March and 14 June 2024, 42 highly pathogenic avian influenza (HPAI) A(H5) virus detections were reported in domestic (15) and wild (27) birds across 13 countries in Europe. Although the overall number of detections in Europe has not been this low since the 2019–2020 epidemiological year, HPAI viruses continue to circulate at a very low level. Most detections in poultry were due to indirect contact with wild birds, but there was also secondary spread. Outside Europe, the HPAI situation intensified particularly in the USA, where a new A(H5N1) virus genotype (B3.13) has been identified in > 130 dairy herds in 12 states. Infection in cattle appears to be centred on the udder, with milk from infected animals showing high viral loads and representing a new vehicle of transmission. Apart from cattle, HPAI viruses were identified in two other mammal species (alpaca and walrus) for the first time. Between 13 March and 20 June 2024, 14 new human cases with avian influenza virus infection were reported from Vietnam (one A(H5N1), one A(H9N2)), Australia (with travel history to India, one A(H5N1)), USA (three A(H5N1)), China (two A(H5N6), three A(H9N2), one A(H10N3)), India (one A(H9N2)), and Mexico (one fatal A(H5N2) case). The latter case was the first laboratory-confirmed human infection with avian influenza virus subtype A(H5N2). Most of the human cases had reported exposure to poultry, live poultry markets, or dairy cattle prior to avian influenza virus detection or onset of illness. Human infections with avian influenza viruses remain rare and no human-to-human transmission has been observed. The risk of infection with currently circulating avian A(H5) influenza viruses of clade 2.3.4.4b in Europe remains low for the general public in the EU/EEA. The risk of infection remains low-to-moderate for those occupationally or otherwise exposed to infected animals or contaminated environments.

©2024 European Food Safety Authority, European Centre for Disease Prevention and Control, European Union Reference Laboratory for Avian Influenza. *EFSA Journal* published by Wiley-VCH GmbH on behalf of European Food Safety Authority.

**Keywords:** avian influenza, captive birds, HPAI, humans, monitoring, poultry, wild birds

**Requestor:** European Commission

**Question number:** EFSA-Q-2024-00174 and Commission request 280 to ECDC (SANTE.B.2/IK/mo (2023)2182203)

Correspondence: [biohaw@efsa.europa.eu](mailto:biohaw@efsa.europa.eu) and [ECDC.influenza@ecdc.europa.eu](mailto:ECDC.influenza@ecdc.europa.eu)

**Acknowledgements:** In addition to the listed authors, EFSA, ECDC and the EURL wish to thank the Member State representatives who provided epidemiological data on avian influenza outbreaks or shared sequence data: Aldin Lika (Albania); Sandra Revilla-Fernández, Janna Vogelgesang and Irene Zimpernik (Austria); Ingeborg Mertens, Mieke Steensels and Steven Van Borm (Belgium); Aleksandra Miteva and Emiliya Ivanova (Bulgaria); Savić Vladimir (Croatia); Vasiliki Christodoulou (Cyprus); Tomáš Jarosil, Alexander Nagy and Luděk Závada (Czechia); Heidi Huus Petersen, Charlotte Kristiane Hjulsager, Yuan Liang and Lone Thing Mortensen (Denmark); Tuija Gadd, Lauri Kareinen, Ari Kauppinen and Niina Tammiranta (Finland); Camille Boyer, François-Xavier Briand, Béatrice Grasland, Éric Niquex and Audrey Schmitz (France); Christoph Staubach, Timm Harder, Anne Pohlmann and Carola Sauter-Louis (Germany); Bálint Ádám, Helyes Georgina and Zsofia Szepesine Kokany (Hungary); Laura Garza Cuartero and Audrey Jenkinson (Ireland); Isabella Monne, Calogero Terregino, Lara Cavicchio, Ambra Pastori and Bianca Zecchin (Italy); Vicky Bink, Guillaume Fournier and Chantal Snoeck (Luxembourg); Oxana Groza, Oxana Popa and Vitalie Caraus (Moldova); Nancy Beerens and Marcel Spiereburg (Netherlands); Britt Gjerset, Silje Granstad and Lars Erik Lundblad Rondestveit (Norway); Krzysztof Śmietanka, Katarzyna Domańska-Blicharz and Edyta Swieton (Poland); Dan Alexandru Enache and Iuliana Onita (Romania); Martin Tinak (Slovakia); Luis Gomero, Germán Cáceres Garrido, Elena García Villacieros, Isabel Guijarro Torvisco, Montserrat Agüero García and Azucena Sánchez (Spain); Malin Grant and Siamak Zohari (Sweden); Arlette Szelecsenyi and Claudia Bachofen (Switzerland); Anil Demeli (Türkiye). The authors also wish to thank Ron Fouchier from Erasmus Medical Center (Netherlands); Ashley Banyard from the Animal and Plant Health Agency (United Kingdom); Camille Delavenne from Ausvet Europe for conducting the data analysis under the contract OC/EFSA/ALPHA/2021/02; the authors, originating and submitting laboratories of the sequences from GISAID's EpiFlu™ Database, which is used for this assessment (Annex C); Paolo Calistri and Christian Gortázar from EFSA's Panel on Animal Health and Welfare (AHAW); Erik Alm, Angeliki Melidou and Edoardo Colzani from ECDC, as well as Inma Aznar, Francesca Baldinelli and Barbara Lanfranchi from EFSA for the support provided to this scientific output.

**Declarations of interest:** If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact [interestmanagement@efsa.europa.eu](mailto:interestmanagement@efsa.europa.eu)

**Suggested citation:** EFSA (European Food Safety Authority), ECDC (European Centre for Disease Prevention and Control), EURL (European Union Reference Laboratory for Avian Influenza), Alexakis L, Fusaro A, Kuiken T, Mirinavičiūtė G, Ståhl K, Staubach C, Svartström O, Terregino C, Willgert K, Delacourt R, Goudjihounde SM, Tampach S and Kohnle L, 2024. Scientific report: Avian influenza overview March–June 2024. *EFSA Journal* 2024;22(7):8930, 72 pp. <https://doi.org/10.2903/j.efsa.2024.8930>

**ISSN:** 1831-4732

©2024 European Food Safety Authority, European Centre for Disease Prevention and Control, European Union Reference Laboratory for Avian Influenza. *EFSA Journal* published by Wiley-VCH GmbH on behalf of European Food Safety Authority.

This is an open access article under the terms of the [Creative Commons Attribution-NoDerivs](#) Licence, which permits use and distribution in any medium, provided the original work is properly cited and no modifications or adaptations are made.

**Maps disclaimer:** The designations employed and the presentation of material on any maps included in this scientific output do not imply the expression of any opinion whatsoever on the part of the European Food Safety Authority concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

## Table of Contents

<b>Abstract</b> .....	<b>1</b>
<b>1. Introduction</b> .....	<b>6</b>
<b>2. Assessment</b> .....	<b>6</b>
2.1 HPAI virus detections in birds.....	6
2.1.1 HPAI virus detections in birds in Europe.....	6
2.1.2 HPAI virus detections in birds outside Europe .....	16
2.1.3 Genetic characteristics of HPAI viruses of the A(H5Nx) subtype in avian species .....	19
2.2 HPAI virus detections in non-human mammals.....	22
2.2.1 HPAI virus detections in non-human mammals worldwide.....	22
2.2.2 Genetic characteristics of HPAI viruses of the A(H5Nx) subtype circulating in non-human mammals 31	
2.3 Food safety aspects related to HPAI .....	33
2.4 Avian influenza virus infections in humans.....	35
2.4.1 Most recent human infections with avian influenza A(H3N8), A(H5N1), A(H5N6), A(H9N2) and A(H10N5) viruses.....	36
2.4.2 Human A(H3N8) cases, summary.....	37
2.4.3 Human A(H5N1) cases, summary.....	37
2.4.4 Human A(H5N6) cases, summary.....	40
2.4.5 Human A(H9N2) cases, summary.....	41
2.4.6 Human A(H10N3) cases, summary.....	42
2.4.7 Human A(H5N2) cases, summary.....	42
2.4.8 Genetic characteristics of avian influenza viruses from humans.....	43
2.4.9 Additional information relevant for public health and international risk assessments .....	45
2.4.10 ECDC risk assessment .....	47
<b>3. Conclusions</b> .....	<b>48</b>
3.1 Birds.....	48
3.2 Mammals.....	50
3.3 Food.....	51
3.4 Humans .....	51
<b>4. Options for response</b> .....	<b>51</b>
4.1 Birds.....	51
4.2 Mammals.....	52
4.3 Humans.....	53
<b>References</b> .....	<b>55</b>
<b>Appendix A – Terms of Reference</b> .....	<b>68</b>

A.1. Background and Terms of Reference as provided by the requestor.....	68
A.2 Interpretation of the Terms of Reference .....	69
<b>Appendix B – Data and Methodologies .....</b>	<b>70</b>
B.1 Data on animals.....	70
B.1.1 Overview of avian influenza outbreaks in Europe .....	70
B.1.2 Overview of avian influenza outbreaks in other countries not reporting via ADIS.....	70
B.1.3 Genetic characterisation of avian influenza viruses: description of the nomenclature of the HPAI A(H5) viruses used in the document .....	70
B.2 Data on humans .....	71
<b>Annex A – Data on Birds .....</b>	<b>72</b>
<b>Annex B – Data on poultry outbreaks.....</b>	<b>72</b>
<b>Annex C – Acknowledgements.....</b>	<b>72</b>

## 1. Introduction

This Scientific Report provides an overview of highly pathogenic avian influenza (HPAI) virus detections in poultry<sup>1</sup>, captive<sup>2</sup> and wild birds that occurred in and outside Europe between 16 March and 14 June 2024, as well as HPAI virus detections in mammals up until 24 June 2024 and human cases due to avian influenza infection between 13 March and 20 June 2024. Detections of low pathogenic avian influenza (LPAI) virus are discussed whenever they are of concern and relevant to be mentioned.

The background, Terms of Reference (TORs), and interpretation thereof are described in Appendix A, whereas the data and methodologies used are reported in Appendix B.

Scientific species names of wild birds and mammals mentioned in this report are listed in Table A.3 (Annex A) and Table 3, respectively.

## 2. Assessment

### 2.1 HPAI virus detections in birds

#### 2.1.1 HPAI virus detections in birds in Europe

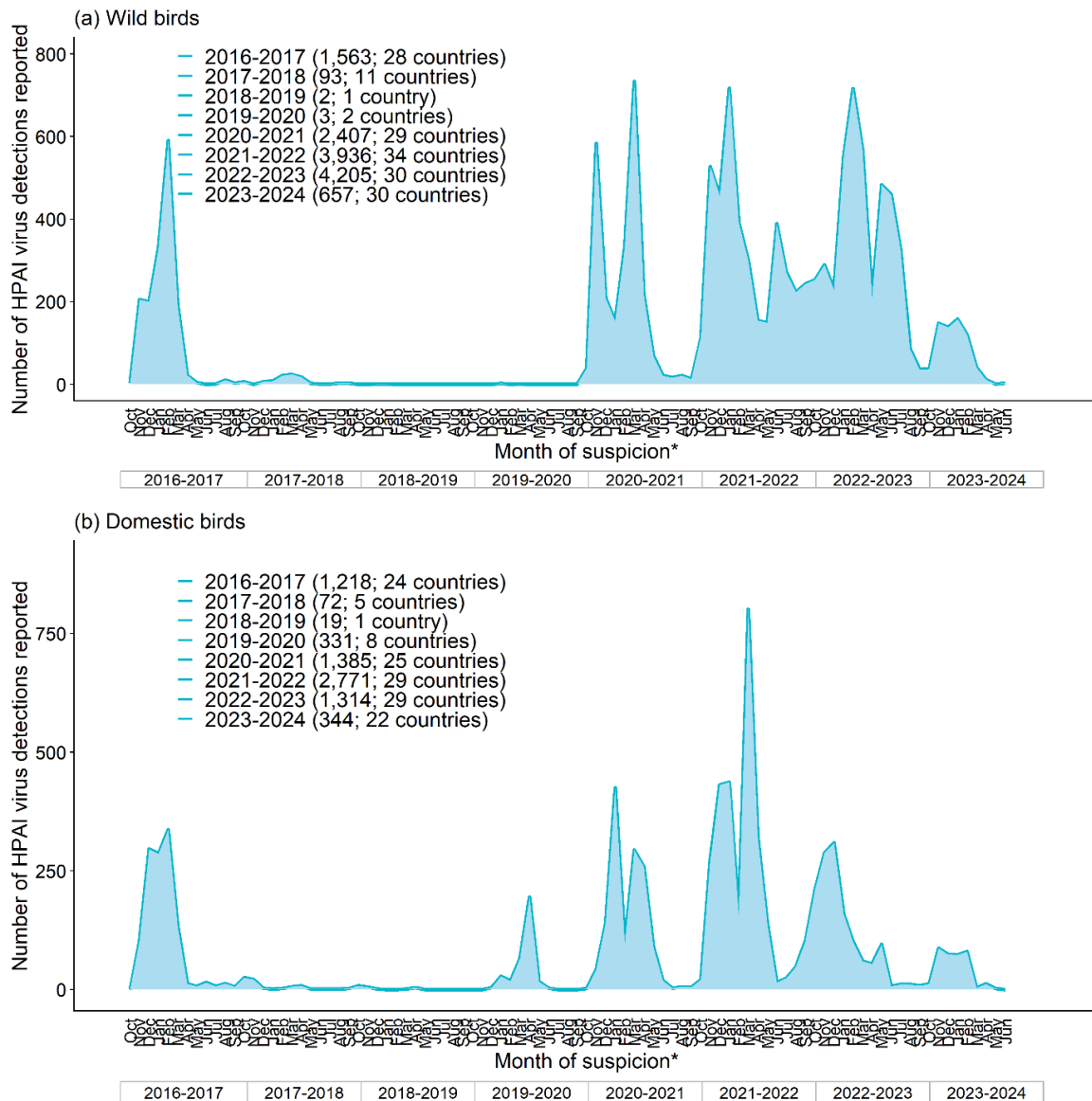
Figure 1 shows all HPAI virus detections in birds in Europe that were reported via the European Union (EU) Animal Disease Information System (ADIS) or the World Animal Health Information System (WOAH-WAHIS) of the World Organisation for Animal Health (WOAH) for the last seven and the current epidemiological years<sup>3</sup> by month of suspicion. For the current epidemiological year 2023–2024, starting on 1 October 2023, data reported are truncated on 14 June 2024.

---

<sup>1</sup> According to Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March 2016, point (9), ‘poultry’ means birds that are reared or kept in captivity for: (a) the production of: (i) meat; (ii) eggs for consumption; (iii) other products; (b) restocking supplies of game birds; (c) the purpose of breeding of birds used for the types of production referred to in points (a) and (b).

<sup>2</sup> According to Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March 2016, point (10), ‘captive birds’ means any birds other than poultry that are kept in captivity for any reason other than those referred to in point (9), including those that are kept for shows, races, exhibitions, competitions, breeding or selling.

<sup>3</sup> In this document an ‘epidemiological year’ refers to the period starting in week 40 (the beginning of October) and ending in week 39 (the end of September) of the following year, based on the dates on which the first HPAI virus detections were observed in wild birds in Europe in 2016–2017, 2020–2021 and 2021–2022.



\*If the date of suspicion was not available, the date of confirmation was used to assign the week of suspicion. United Kingdom data are from the Animal Disease Notification System (ADNS, former ADIS) up until 31 December 2020. From 1 January 2021 onwards, the data source was WOA for the United Kingdom (excluding Northern Ireland) and ADNS/ADIS for the United Kingdom (Northern Ireland)<sup>4</sup>. Source: ADNS/ADIS and WOA (data extraction carried out on 14 June 2024).

**Figure 1:** Distribution of the number of HPAI virus detections in wild (12,866) (a) and domestic (7,454) (b) birds reported in Europe during eight epidemiological years by month of suspicion, from 1 October 2016 to 14 June 2024 (20,320)

The decline and corresponding very low number of HPAI virus detections reported in birds in Europe between 16 March and 14 June 2024 is consistent with the trend observed in previous years (Figure 1). Of note, the total number of HPAI virus detections in wild and domestic birds has not been this low since the 2019–2020 epidemiological year. In 2024, the decline in the number of HPAI virus detections began already in March and continued throughout the course of the current reporting period.

<sup>4</sup> In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and in particular with the Windsor Framework, the EU requirements on data sampling are also applicable to the United Kingdom (Northern Ireland).

However, compared to these earlier years, HPAI viruses now appear to be circulating in wild birds year-round, albeit at very low levels.

Among the possible reasons for this change are flock immunity acquired by certain wild bird species, depletion of some wild bird populations, reduced viral contamination of the environment, changing composition of circulating HPAI virus genotypes, and decreased detection of dead wild birds.

Considering the current reporting period from 16 March to 14 June 2024, 46 HPAI virus detections were reported in poultry (15) and wild birds (27), whereas no HPAI virus detections were reported in captive birds (Table 1, Figure 2).

**Table 1:** Number of HPAI outbreaks reported in Europe, by country, virus subtype and affected sub-population, from 16 March to 14 June 2024. Cumulative numbers since the start of the 2023–2024 epidemiological year are reported in parentheses (1 October 2023 to 14 June 2024)

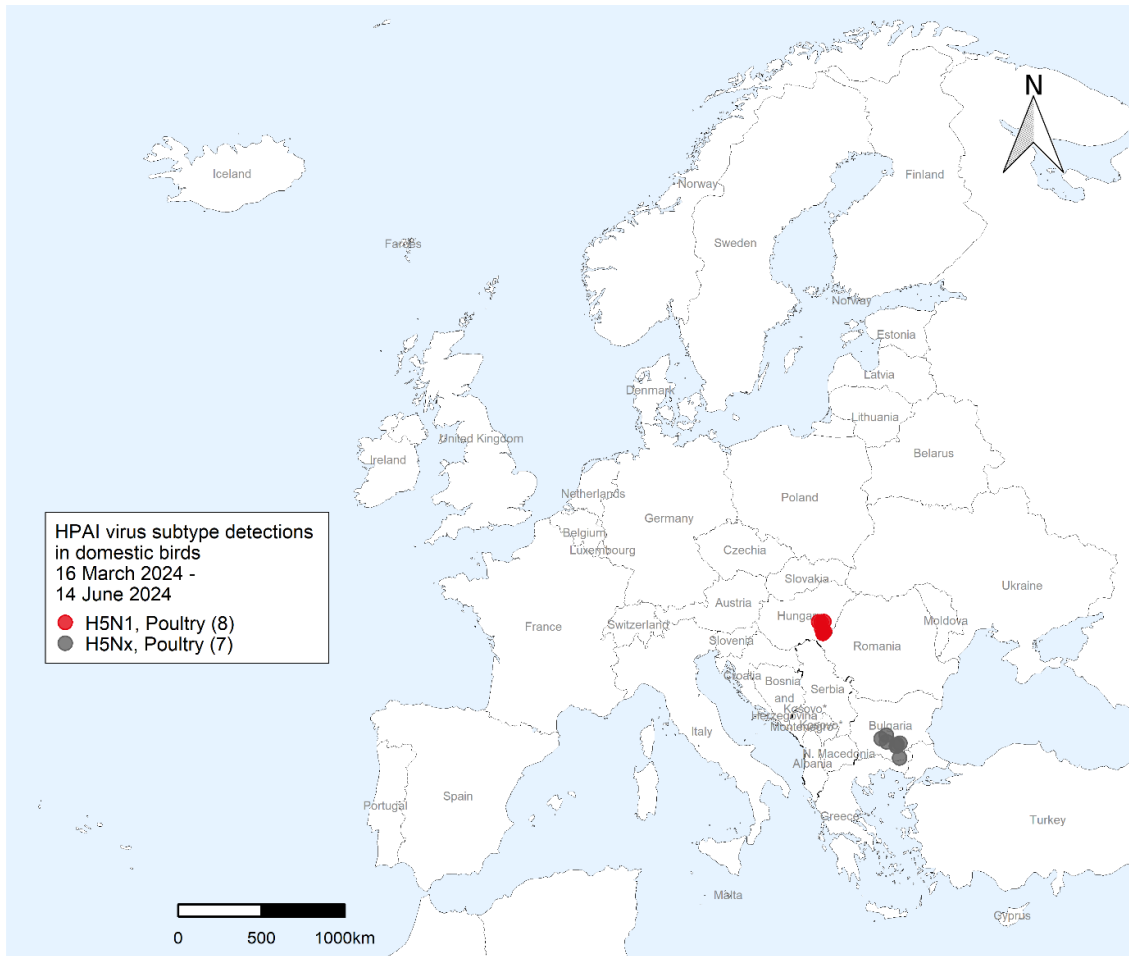
Reporting country	Captive birds		Poultry			Wild birds					Total
	A(H5N1)	A(H5N5)	A(H5N1)	A(H5Nx)	A(Not typed)	A(H5N1)	A(H5N5)	A(H5N8)	A(H5Nx)	A(Not typed)	
Austria	0 (4)	-	-	-	-	0 (23)	-	-	0 (2)	-	<b>0 (29)</b>
Belgium	-	-	0 (4)	-	-	0 (6)	-	-	0 (1)	-	<b>0 (11)</b>
Bosnia and Herzegovina	-	-	-	-	-	0 (1)	-	-	-	-	<b>0 (1)</b>
Bulgaria	-	-	0 (5)	7 (19)	-	-	-	-	1 (1)	-	<b>8 (25)</b>
Croatia	-	-	0 (2)	-	-	0 (7)	-	-	-	-	<b>0 (9)</b>
Cyprus	-	-	-	-	-	0 (1)	-	-	-	-	<b>0 (1)</b>
Czechia	0 (23)	-	0 (5)	-	-	0 (7)	-	-	-	-	<b>0 (35)</b>
Denmark	0 (1)	-	0 (11)	-	-	1 (80)	-	-	-	-	<b>1 (92)</b>
Faroe Islands	-	0 (1)	-	-	-	-	-	-	-	-	<b>0 (1)</b>
Finland	-	-	-	-	-	0 (4)	-	-	-	-	<b>0 (4)</b>
France	-	-	0 (10)	-	-	-	-	-	1 (15**)	-	<b>1 (25)</b>
Germany	0 (11)	-	0 (26)	-	-	13 (175)	0 (2)	0 (1)	0 (2)	-	<b>13 (217)</b>
Hungary	-	-	8 (84)	-	-	0 (50)	-	-	-	-	<b>8 (134)</b>
Iceland	-	-	-	-	-	-	0 (4)	-	-	-	<b>0 (4)</b>
Italy	-	-	0 (6)	-	-	0 (19)	-	-	-	-	<b>0 (25)</b>
Kosovo*	-	-	0 (1)	-	-	-	-	-	-	-	<b>0 (1)</b>
Latvia	-	-	-	-	-	1 (1)	-	-	-	-	<b>1 (1)</b>
Lithuania	-	-	0 (1)	-	-	0 (1)	-	-	-	-	<b>0 (2)</b>
Moldova	-	-	0 (51)	-	0 (7)	1 (31)	-	-	-	-	<b>1 (89)</b>
Netherlands	0 (2)	-	0 (3)	-	-	0 (39)	-	-	0 (1)	-	<b>0 (45)</b>
Norway	0 (1)	-	0 (1)	-	-	1 (3)	0 (4)	-	0 (3)	-	<b>1 (12)</b>
Poland	0 (3)	-	0 (33)	-	-	3 (21)	-	-	-	-	<b>3 (57)</b>
Portugal	-	-	-	-	-	0 (6)	-	-	-	-	<b>0 (6)</b>
Romania	-	-	0 (4)	-	-	1 (34)	-	-	-	-	<b>1 (38)</b>
Serbia	-	-	-	-	-	0 (9)	-	-	-	-	<b>0 (9)</b>
Slovakia	0 (3)	-	0 (6)	-	-	0 (9)	-	-	-	-	<b>0 (18)</b>
Slovenia	-	-	-	-	-	1 (14)	-	-	-	-	<b>1 (14)</b>
Spain	-	-	-	-	-	1 (14)	-	-	-	-	<b>1 (14)</b>



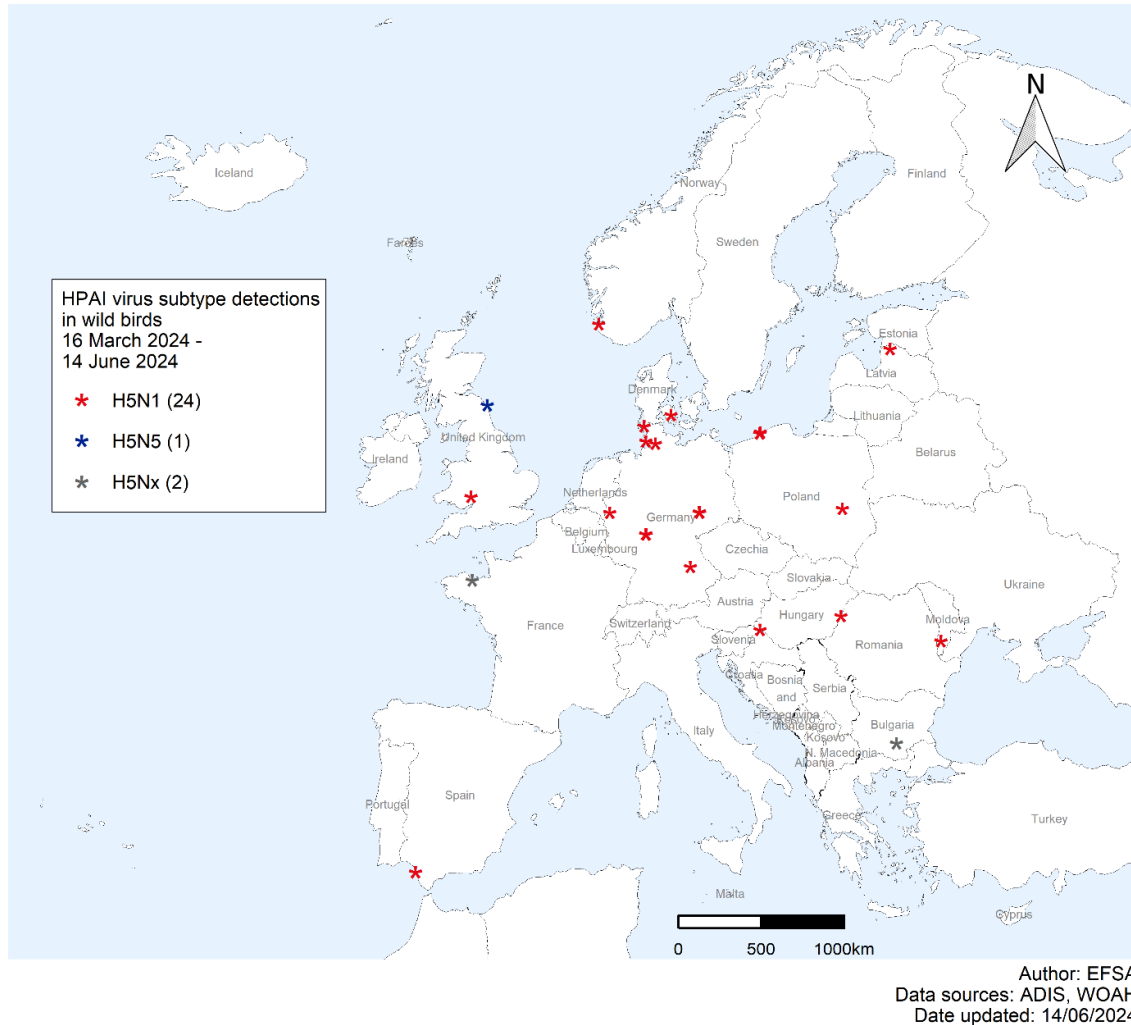
Sweden	-	-	0 (3)	-	-	0 (29)	-	-	0 (4)	-	<b>0 (36)</b>
Switzerland	-	-	-	-	-	0 (1)	-	-	-	-	<b>0 (1)</b>
Ukraine	0 (7)	-	-	-	-	0 (6)	-	-	-	-	<b>0 (13)</b>
United Kingdom	-	-	0 (6)	-	-	1 (18)	1 (7)	-	-	0 (1)	<b>2 (32)</b>
<b>Total</b>	<b>0 (55)</b>	<b>0 (1)</b>	<b>8 (262)</b>	<b>7 (19)</b>	<b>0 (7)</b>	<b>24 (609)</b>	<b>1 (17)</b>	<b>0 (1)</b>	<b>2 (29)</b>	<b>0 (1)</b>	<b>42 (1001)</b>

\*This designation is without prejudice to positions on status and is in line with United Nations Security Council Resolution 1244 and the International Court of Justice Opinion on the Kosovo Declaration of Independence.

\*\*In France, during the current reporting period, 1 A(H5N1) virus detection was reported in wild birds. Since the beginning of the epidemiological year 2023–2024, 11 A(H5N1) and 4 A(H5Nx) virus detections were reported in wild birds. These data have not been updated in ADIS yet.



Author: EFSA  
 Data sources: ADIS, WOAH  
 Date updated: 14/06/2024



\*This designation is without prejudice to positions on status and is in line with United Nations Security Council Resolution 1244 and the International Court of Justice Opinion on the Kosovo Declaration of Independence. United Kingdom data are from ADNS up until 31 December 2020. From 1 January 2021 onwards, the data source was WOA for the United Kingdom (excluding Northern Ireland) and ADNS/ADIS for the United Kingdom (Northern Ireland)<sup>5</sup>.  
Source: ADIS, EFSA and WOA (data extraction carried out on 14 June 2024).

**Figure 2:** Geographic distribution, based on available geocoordinates, of HPAI virus detections in poultry and captive birds (15) (upper panel), and in wild birds (27) (lower panel) reported by virus subtype in Europe from 16 March to 14 June 2024

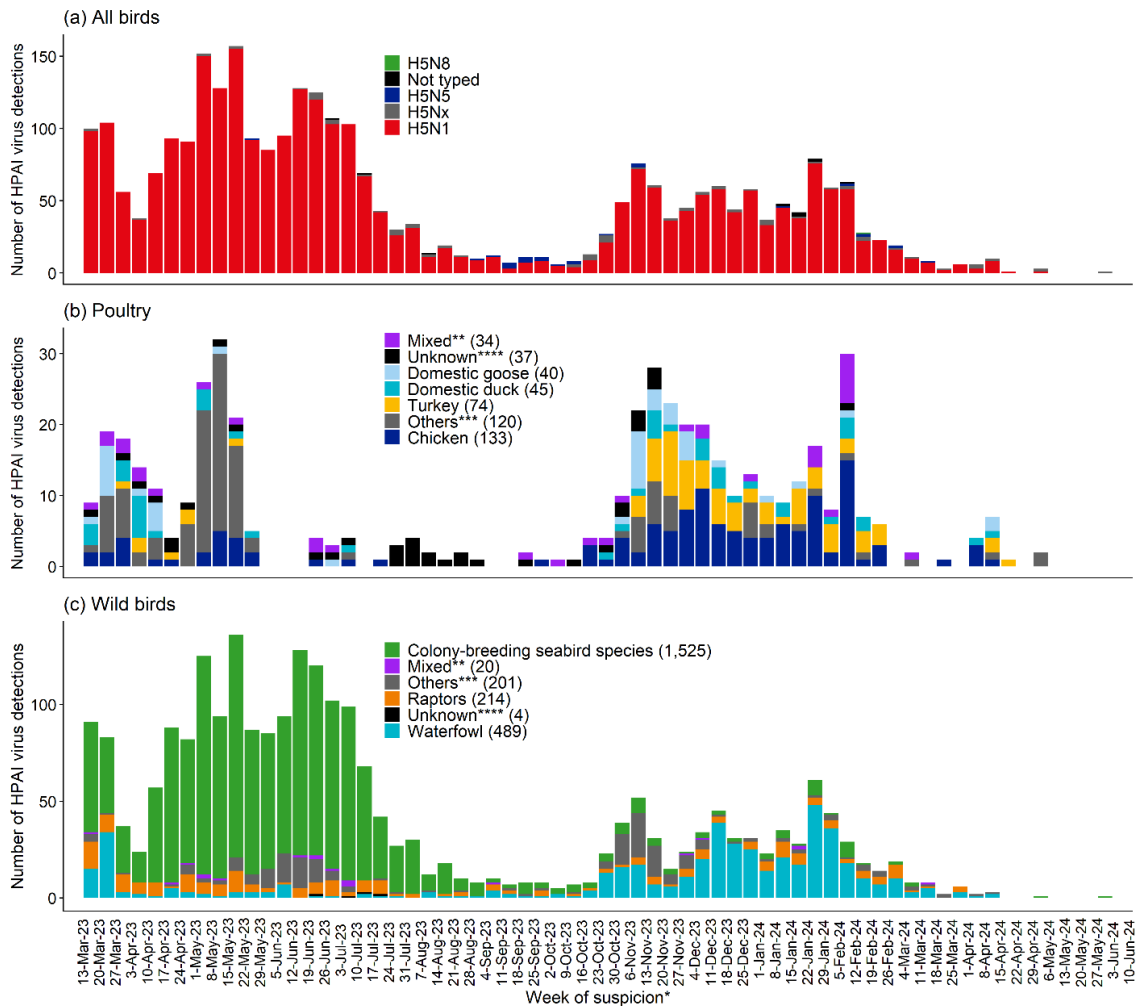
During the current reporting period, HPAI outbreaks in poultry were still concentrated in south-eastern Europe and occurred in two clusters in Bulgaria and Hungary (Table 1, Figure 2). These clusters spatially coincide with HPAI virus detections in two white storks in Bulgaria and Romania (at the border with Hungary), suggesting further presence of the virus in wild birds in the area.

No HPAI outbreaks in captive birds were reported during this reporting period (Table 1).

The spatial pattern in wild birds consisted in only a few HPAI virus detections fairly dispersed in a broad band from north-western to south-eastern Europe, with no detections

<sup>5</sup> In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and in particular with the Windsor Framework, the EU requirements on data sampling are also applicable to the United Kingdom (Northern Ireland).

in north-eastern Europe and only one detection at the south-westernmost tip of the Iberian Peninsula (Figure 2). Although the total number was relatively low, infected wild birds were reported from 12 different European countries (Table 1). The majority of these HPAI virus detections continued to concern waterfowl, while the EA-2022-BB genotype had not completely disappeared and was still occasionally found in colony-breeding seabirds (Figure 3).



United Kingdom data are from ADNS up until 31 December 2020. From 1 January 2021 onwards, the data source was WOHAI for the United Kingdom (excluding Northern Ireland) and ADNS/ADIS for the United Kingdom (Northern Ireland)<sup>6</sup>.

\*If the date of suspicion was not available, the date of confirmation was used to assign the week of suspicion.

\*\*'Mixed' refers to outbreaks in which multiple species or categories were involved.

\*\*\*'Others' groups all other affected categories that are not indicated in the legend.

\*\*\*\*'Unknown' refers to affected categories that were not further specified during reporting.

Source: ADNS/ADIS, EFSA and WOHAI (data extraction carried out on 14 June 2024).

**Figure 3:** Distribution of the total number of HPAI virus detections reported in Europe by week of suspicion (dates indicate the first day of the week) and virus subtype (a), affected poultry categories (b) and affected wild bird categories (c), from 16 March 2023 to 14 June 2024

<sup>6</sup> In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and in particular with the Windsor Framework, the EU requirements on data sampling are also applicable to the United Kingdom (Northern Ireland).

While the majority of HPAI virus detections in birds during this reporting period can be attributed to HPAI A(H5N1) viruses, A(H5N5) viruses were still sporadically present in a mixed wild bird outbreak in the United Kingdom (Table 1, Figure 2, Figure 3).

Spatio-temporal information on all HPAI virus detections reported in Europe since October 2016 is available via EFSA's interactive dashboard<sup>7</sup>.

## Domestic birds

Between 16 March and 14 June 2024, 15 HPAI outbreaks in poultry were reported from two countries in Europe: 8 A(H5N1) from Hungary and 7 A(H5Nx) from Bulgaria (Table 1, Figure 2). This compares to a total of 173 A(H5) outbreaks during the same period in the previous epidemiological year and is the lowest number recorded for this period since 2019. Eleven of those outbreaks were reported as primary and 4 as secondary. For 10 of these outbreaks, indirect contact with wild birds was considered the most likely source of introduction, although for both countries the number of HPAI virus detections in wild birds was very limited (1 in Bulgaria and 0 in Hungary). In total, approximately 1 million birds died or were culled in the HPAI-affected poultry establishments.

In the following paragraphs, a brief description of the HPAI outbreaks in poultry is given by country. This description is based on information collected by EFSA from ADIS, reporting countries (in form of additional data submitted and personal communications) and media reports. In the time period from 16 March to 14 June 2024, 15 HPAI outbreaks in poultry were reported in Europe via ADIS. Additional data on the characteristics of the affected poultry establishments and poultry species reared (Annex B) were collected for all outbreaks in poultry occurred during this reporting period.

### *Bulgaria*

During the current reporting period from 16 March to 14 June 2024, 7 outbreaks in poultry were reported in Bulgaria via ADIS. All outbreaks were primary outbreaks and reported as A(H5Nx). Six of them occurred in commercial mono-species establishments. On 27 March, the first outbreak was confirmed in an establishment keeping laying hens (n = 86,054) without outdoor access. Increased mortality and a decrease in egg production, as well as reduced feed and water intake, were observed. No other clinical signs were present. The most likely source of introduction was indirect contact with wild birds. On 9 April, an outbreak was detected through active surveillance in another establishment keeping laying hens (n = 25,028). Increased mortality and clinical signs, with reduced feed and water intake, were observed, but no decrease in egg production was reported. The most likely source of introduction was indirect contact with poultry, even though the outbreak was reported as primary. No outdoor access for birds was available in the establishment. Two other outbreaks were detected in the two following days: 1 in a backyard flock keeping chickens (n = 98) and 1 in an establishment keeping broilers (n = 396,561). Increased mortality, clinical signs and decreased feed and water intake were reported in both establishments. In each case, the most likely source of introduction was indirect contact with wild birds. Outdoor access was available for the birds in the backyard flock, but not in the commercial broiler establishment. On 16 April, an outbreak was confirmed in an establishment keeping laying hens (n = 153,893) without outdoor access. Increased mortality, clinical signs and decreased feed and water intake were described,

---

<sup>7</sup> <http://hpaiefsa.aus.vet/>

however, no decrease in egg production was reported. The most likely source of introduction was indirect contact with wild birds. On 9 May, the virus was reported in 2 commercial establishments keeping ducks for foie gras production ( $n = 1,800$  and  $n = 6,300$ ). The presence of the virus in these establishments was detected through active surveillance. No increased mortality or clinical signs were observed. Outdoor access for birds was provided in both establishments, with the most likely source of introduction being indirect contact with wild birds. In total, 38 people were reported as exposed.

### *Hungary*

During the current reporting period from 16 March to 14 June 2024, 8 outbreaks in poultry were reported in Hungary via ADIS. Half of them were considered secondary and all of them occurred in commercial mono-species establishments. On 13 April, an A(H5N1) outbreak was detected in an establishment keeping ducks for fattening ( $n = 45,000$ ). The establishment did not provide outdoor access and the most likely source of introduction was indirect contact with wild birds. On 15 April, the following 4 outbreaks were reported: a secondary outbreak, close to the previous one, in an establishment keeping geese for fattening ( $n = 6,150$ ), and another secondary outbreak in an establishment keeping ducks for fattening ( $n = 4,880$ ). This establishment belonged to the same owner who had experienced another outbreak in a different establishment in Hungary two days earlier. On the same day, two primary outbreaks were reported in establishments keeping geese ( $n = 1,700$ ) and turkeys for fattening ( $n = 19,900$ ). Outdoor access for poultry was not available in these establishments. The most likely source of introduction for the last two outbreaks was indirect contact with wild birds. On 18 April, the virus was detected in an establishment keeping turkeys for fattening ( $n = 26,500$ ). These animals were reported to originate from the same establishment as the turkeys that tested positive for A(H5N1) virus three days earlier. Since no animals were present in the holding of origin when the outbreaks were reported, it was not affected by the virus. The outbreak was then defined as secondary, and the most probable source of introduction was indirect contact with poultry. On 20 April 2024, an outbreak was detected in an establishment keeping Mulard ducks for foie gras production ( $n = 2,000$ ). The owner of these animals was the same as the owner of the geese that tested positive for A(H5N1) virus on 15 April. Therefore, the most likely source of introduction was indirect contact with poultry. On 26 April, another outbreak was detected in an establishment keeping turkeys for fattening ( $n = 20,000$ ). Outdoor access for birds was not provided by the establishment and the most probable source of introduction was indirect contact with wild birds. Despite the suspected role of wild birds in virus introduction in 4 outbreaks, no cases of A(H5N1) virus-positive wild birds were reported in the country during the reporting period. Increased mortality and clinical signs were reported in all 8 outbreaks. Decreased feed and water intake were observed in all establishments, except the 3 keeping turkeys. No information on the number of exposed people was available at the time of production of this report.

### *Sweden*

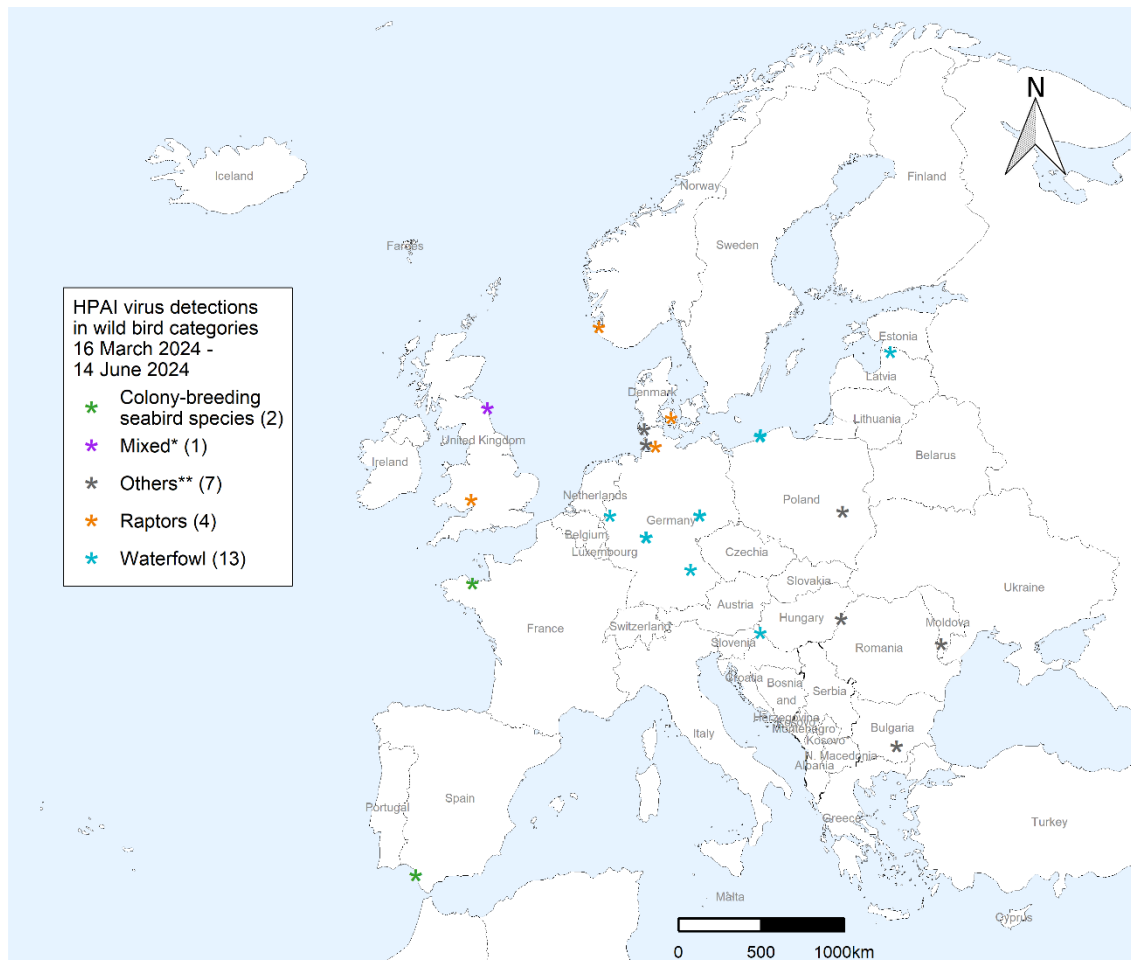
On 14 March 2024, 1 outbreak in poultry was suspected in Sweden, which had not yet been included in the previous report. It occurred during the previous reporting period (from 2 December 2023 to 15 March 2024), was confirmed on 16 March and reported via ADIS on 17 March. Therefore, this outbreak is not part of the data presented in the figures and tables of this report, but it is discussed in this paragraph for completeness. The A(H5N1) outbreak was confirmed in a multi-species establishment keeping pheasants for breeding

(n = 218), domestic pigeons (n = 25) and ornamental birds (n = 43), as well as dogs (n = 2) and ferrets (n = 4). All animals present in the establishment were tested, but only pheasants tested positive for A(H5N1) virus. Increased mortality and clinical signs were only reported in pheasants. Outdoor access was available for all animals in the establishment. The most likely source of introduction was indirect contact with wild birds, with several wild bird species observed near the establishment. Five people were reported as exposed.

## Wild birds

During the time period from 16 March to 14 June 2024, a total of 24 A(H5N1), 1 A(H5N5) and 2 A(H5Nx) virus detections were reported from Germany (13), Poland (3), the United Kingdom (2) and, one each, from Bulgaria, Denmark, France, Latvia, Moldova, Norway, Romania, Slovenia and Spain (Table 1, Figure 2).

The overall number of HPAI virus detections in wild birds (27) was about 16 times lower than in the previous reporting period (2 December 2023 to 15 March 2024). Of note, HPAI virus detections were only recorded in 3 colony-breeding seabirds identified to species (Figure 4): a European herring gull in France (A(H5Nx)), a sandwich tern in Spain (A(H5N1)) and another European herring gull in the United Kingdom (A(H5N5)).



Author: EFSA  
Data sources: ADIS, WOH  
Date updated: 14/06/2024

\*This designation is without prejudice to positions on status and is in line with United Nations Security Council Resolution 1244 and the International Court of Justice Opinion on the Kosovo Declaration of Independence.

Note that the unit reported is the number of HPAI virus detections in different wild bird categories and not the number of HPAI virus detections in wild birds (as more than one species can be involved in one single HPAI virus detection reported).

\*\*Mixed' refers to outbreaks in which multiple categories were involved.

\*\*\*Others' groups all other affected categories that are not indicated in the legend.

Source: ADIS, EFSA and WOA (data extraction carried out on 14 June 2024).

**Figure 4:** Geographic distribution, based on available geocoordinates, of HPAI virus detections in different categories of wild birds in Europe, by species category, from 16 March to 14 June 2024

Therefore, in contrast to previous epidemiological years, there was no indication of increased mortality from HPAI in this category of wild birds (including black-headed gulls), even though they were aggregating at breeding colony sites from April onwards. While the majority of HPAI virus detections in wild birds were due to A(H5N1) virus, there was a single detection of A(H5N5) virus in a mixed outbreak involving a European herring gull and a peregrine falcon in the United Kingdom.

Overall, these data suggest that HPAI viruses were only circulating at a low level, if at all, without causing mass mortality events in wild bird populations in Europe during the current reporting period. Possible explanations are acquired flock immunity after previous infections, depletion of certain wild bird populations and underreporting due to decreased detection of dead wild birds in certain countries. HPAI virus detections in wild birds are generally underestimated. Therefore, the numbers provided are not representative of the number of wild birds that actually died from A(H5) virus infection.

The few wild birds in which HPAI viruses were detected belonged to six different orders, mainly Anseriformes (13), Charadriiformes (6), and Ciconiiformes (4) (Figure A.1 in Annex A). No new wild bird species were reported as infected in Europe during the current reporting period. The most common waterfowl identified to species were the mute swan (3 in the current vs 106 in the previous reporting period) and greylag goose (2 vs 21) (Figure A.1 in Annex A), while it is concerning that 8 waterfowl in which HPAI viruses were reported were not identified to species. The three raptors identified to species in which HPAI virus detections were reported were the common buzzard (2 vs 31), Eurasian eagle-owl (1 vs 1), and Eurasian sparrowhawk (1 vs 3). The only two colony-breeding seabirds identified to species in which HPAI virus detections were reported were the European herring gull (2 vs 15) and sandwich tern (1 vs 0). The main species in the 'other' wild bird category was the white stork (4 vs 1).

The complete list of wild bird species found as HPAI virus-infected from 16 March to 14 June 2024 is reported in Figure A.1 in Annex A. The number of HPAI virus-affected wild birds that were not identified to species was 11/28 (39.3%), a large increase compared to the previous reporting period (98/454, 21.6%) (Figure A.2 in Annex A). This was especially the case in Germany, where identification of wild bird species in ADIS is based on the immediate report of the district veterinary officer to the German animal disease information system (TSN) shortly after confirmation in the national reference laboratory (NRL). The more precise information on the species is later entered into the German AI surveillance database (AI-DB) by the federal state laboratory.

Note that Figure 4 and Figures A.1–A.2 in Annex A provide information on the numbers of wild bird categories/families/species that were detected as HPAI virus-infected at single bird level, as more than one bird can be involved in one single HPAI virus detection reported.

### 2.1.2 HPAI virus detections in birds outside Europe

An overview of the HPAI virus detections in birds that were notified from other countries not reporting via ADIS but via WOA from 16 March to 14 June 2024 is presented in Table 2 and Figure 5.

**Table 2:** Number of HPAI virus detections in non-European countries, by virus subtype and country, from 16 March to 14 June 2024

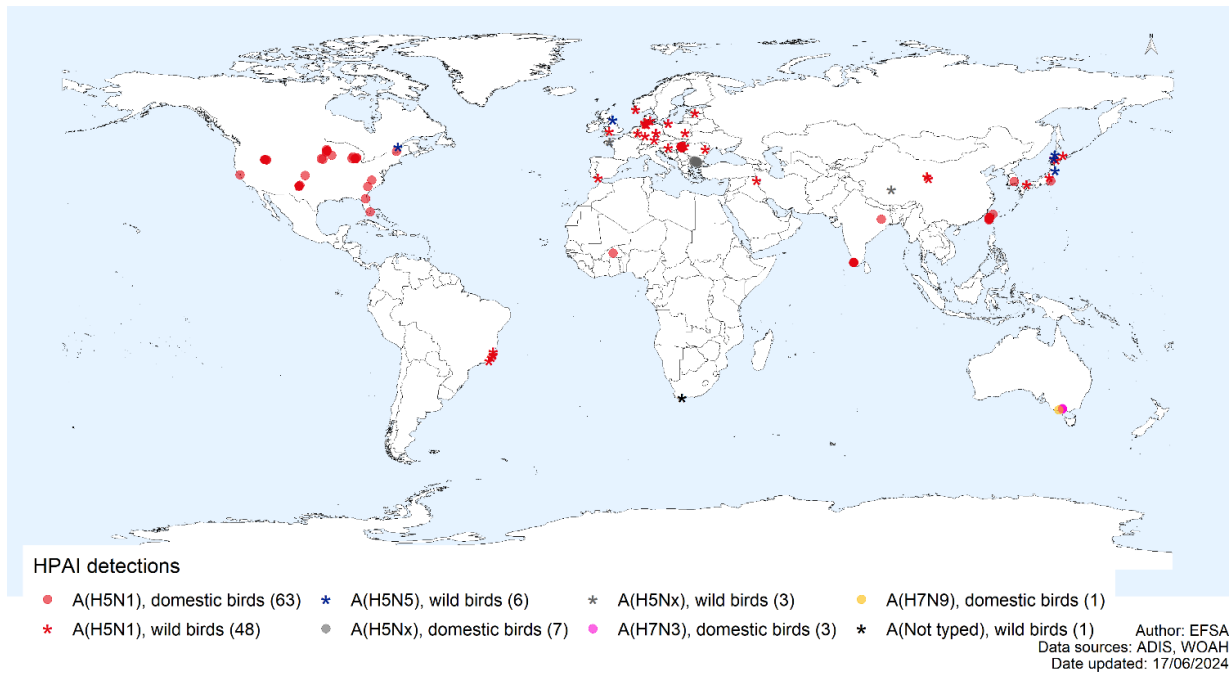
Region	Country	Domestic birds								Wild birds					Total
		A(H5N1)	A(H5N2)	A(H5N6)	A(H5Nx)	A(H7N3)	A(H7N6)	A(H7N9)	A(Not typed)	A(H5N1)	A(H5N5)	A(H5N6)	A(H5Nx)	A(Not typed)	
Africa (36)	Burkina Faso	1 (2)	-	-	-	-	-	-	-	-	-	-	-	-	1 (2)
	Nigeria	0 (3)	-	-	-	-	-	-	-	-	-	-	-	-	0 (3)
	South Africa	-	-	-	-	-	0 (21)	-	0 (8)	-	-	-	-	1 (2)	1 (31)
Americas (506)	Argentina	-	-	-	-	-	-	-	-	-	-	-	0 (1)	-	0 (1)
	Brazil	-	-	-	-	-	-	-	-	5 (44)	-	-	-	-	5 (44)
	Canada	1 (52)	-	-	-	-	-	-	-	0 (10)	1 (2)	-	0 (1)	-	2 (65)
	Colombia	-	-	-	0 (13)	-	-	-	-	-	-	-	0 (1)	-	0 (14)
	Costa Rica	-	-	-	-	-	-	-	-	-	-	-	0 (2)	-	0 (2)
	Ecuador	0 (2)	-	-	-	-	-	-	-	0 (2)	-	-	-	-	0 (4)
	Mexico	0 (7)	0 (1)	-	-	-	-	-	-	0 (9)	-	-	-	-	0 (17)
	Peru	-	-	-	0 (36)	-	-	-	-	-	-	-	0 (4)	-	0 (40)
	United States of America	35 (308)	-	-	-	-	-	-	-	2 (10)	-	-	-	-	37 (318)
Uruguay	-	-	-	-	-	-	-	-	0 (1)	-	-	-	-	0 (1)	
Antarctica (8)	Antarctica	-	-	-	-	-	-	-	-	0 (1)	-	-	0 (1)	-	0 (2)
	Falkland Islands	-	-	-	-	-	-	-	-	0 (1)	-	-	-	-	0 (1)
	South Georgia and the South Sandwich Islands	-	-	-	-	-	-	-	-	0 (5)	-	-	-	-	0 (5)
Asia (302)	Cambodia	0 (12)	-	-	-	-	-	-	-	-	-	-	-	-	0 (12)
	China	-	-	-	-	-	-	-	-	2 (3)	-	-	1 (1)	-	3 (4)
	Hong Kong	-	-	-	-	-	-	-	-	0 (6)	-	-	-	-	0 (6)
	India	7 (10)	-	-	-	-	-	-	-	-	-	-	-	-	7 (10)
	Iraq	-	-	-	-	-	-	-	-	1 (1)	-	-	-	-	1 (1)



	Israel	0 (3)	-	-	-	-	-	-	-	0 (9)	-	-	-	-	<b>0 (12)</b>
	Japan	1 (10)	-	0 (1)	-	-	-	-	-	14 (11 2)	4 (31)	0 (1)	-	-	<b>19 (155)</b>
	Kazakhstan	-	-	-	-	-	-	-	-	-	-	-	0 (1)	-	<b>0 (1)</b>
	Korea	1 (7)	-	0 (26)	-	-	-	-	-	0 (6)	-	0 (11)	-	-	<b>1 (50)</b>
	Philippines	0 (7)	-	-	-	-	-	-	-	-	-	-	-	-	<b>0 (7)</b>
	Taiwan	9 (41)	-	-	-	-	-	-	-	0 (3)	-	-	-	-	<b>9 (44)</b>
Europe (3)	Russia	0 (3)	-	-	-	-	-	-	-	-	-	-	-	-	<b>0 (3)</b>
Oceania (4)	Australia	-	-	-	-	3 (3)	-	1 (1)	-	-	-	-	-	-	<b>4 (4)</b>
<b>Total</b>		<b>55 (46 7)</b>	<b>0 (1)</b>	<b>0 (27)</b>	<b>0 (49)</b>	<b>3 (3)</b>	<b>0 (21)</b>	<b>1 (1)</b>	<b>0 (8)</b>	<b>24 (22 3)</b>	<b>5 (33)</b>	<b>0 (12)</b>	<b>1 (12)</b>	<b>1 (2)</b>	<b>90 (859)</b>

'-' means that no HPAI outbreaks were notified to WOAHA.

Source: WOAHA (data extraction carried out on 14 June 2024).



**Figure 5:** Geographic distribution, based on available geocoordinates, of HPAI virus detections reported worldwide in domestic (74) and wild (58) birds by virus type, from 16 March to 14 June 2024

In the tables and figures of the present report, only data extracted from WOAHA on 14 June 2024 are presented. However, HPAI virus detections in poultry and wild birds are also reported to the public via different means. This additional information on HPAI virus detections available from sources other than WOAHA-WAHIS has been integrated in the text below.

In comparison to the previous reporting period from 2 December 2023 to 15 March 2024 (EFSA, ECDC and EURL, 2024a), the total number of HPAI outbreaks in domestic and wild birds officially notified to WOAHA dropped considerably from 378 to 90, and the number

of countries outside Europe from 22 to 12 (Table 2, Figure 5). The official figures reported to WOAHP during the current reporting period were also lower than the number of outbreaks reported between 29 April and 23 June in 2023 (90 vs 121 outbreaks) (EFSA, ECDC and EURL, 2023). In contrast to previous years, no outbreaks in Russia were reported to WOAHP in the period from 16 March to 14 June 2024. In addition to Canada and the United States of America (USA), which reported HPAI A(H5) in poultry and wild birds, of the South American countries only Brazil reported cases, all of which occurred in wild birds. In addition, A(H5) was detected in wild birds in only three further countries that were also previously affected, namely China, Iraq and South Africa. Overall, HPAI outbreaks in domestic birds officially reported to WOAHP (59 vs 234) as well as the number of cases in wild birds (31 vs 144) decreased significantly in the current vs the previous reporting period.

No further outbreaks in poultry were reported from South Africa, but A(HxNx) was detected in a greater crested tern. The outbreak of A(H5N1) in Burkina Faso continued and the virus was detected in a backyard flock in a previously affected area.

The large epidemic of A(H5N1) in the USA and Canada continued in poultry establishments of all sizes on a high level and accounted for 59% of the reported outbreaks in domestic birds outside Europe. At the end of March and beginning of April 2024, A(H5N1) virus was detected in very large poultry flocks with a population size of between 1.8 and 2.5 million birds. At the end of May, the Iowa Department of Agriculture reported that one of the biggest table egg producers in the country (4.2 million poultry) and a large turkey farm with over 100,000 birds were infected with HPAI virus (Des Moines Register, online). The outbreaks in Iowa were the first since December 2023, when a backyard flock was infected. Since 2022, Iowa poultry producers have lost 23.3 million birds to the disease and the United States Department of Agriculture (USDA) estimated that the virus has killed 96.6 million birds nationwide (Des Moines Register, online). Furthermore, medium- and some small-scale farms were affected by the epidemic in the rest of North America as well as live bird markets (UNMC, online-a). The USDA also reported the detection of A(H5) in 106 captive and 213 wild birds, comprising a total of 55 different species, in the period from 16 March to 17 June 2024 (Figures A.3 and A.7–A.10 in Annex A) (USDA, online-a). Canada notified to WOAHP an outbreak of A(H5N1) in a small establishment with captive birds, and a case of A(H5N5) was detected in an American crow. Furthermore, only the media reported an outbreak of HPAI A(H5N2) in a backyard poultry flock in the state of Michoacán, Mexico, and two outbreaks of LPAI A(H5N2) in Temascalapa and Texcoco in the state of Mexico, respectively (GovMEX, online; WHO, online-a). In contrast to the previous reporting period, only Brazil from the South American countries notified A(H5N1) virus detections in terns (common tern and Cabot's tern) at previously affected locations on the Brazilian Atlantic coast.

In the period from 16 March to 14 June 2024, several countries in Asia reported outbreaks of HPAI to WOAHP from previously affected areas. Japan detected A(H5N1) in a large poultry establishment, and A(H5N5) in large-billed crows and European herring gulls. Furthermore, the outbreaks of A(H5N1) of clade 2.3.4.4b in poultry establishments of all sizes and wild birds in Taiwan continued. However, in contrast to the previous reports, no outbreaks of the Taiwanese lineage A(H5N2) were reported in wild birds (EFSA, ECDC and EURL, 2021). Korea notified an outbreak of A(H5N1) in a large poultry establishment to WOAHP, and China detected A(H5) and A(H5N1) in several, not further specified European wild bird species. The latter report is of concern due to their migration to breeding areas

in northern Asia and subsequent autumn migration south to the Americas, Asia and Europe. In contrast to the previous reporting period, Iraq detected A(H5N1) in a gull. Seven outbreaks of A(H5N1) in poultry in India were notified to WOA, with high mortality in ducks and chickens described (Hindustan Times, online). Six outbreaks were detected in Kerala state and one in Jharkhand state. Additionally, in June, media reported about mass mortality in wild birds in different districts of Kerala state due to the virus. HPAI virus-positive crows, kites, herons and quails were reported, without precise information on the species affected, the number of individuals or the detected subtype (The Hindu, online). Furthermore, only the media reported outbreaks of A(H5N1) in domestic birds in the Philippines (Noticias Agrícolas, online) and Vietnam (CIDRAP, online-a), countries that have been affected in previous epidemiological years.

Australia officially notified to WOA three outbreaks of A(H7N3) and one outbreak of A(H7N9) in very large layer farms in the state of Victoria. Furthermore, the Australian government and media reported about two further outbreaks of A(H7N3) in layer farms and one outbreak in a duck farm (GovAU, online; The Poultry Site, online). Finally, yet another subtype, A(H7N8), was detected in layers in the state of New South Wales (The Guardian, online-a; GovAU, online). Presumably, these HPAI outbreaks occurred after incursion of LPAI A(H7) viruses from free-living wild waterfowl into commercial poultry establishments, followed by on-farm conversion to HPAI A(H7) viruses (Scott et al., 2020).

Although no HPAI from the Antarctic region was reported to WOA during the current reporting period since 16 March 2024, the detection of HPAI virus has been confirmed in skuas (brown and/or Antarctic) on several islands (Paulet, Beak, Devil) on the northeastern coast of the Antarctic Peninsula (SCAR, online). However, the authors of a recent publication did not detect any infections on the South Shetland Islands (Muñoz et al., 2024a). In another publication, the authors suspected A(H5N1) in penguins and shags on the Antarctic Peninsula and West Antarctic Coast (León et al., 2024). Furthermore, research expeditions and studies exploring the impact of A(H5N1) on birdlife of the Antarctic region are still ongoing (FLI, 2024; Reuters, online-a).

The list of wild bird species that have been reported to WOA as HPAI virus-infected from 16 March to 14 June 2024 is presented in Table A.1 in Annex A.

### 2.1.3 Genetic characteristics of HPAI viruses of the A(H5Nx) subtype in avian species

Details on the nomenclature of the HPAI A(H5) viruses used in this section are reported in Appendix B. Genotypes are assigned using the criteria described in Fusaro et al. (2024). Mutation analyses of the A(H5N1) viruses have been performed using FluMut (Github izsvenezie-virology, online-a, b) with FluMutDB v5.0 mutation database.

#### **Genetic diversity of HPAI A(H5Nx) viruses in avian species in Europe**

Since October 2023, complete genome sequences of > 650 European clade 2.3.4.4b A(H5) viruses have been characterised. The vast majority (> 90%) belong to six different A(H5N1) and one A(H5N5) genotypes, namely EA-2021-AB (H5N1 A/duck/Saratov/29-02/2021-like), EA-2022-BB (H5N1-A/Herring\_gull/France/22P015977/2022-like), EA-2023-DA (H5N1-A/mute\_swan/Slovenia/PER1486-23TA\_23VIR10323-22/2023-like), EA-2023-DB (H5N1-A/herring\_gull/Germany-NI/2023AI08764/2023-like), EA-2023-DG (H5N1-A/Gallus\_gallus/Belgium/11307\_0002/2023-like), EA-2024-DI (H5N1 A/mute\_swan/Poland/MB008-1/2024-like) and EA-2021-I (H5N5

A/whooper\_swan/Romania/10123\_21VIR849-1/2021-like). Three of these genotypes (EA-2021-AB, EA-2022-BB and EA-2021-I) have persistently been circulating in Europe from previous epidemiological years, while four have newly emerged from reassortment events of the internal gene segments with LPAI viruses. Whether these new genotypes have originated in Europe or represent new virus introductions cannot be assessed, given the limited data available from other countries outside Europe.

Interestingly, genotype EA-2022-BB, which circulated extensively among Laridae in Europe in summer 2023, and was responsible for all of the outbreaks reported in fur farms in Europe in 2022–2023 (Spain and Finland), has only been detected at low level in the current epidemiological year. Since December 2023, this genotype has only been reported in France and Spain, with the last case identified in a European herring gull in France in March 2024. Of note, a novel genotype (EA-2023-DT) originating from a reassortment event of the PB1 gene between the EA-2022-BB and a gull-adapted H13 subtype has been circulating among Laridae and Sulidae in Spain since November 2023.

On the other hand, an increase in the number of detections in Laridae of subtype A(H5N5), genotype EA-2021-I, was observed. This genotype, which emerged in Europe in 2021, has been detected in Norway since the 2021–2022 epidemiological year. In September 2023, viruses of this genotype, highly related to the Norwegian viruses, were identified in Iceland, Greenland and the United Kingdom, followed by the Netherlands and Germany in January and February 2024, which suggests a geographic expansion of this variant. Based on the data available in GISAID (accessed on 3 June 2024), the EA-2021-I was identified also in Canada in the first half of 2023 and in Japan in 2023–2024, indicating the spread of this genotype from Europe to northern areas of other continents. Most of these cases have been identified in scavengers and raptors of the orders Charadriiformes, Accipitriformes, Procellariiformes and Passeriformes, with Laridae in Europe and Canada, and large-billed crows in Japan as the most affected species.

A single virus of the A(H5N8) subtype was identified in a red knot in Germany in February 2024. Genetic data indicate that this virus originated from a novel reassortment event with an LPAI virus, likely occurring in this host species.

Based on the available data, the A(H5N1) collected from poultry outbreaks during the current epidemiological year belong to 15 genotypes, with genotypes EA-2021-AB, EA-2023-DA, EA-2023-DB, EA-2023-DG and EA-2024-DI collected in four or more countries. In Bulgaria, data available so far indicate multiple virus introductions into the poultry population as well as a persistent circulation of viruses of the EA-2023-DA genotype in domestic birds, suggesting a possible farm-to-farm virus transmission.

### **Mutations identified in HPAI A(H5Nx) viruses from avian species in Europe**

Molecular analyses of the A(H5N1) viruses circulating in birds in Europe during the 2023–2024 epidemiological year indicate that these viruses continue to be well-adapted to avian species, as they retain a preferential binding for avian-like receptors. However, several mutations, previously described in literature (Du et al., 2018; Suttie et al., 2019; Pinto et al., 2023) have been identified as being associated with i) enhanced polymerase activity and replication in mammals or mammalian cells, ii) increased virulence, iii) increased/conferred resistance towards antiviral drugs, iv) increased in vitro binding to human-type receptors alpha2,6-SA, v) decreased antiviral response in ferrets, vi) evasion of human butyrophilin subfamily 3 member A3 (BTN3A3) and vii) disruption of the second

sialic acid (SIA) binding site in the neuraminidase protein, with a frequency varying by the distinct mutations. The net effect of these mutations on the biological characteristics of the viruses is still unknown and further studies are needed to improve existing knowledge. Since October 2023, mutations in the PB2 protein associated with virus adaptation in mammals (E627K, D701N or K526R) have been detected in 16 European viruses collected from birds, more specifically in i) nine genetically related A(H5N5) viruses (genotype EA-2021-I) collected from wild birds in Norway, the Netherlands, England and Germany in January–February 2024; ii) six A(H5N1) viruses collected between October 2023 and March 2024 from separate outbreaks in domestic birds in Poland (genotypes EA-2022-CH and EA-2022-AB), Denmark (genotype EA-2023-DB), Czechia (genotype EA-2024-DI) and Romania (genotype EA-2023-DA); iii) one A(H5N1) virus collected from a wild bird in France in February 2024 (genotype EA-2022-BB). Of note, the emergence of mutations PB2-E627K and PB2-D701N have also been observed in several A(H5N5) viruses (genotype EA-2021-I) collected from wild birds and mammal species in Canada and Japan. Phylogenetic clustering suggests that these mammalian adaptive markers have emerged independently in the different continents.

Among the mutations in the HA protein that have proved to increase in vitro binding to human-type receptors, some (i.e. S133A, S154N, T156A and H5 numbering) have been identified in the majority of the A(H5N1) viruses which have been circulating in Europe since October 2023, while others (i.e. E251K, E75K-S123P, P235S, V210I and S155N) have only been sporadically observed. The impact of these HA mutations on the biological characteristics of the circulating viruses is still unknown; however, none of them has been demonstrated to cause a shift from avian-like to human-like receptor binding preference. Moreover, the majority of the A(H5N1) viruses belonging to the EA-2022-BB and EA-2023-DT genotypes contain mutations NP-Y52N and NA-S369I, which are also associated with increased zoonotic potential. In addition, all the currently circulating A(H5N5) viruses (genotype EA-2021-I) contain a deletion in the NA stalk region, which is a virulence determinant in chickens (Stech et al., 2015). Mutations associated with antiviral resistance have rarely been identified in the circulating strains (about 3%).

### **Genetic characteristics of zoonotic avian influenza viruses in birds outside Europe**

The recent A(H10N3) virus human infection in China has increased interest in this subtype and in the threat it poses to public health. Recent studies (Zhang et al., 2023a; Liu et al., 2024a) investigated the genetic and biological features of the A(H10N3) viruses that had circulated in domestic birds in China between 2014 and 2022. Phylogenetic analyses indicate that the HA and NA genes of all the A(H10N3) viruses collected in the country since 2019 formed a monophyletic group with the Eurasian lineage. In contrast, the internal genes originated from multiple reassortment events with A(H9N2) viruses. Most of these viruses contain several amino acid mutations associated with mammalian adaptation in the polymerases (i.e. R340K, R477G, I495V, A588V and E627V in the PB2, I368V and S622G in the PB1, A100V, P224S, K356R, K142R and S409N in the PA) and surface glycoproteins, including G228S (H3 numbering) in the receptor binding site of the HA, which could enhance the binding capacity for both avian and human receptors. Moreover, these studies demonstrated that some of the poultry A(H10N3) viruses are highly virulent or lethal to mice and could be transmitted between guinea pigs via direct contact or respiratory droplets. The A(H10N3) virus responsible for the recent human case is highly related to the viruses circulating in poultry. However, compared to these strains.

the virus from the human case contains the additional mutations HA-Q226L (H3 numbering) and PB2-D701N associated with increased virus adaptation to mammals.

## 2.2 HPAI virus detections in non-human mammals

### 2.2.1 HPAI virus detections in non-human mammals worldwide

From 16 March to 24 June 2024, HPAI A(H5N1) viruses were reported in wild and domestic mammals in Europe and the USA. The data described were actively collected from Member States and other European countries, retrieved through WOA-H-WAHIS and from the USDA websites (for cases occurred in the USA), and supplemented with information from media reports (Table 3).

**Table 3:** Avian influenza A(H5Nx) virus detections in mammalian species other than humans related to circulating viruses worldwide, 2016–2024

Virus	Animal (order, family, species)		Country	Reference	
A(H5N1) or A(H5Nx) clade 2.3.4.4b	Artiodactyla	Bovidae	Cattle ( <i>Bos taurus</i> )	United States of America	WOAH USDA
			Goat ( <i>Capra hircus</i> )	United States of America	WOAH USDA
		Camelidae	Alpaca ( <i>Lama pacos</i> )	United States of America	USDA, online-g
		Suidae	Pig ( <i>Sus scrofa</i> )*	Italy	Rosone et al. (2023)
	Carnivora	Canidae	Arctic fox ( <i>Vulpes lagopus</i> )	Finland	WOAH
			Common raccoon dog ( <i>Nyctereutes procyonoides</i> )	Finland, Japan, Sweden*	WOAH Personal communication by Malin Grant (SVA, 2024)
			Coyote ( <i>Canis latrans</i> )	United States of America	WOAH
			Dog ( <i>Canis lupus familiaris</i> )	Canada, Italy*, Poland	WOAH Szaluś-Jordanow et al. (2024)
			Japanese raccoon dog ( <i>Nyctereutes viverrinus</i> )	Japan	WOAH
			Red fox ( <i>Vulpes vulpes</i> )	Belgium, Canada, Denmark, Estonia, Finland, France, Germany, Ireland, Italy, Japan, Latvia, Netherlands, Norway, Sweden**, United Kingdom (Northern Ireland), United Kingdom, United States of America	WOAH
			South American bush dog ( <i>Speothos venaticus venaticus</i> )	United Kingdom	WOAH
		Felidae	Amur leopard ( <i>Panthera pardus</i> )	United States of America	WOAH
			Amur tiger ( <i>Panthera tigris</i> )	United States of America	WOAH
			Bobcat ( <i>Lynx rufus</i> )	United States of America	WOAH

Virus	Animal (order, family, species)	Country	Reference		
	Caracal ( <i>Caracal caracal</i> )	Poland	WOAH		
	Cat ( <i>Felis catus</i> )	Canada, France, Hungary**, Italy*, Korea, Poland, United States of America	WOAH		
	Eurasian lynx ( <i>Lynx lynx</i> )	Finland, Sweden*	WOAH Personal communication by Malin Grant (SVA, 2024)		
	Lion ( <i>Panthera leo</i> )	Peru	WOAH		
	Mountain lion ( <i>Puma concolor</i> )	United States of America	WOAH		
	Mephitidae	Striped skunk ( <i>Mephitis mephitis</i> )	Canada, United States of America	WOAH	
	Mustelidae	American marten	United States of America	WOAH	
		American mink ( <i>Neovison vison</i> )	Canada, Finland, Spain	WOAH	
		Beech marten ( <i>Martes foina</i> )	Netherlands	GISAID (online)	
		Eurasian otter ( <i>Lutra lutra</i> )	Netherlands, Finland, Sweden, United Kingdom	WOAH	
		European badger ( <i>Meles meles</i> )	Netherlands	WOAH	
		European pine marten ( <i>Martes martes</i> )	Germany	WOAH	
		European polecat ( <i>Mustela putorius</i> )	Belgium, Netherlands	WOAH	
		Ferret ( <i>Mustela furo</i> )	Belgium, Poland, Slovenia	WOAH Golke et al. (2024)	
		Fisher ( <i>Pekania pennanti</i> )	United States of America	WOAH	
		Marine otter ( <i>Lontra felina</i> )	Chile	WOAH	
		North American river otter ( <i>Lontra canadensis</i> )	United States of America	WOAH	
		Sable ( <i>Martes zibellina</i> )*	Finland	WOAH	
		Southern river otter ( <i>Lontra provocax</i> )	Chile	WOAH	
		Otariidae	Antarctic fur seal ( <i>Arctocephalus gazella</i> )	South Georgia and the South Sandwich Islands	WOAH
			Northern fur seal ( <i>Callorhinus ursinus</i> )	Russia	WOAH
			South American fur seal ( <i>Arctocephalus australis</i> )	Argentina, Brazil, Peru, Uruguay	WOAH
	South American sea lion ( <i>Otaria flavescens</i> )		Argentina, Brazil, Chile, Peru, Uruguay	WOAH	
	Walrus ( <i>Odobenus rosmarus</i> )		Norway	WOAH	
	Phocidae	Caspian seal ( <i>Pusa caspica</i> )	Russia	WOAH	
		Grey seal ( <i>Halichoerus grypus</i> )	Canada, Germany, Netherlands, Poland,	WOAH	

Virus	Animal (order, family, species)		Country	Reference		
A(H5N5) clade 2.3.4.4b			Sweden**, United Kingdom, United States of America			
			Harbour seal ( <i>Phoca vitulina</i> )	Canada, Denmark, Germany, United Kingdom, United States of America	WOAH	
			Southern elephant seal ( <i>Mirounga leonina</i> )	Argentina, South Georgia and the South Sandwich Islands	WOAH	
		Procyonidae	Raccoon ( <i>Procyon lotor</i> )	Canada, Germany, United States of America	WOAH	
			South American coati ( <i>Nasua nasua</i> )	Germany, Uruguay	WOAH	
		Rodentia	Abert's squirrel ( <i>Sciurus aberti</i> )	United States of America	WOAH	
			House mouse ( <i>Mus musculus</i> )	United States of America	WOAH USDA	
		Ursidae	American black bear ( <i>Ursus americanus</i> )	Canada, United States of America	WOAH	
			Asian black bear ( <i>Ursus thibetanus</i> )	France	WOAH	
			Brown bear ( <i>Ursus arctos</i> )	United States of America	WOAH	
			Kodiak grizzly bear ( <i>Ursus arctos horribilis</i> )	United States of America	WOAH	
			Polar bear ( <i>Ursus maritimus</i> )	United States of America	WOAH	
		Cetacea	Delphinidae	Bottlenose dolphin ( <i>Tursiops truncatus</i> )	Peru, United States of America	WOAH
				Chilean dolphin ( <i>Cephalorhynchus eutropia</i> )	Chile	WOAH
				Common dolphin ( <i>Delphinus delphis</i> )	Peru, United Kingdom	WOAH Leguia et al. (2023)
	White-sided dolphin ( <i>Lagenorhynchus acutus</i> )			Canada	WOAH	
	Phocoenidae		Burmeister's porpoise ( <i>Phocoena spinipinnis</i> )	Chile	WOAH	
		Harbour porpoise ( <i>Phocoena phocoena</i> )	Sweden, United Kingdom	WOAH		
	Didelphimorphia	Didelphidae	Virginia opossum ( <i>Didelphis virginiana</i> )	United States of America	WOAH USDA	
	Carnivora	Canidae	Red fox ( <i>Vulpes vulpes</i> )	Canada, Norway	WOAH	
		Procyonidae	Raccoon ( <i>Procyon lotor</i> )	Canada	WOAH	

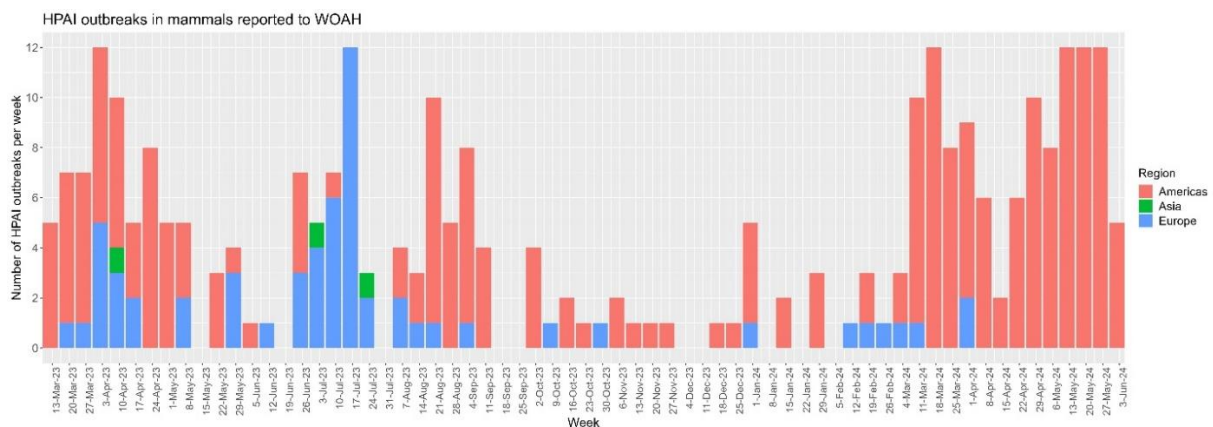


Virus	Animal (order, family, species)		Country	Reference	
A(H5N6) clade 2.3.4.4b	Carnivora	Canidae	Dog ( <i>Canis lupus familiaris</i> )	China	Yao et al. (2023)
A(H5N8) clade 2.3.4.4b	Artiodactyla	Suidae	Pig (domestic) ( <i>Sus scrofa</i> )*	France	Herve et al. (2021)
			Pig (wild boar) ( <i>Sus scrofa</i> )*	Germany	Schülein et al. (2021)
	Carnivora	Canidae	Red fox ( <i>Vulpes vulpes</i> )	United Kingdom	WOAH
		Phocidae	Grey seal ( <i>Halichoerus grypus</i> )	Poland, Sweden, United Kingdom	SVA Shin et al. (2019), Floyd et al. (2021) Personal communication by Siamak Zohari (SVA)
		Harbour seal ( <i>Phoca vitulina</i> )	Denmark, Germany, United Kingdom	WOAH Floyd et al. (2021), Ärztblatt (online), Avian Flu Diary (online), Outbreak News (online)	

\*Serological detection.

\*\*Both virological and serological detection.

Overall, the HPAI situation in mammals has intensified in the Americas in the last two years, placing the current focus is outside Europe, as displayed in Figure 6.



Source: WOA (data extraction carried out on 24 June 2024; data on notifications according to Article 1.1.3 of the WOA Terrestrial Animal Health Code are included; data on notifications according to Article 1.1.5 and positive serological detections of HPAI in fur animals in Finland are not included – the latter were not considered active outbreaks at the time of detection)

**Figure 6:** Distribution of the total number of HPAI A(H5) outbreaks in mammals per region and week since 16 March 2023 (dates indicate the first day of the week).

Almost all HPAI A(H5N1) virus detections in Europe since the beginning of 2024 have been reported in wildlife: 1 red fox in Denmark, 4 red foxes and 1 raccoon in Germany, and 1 Eurasian otter in Sweden. The latter was the only animal testing positive out of the 192 mammals tested with molecular methods in Sweden since the beginning of the year.

The otter was found in a coastal area where wild birds are abundant. Denmark reported the infection of 4 harbour seals that had already been sampled in late summer 2023. At the same time, HPAI virus was found for the first time in a walrus on Svalbard Islands, Norway. The sample material was too limited to confirm the exact A(H5) clade 2.3.4.4b subtype involved. Additionally, unofficial articles reported that about six walruses were found dead for unknown reasons on the same island in the previous year, and with no tests performed, their deaths could potentially have been caused by the same virus (UNMC, online-b; The Guardian, online-b). In Hungary, A(H5N1) virus was detected in one cat (kitten) of a group of 21 cats in a breeding establishment, which developed clinical signs and eventually died. All other cats of the same group were RT-PCR-negative (fecal and tracheal swabs), but 2 out of 3 cats (including the mother) from which blood samples were taken were positive by enzyme-linked immunosorbent assay (ELISA). The suspected source of infection was indirect contact with wild birds, as outdoor access for the cats was available (Nébih, online). A serological survey (hemagglutination inhibition, HI) conducted in Sweden resulted in the detection of antibodies to influenza A virus in 4 red foxes (4/32), 2 Eurasian lynx (2/100), 1 common raccoon dog (1/1) and 1 grey seal (1/9), whereas no antibodies were found in American mink (0/1), Eurasian otters (0/6), European badgers (0/2), European pine marten (0/1), European polecats (0/8), harbour seals (0/6) and porpoises (0/9) (Malin Grant, SVA, personal communication by email).

No HPAI virus detections in the current reporting period were declared by Austria, Belgium, Cyprus, Czechia, France, Ireland, Luxembourg, Norway, Romania, Slovakia, Spain, Switzerland, and Türkiye. The other European countries not listed above have not confirmed the absence or presence of A(H5N1) viruses in mammals, but it can be assumed that no detections were reported in those countries. In Austria, 89 mammals (43 foxes, 33 swine, 4 horses, 2 badgers, 2 bats, 1 cattle, 1 marten, 1 raccoon, 1 wild boar and 1 wolf) were tested and all found negative (Sandra Revilla-Fernández, AGES, personal communication by email). In Belgium, from 1 January to 14 June 2024, 101 foxes were tested and all found negative.

Outside Europe, after the first natural HPAI virus infections in ruminants (goats) were detected in the USA during the last reporting period, on 25 March 2024 the first natural HPAI virus infections in cattle were reported from commercial dairy herds in Texas, USA, to the Animal and Plant Health Inspection Service of the USDA (USDA-APHIS). At that time, an unknown number of primarily older dairy cows were reported sick, with the main clinical findings being decreased lactation and low appetite with unknown cause. Detection of a new A(H5N1) virus genotype (B3.13) was then confirmed in clinical samples of milk from sick cows and from an oropharyngeal swab (USDA-APHIS, online-a). Genetic analyses suggest that, at that time, A(H5N1) virus had already been circulating in the US dairy cattle population for several months (Figures A.4–A.6 in Annex A) (Nguyen et al., 2024).

Since the first detection and as of 25 June 2024, 132 dairy herds across 12 states (Colorado, Idaho, Iowa, Kansas, Michigan, Minnesota, New Mexico, North Carolina, Ohio, South Dakota, Texas and Wyoming) have been affected by A(H5N1) (USDA-APHIS, online-b). Data on the disease prevalence at farm level and the overall prevalence of A(H5N1) in cattle at country level are lacking. Based on genetic analyses, it is likely that a single spillover event from wild birds into cattle occurred in the Texas Panhandle (Figures A.4–A.6 in Annex A), while between-herd spread has probably been due to the movement of animals (mostly long-distance spread) or the movement of people, vehicles, equipment and fomites (mostly short-distance spread) (Caserta et al., 2024; Nguyen et al., 2024).

According to the latest epidemiological investigation performed by the USDA, animal movement, shared farm personnel or vehicles, and frequent visitors, are recognised risk factors for disease transmission (USDA, online-b, c). Not only cattle-to-cattle but also cattle-to-poultry transmission has been described in this context (USDA, online-c). Within affected farms, spread is suspected to have occurred through indirect cattle-to-cattle transmission, and in particular through milking equipment during the milking process (Le Sage et al., 2024; USDA, online-c), due to the very elevated levels of A(H5N1) virus detected in milk. Among many different samples tested, the highest viral loads were detected in milk (Caserta et al., 2024), while among the post mortem tissue samples examined, virus antigen expression was the highest in mammary glands (Kristensen et al., 2024). Two pre-prints and one peer-reviewed study investigating the distribution of influenza A receptors in cows have recently been published (Kristensen et al., 2024; Ríos Carrasco et al., 2024; Nelli et al., 2024) and are discussed in Annex A. Although direct transmission through other body secretions than milk has been suggested, the exact mechanisms remain unclear. Detection of the virus in nasal swabs and urine samples was at lower levels, and also manure did not seem to be a significant source of the virus and is unlikely to facilitate transmission (USDA, online-c). A study released recently suggests that various A(H5N1) virus genotypes, including an European A(H5N1) virus, might be capable of infecting the respiratory tract of cattle (Bordes et al., 2024). The potential role of semen in cattle-to-cattle transmission is currently being investigated.

For the confirmed HPAI outbreaks discussed in the USDA's National Epidemiologic Brief (USDA, online-c), more than 80% of dairy farms reported abnormal lactation and decreased feed intake, and more than 90% of dairy farms reported thickened or clotted milk. Flakes were visible in 46% of dairy farms with abnormal milk symptoms. Other clinical signs reported affected different body systems and included: decreased rumen motility, diarrhea/loose manure, tacky dry manure, constipation, increased respiratory rate, laboured breathing, nasal discharge, epistaxis, pneumonia, neurological signs, blisters or ulcers, abortions, lameness, fever and dehydration. Within-farm morbidity was estimated at < 10%, and mortality or culling was  $\leq$  2%, in the dairy herds investigated by the USDA (USDA, online-c), however no mortality solely attributable to HPAI has been reported. Before the first confirmation of HPAI in cattle, farmers in New Mexico were culling dairy cows due to decreased milk production (Reuters, online-a). In some cases, dairy cows in Colorado, Michigan and South Dakota were culled due to secondary infections, failure to recover from the virus, or inability to return to milk production. Affected dairy herds in Ohio and Texas reported mortality attributed to secondary infections (CIDRAP, online-b; Reuters, online-a). Decreased lactation lasted for an average of 8 days (range: 0–15 days), whereas other clinical signs lasted for an average of 6 days (range: 0–17 days). Among dairy cattle, most affected animals presenting clinical signs were either first-lactation (4%), second-lactation (7%), third- or higher-lactation cows (9%), or dry dairy cows (5%). From these animals, 2%, 3%, 4% and 3% recovered, respectively (USDA, online-c). As part of the affected dairy cows showing a sudden decrease in milk production are sent for slaughter, the severity of disease and level of mortality from A(H5N1) infection in dairy cattle may be underestimated.

According to the USDA, animals presenting clinical signs are usually isolated together with other affected animals in isolation pens, where they remain until clinical signs resolve. In 33% (5/15) of the affected dairy farms in Michigan, waste milk was fed to calves, while 73% (11/15) of the affected dairy farms were disposing of milk from affected individuals in lagoons (USDA, online-b). No major changes in the handling of manure from affected

animals was observed after the onset of clinical signs (USDA, online-c). To prevent further spread of A(H5N1) among dairy cattle, a Federal Order was issued by USDA-APHIS on 24 April 2024, requiring mandatory testing prior interstate movement (USDA-APHIS, online-d). In addition, a voluntary testing programme was implemented on 30 May 2024. It allows farmers to move their animals without the additional pre-movement testing mandated by the Federal Order after their herds have tested A(H5N1) virus-negative for three consecutive weeks using on-farm bulk tank milk samples or similar representative milk samples tested at a National Animal Health Laboratory Network (NAHLN) laboratory (USDA, online-e). As of 25 June 2024, dairy herds from Kansas, Nebraska, New Mexico and Texas are enrolled in the voluntary testing programme (CIDRAP, online-b).

In and around affected dairy herds, mortality events have been described in wild birds (great-tailed grackles), peridomestic birds (pigeons), domestic birds (chickens), wild mammals (raccoons), peridomestic mammals (house mice) and domestic mammals (cats) (Caserta et al., 2024). In more than one dairy farm (exact number is unknown) in Texas, mortality was reported in half of the population of cats that were fed raw colostrum and milk from sick cows. Ante mortem clinical signs in affected cats were depression, rigid body movements, ataxia, vision loss, moving in circles, and excessive discharge from eyes and nose (Burrough et al., 2024). Overall, over 80% of the dairy herd premises investigated in the USDA's National Epidemiologic Brief kept cats, while 20% kept chickens (USDA, online-c). More than half of the cats and nearly all of the poultry on these premises were found sick or dead (USDA, online-c). The most frequently observed wild birds around dairy farms were pigeons and doves, blackbirds, crows, cowbirds and grackles, and small perching birds (USDA, online-c).

Quantification of the movement of HPAI among six host categories (domestic and wild mammals, domestic and wild birds, and humans) in the USA supported the assertion that HPAI virus infections in cattle led to infections in several other species. For example, multiple transmission events have been described from cattle to cat, raccoon, poultry and wild birds, respectively (Nguyen et al., 2024). However, blackbirds found dead near a dairy farm in Texas tested positive for a virus closely related to the one circulating in dairy cows in farms in Texas and Kansas, suggesting possible vice versa transmission from wild birds to cattle beyond the first spillover event. Still, the possibility that these blackbirds became infected from cattle in the first place cannot be ruled out (Caserta et al., 2024). Additionally, in Michigan, although no genomic evidence indicating the role of migratory birds in spreading HPAI virus in the state is available, the risk that resident wild or peridomestic bird species might move and transmit the virus between dairy herds remains a concern, particularly for farms situated in close proximity (USDA, online-b). Based on the epidemiological investigations of HPAI in Michigan dairy herds and poultry flocks (USDA, online-b), all dairy herds reported the presence of wild, peridomestic or domestic birds or mammals, with many of them regularly accessing cattle feed. To this end, A(H5N1) virus has been detected in cats (number unknown), pigeons (number unknown), 1 starling, 1 raccoon, 2 Virginia opossums and 5 foxes in or around five affected dairy farms and one affected poultry establishment that participated in on-farm sampling (USDA, online-b, f). However, only a small number of these animals were found positive out of the numerous samples collected (USDA, online-b). Additionally, A(H5N1) virus was detected in 1 raccoon associated with an infected dairy cattle farm in New Mexico (Caserta et al., 2024).

Finally, between 18 March and 18 June 2024, A(H5N1) virus was detected in the following mammal species in the USA that were not necessarily associated with dairy

herds: cats (30), red foxes (3), bobcat (1), raccoon (1) and striped skunk (1). Some of the above-mentioned cases in cats (exact number is unknown) might have been associated with dairy herds in Kansas, Michigan, New Mexico and Texas. Of note, a total of 4 out of 18 alpacas that were associated with affected poultry establishments in Idaho were found infected with A(H5N1) virus in May 2024 (USDA, online-g). This represents the first HPAI virus detection in this species and none of the animals showed clinical signs. Finally, A(H5N1) virus detections in 66 peridomestic house mice were reported from New Mexico, all from the same location where HPAI virus had also been detected in poultry.

The US Centers for Disease Control and Prevention (CDC) conducted a study using ferrets to assess the severity and transmission efficiency of the A(H5N1) virus isolated from a human case in Texas. The study revealed that the virus caused severe illness and mortality in all six infected ferrets. It spread efficiently to 100% of ferrets (3/3) in direct contact with infected ones, but was less capable of spreading via respiratory droplets, with only 1 out of 3 ferrets (33%) in adjacent enclosures becoming infected (CDC, online-a). These results also align with another recent study of ferrets that were experimentally infected with an A(H5N1) virus from an outbreak in farmed American mink in Spain, where respiratory droplet transmission was observed in 3 out of the 8 ferrets (37.5%) (Restori et al., 2024). Another recent study in ferrets that had been exposed to A(H5N1) virus isolated from a human case in Chile demonstrated efficient spread through direct contact, but no spread via respiratory droplets (Pulit-Penalosa et al., 2024).

In response to the ongoing HPAI situation in dairy cows in the USA, several European countries have initiated testing of and/or surveillance in cattle and milk. Germany has already tested about 1,400 cattle sera from high-risk areas and > 450 bulk milk samples from different states, all of which resulted negative (FLI, online). Bulk milk samples will continue to be tested up to a target of 1,500 allowing exclusion of a prevalence of 0.2%. Furthermore, Germany is currently conducting at the Friedrich-Loeffler-Institut (FLI) an infection study with recent A(H5N1) virus isolates from the USA, and from a wild bird in Germany, in dairy cows. First results indicate that both isolates, upon direct instillation into the udder, were able to multiply very well in the udder and induced signs of disease as described from the USA (FLI, online). Italy has tested approximately 3,200 sera from cattle and goats in provinces where A(H5N1) viruses have circulated extensively in recent years, all of which were negative (Calogero Terregino, EURL for Avian Influenza and Newcastle Disease, personal communication by email). The Dutch Animal Health Service is conducting a retrospective serological study in ruminants in the Netherlands to detect any past infections with HPAI. Results are expected shortly after summer 2024. Sweden is also considering analysing bulk milk samples that had been collected and stored for different screening purposes. Moreover, 403 samples collected from cattle with respiratory signs since the beginning of the year were tested for influenza A viruses and were all found negative (Malin Grant, SVA, personal communication by email). Norway is currently testing ruminant application of common diagnostic tests. To this end, a pilot serosurvey of samples from cattle and sheep in HPAI-affected areas will be initiated. Norway has also published recommendations on the circumstances under which cats or cattle should be tested for HPAI viruses (Mattilsynet, online). Spain has raised awareness among its bovine sector and reinforced passive surveillance. Otherwise, passive surveillance in wild carnivores, American mink and swine continues in case of increased epidemiological risk in a certain area. Other countries such as Belgium and France are preparing for similar activities.

In Canada, since 2 February 2024, A(H5N5) virus has been reported in 3 raccoons, 3 striped skunks and 1 red fox. A(H5N1) virus has also been reported in 8 striped skunks and 1 red fox. Another red fox tested positive for HPAI virus, but the subtype was not identified. These outbreaks were reported in four different locations, and all infected animals were reported dead, except for 2 striped skunks for which the information was not available (CFIA, online; WOA, online).

The recent detections of A(H5N1) virus in dairy cows in the USA have raised questions about the potential risk of viral transmission through the consumption of milk and meat from infected animals (see Section 2.3). To date, the vast majority of HPAI spillovers from birds to mammals have been reported in scavenging species, where the most likely source of infection was feeding on infected birds (Falchieri et al., 2024). Therefore, carnivorous species, especially those that prey on wild birds, are considered particularly at risk of contracting HPAI. A recent study conducted from March to June 2023 in the state of Washington, USA, highlighted that, out of 196 hunting dogs serologically investigated, four had antibodies to A(H5N1) (Brown et al., 2024). These seropositive dogs were reported to have all hunted in areas where waterfowl had tested positive for HPAI virus, and three of them had hunted dead waterfowl (without evidence of having been hunted or shot) or waterfowl that showed neurological signs. In November 2022, A(H5N1) virus was detected by RT-PCR in an enclosure of 15 captive bush dogs in the United Kingdom (Falchieri et al., 2024). Ten of the animals died suddenly or were euthanised on welfare grounds, with some showing neurological signs. The rapid development of the disease and the severity of signs suggest a high viral load in the bush dogs. Outdoor access without net was available for the bush dogs in the enclosure. Wild bird activity (e.g. gulls, geese and corvids) was described in the vicinity. The bush dogs were fed with frozen, shot wild game. Based on this information and the high viral load detected in the infected animals, the most likely source of introduction was the ingestion of infected meat, either through the frozen wild game given to the dogs or by scavenging wild bird carcasses or sick birds that fell into the enclosure. Additionally, five domestic ferrets from one and the same owner were found positive to A(H5N1) virus in Poland in July 2023 after being fed raw poultry meat (Golke et al., 2024), during the same period when cats were also found positive to A(H5N1) in Poland (Rabalski et al., 2023). The three juvenile ferrets showed respiratory and neurological signs, with one case being fatal, while the two adults were asymptomatic. All tested positive for antigens and by RT-PCR. Although other infection route besides feeding with raw meat cannot be excluded, this scenario appears to be the most probable. The fact that the ferrets were kept indoors, that clinical signs began 12–15 hours after the last meal, and that cats in Poland were found positive to A(H5N1) after consuming raw poultry meat support this hypothesis (Rabalski et al., 2023). Also, it cannot be excluded that the immunological memory and the degree of development of the immune system explain the difference in the course of infection between adults and juveniles. However, considering that adults were fed from a different batch than juveniles, the rapid development of signs in juveniles suggesting a high viral load, and previous studies highlighting the probable mammal-to-mammal transmission of A(H5N1) (Thanawongnuwech et al., 2005; Lindh et al., 2023; Plaza et al., 2024a) make a scenario in which juveniles were infected through ingestion of contaminated raw meat and subsequently transmitted the virus to adults the most probable transmission scenario (Golke et al., 2024).

Also the studies summarising the HPAI events in mammals in South America in recent years suggest possible mammal-to-mammal transmission, even across borders, and mammal-to-bird transmission, which is of concern due to the possible spillback of

mutations associated with mammalian adaptation. Between the end of 2022 and 2023, at least 30,000 South American sea lions were reported dead along the coasts of Peru, Chile, Argentina, Uruguay and Brazil due to A(H5N1) virus infections (Uhart et al., 2024). In October 2023, the largest mortality event affecting southern elephant seals was recorded in Península Valdés, Argentina, caused by the same virus. More than 17,000 southern elephant seal pups (with an estimated mortality rate of 96% in early November 2023) died with the infection, along with an unknown number of adults (Campagna et al., 2024). Genomic epidemiological studies suggest that the outbreaks reported in marine mammals along the South American coasts are a continuous of the first outbreak detected in Peru (Plaza et al., 2024a; Tomás et al., 2024). The virus found in Peru migrated from the south to the north along the Pacific Ocean coasts, until August 2023, when the virus was found in Argentina and started to spread from the south to the north along the Atlantic Ocean. Other marine mammal species were reported infected by the same virus and related to these cases, including porpoises, dolphins and otters, but in smaller numbers (Pardo-Roa et al., 2023; Plaza et al., 2024a). The A(H5N1) virus belonging to the marine mammal clade has also been described in a human in Chile (Castillo et al., 2023). Additionally, the virus has caused damage to many seabird species, such as the death of 2,788 Humboldt penguins in Chile between January and August 2023 (Muñoz et al., 2024b), that, together with other factors, has led to the designation of the Humboldt penguin as the 18th most vulnerable penguin species in the world (BusinessDay, online). While the most plausible route of the initial virus introduction in South American sea lions is through cohabitation and feeding on infected birds, epidemiological and phylogenetical studies provided evidence of mammal-to-mammal transmission with occasional mammal-to-bird spillover. Furthermore, viral genomic data isolated from pinnipeds, as well as other marine mammals and seabirds, and even from the infected human, revealed numerous mammalian adaptations (Plaza et al., 2024a; Rimondi et al., 2024; Tomás et al., 2024). Since October 2023, mass mortality of southern elephant seals and Antarctic fur seals caused by A(H5N1) virus has been reported in the Antarctic region. Further analyses need to be conducted to determine if these infections were caused by the virus belonging to the marine mammal clade responsible for the outbreak in pinnipeds in South America, or to the clade circulating in brown skuas in Argentina, which clusters with avian viruses from inland Argentina, and appears not to have mutations associated with increased virulence, transmission or adaptation to mammalian hosts (Bennison et al., 2023; Uhart et al., 2024).

### 2.2.2 Genetic characteristics of HPAI viruses of the A(H5Nx) subtype circulating in non-human mammals

Details on the nomenclature of the HPAI A(H5) viruses used in this section are reported in Appendix B. Genotypes are assigned using the criteria described in Fusaro et al. (2024). Mutation analyses of the A(H5N1) viruses have been performed using FluMut (Github izsvenezie-virology, online-b) with FluMutDB v5.0 mutation database.

#### **Genetic diversity of HPAI A(H5Nx) viruses in non-human mammals in Europe**

Since October 2020, the complete genome sequences of about 250 A(H5) viruses of clade 2.3.4.4b collected from 17 distinct mammalian species (i.e. American mink, Arctic fox, Asian black bear, beech marten, bush dog, caracal, cat, common raccoon dog, European badger, Eurasian lynx, Eurasian otter, European polecat, ferret, grey seal, harbour porpoise, harbour seal, red fox and South American coati) have been generated. The characterised viruses belong to 10 different A(H5N1) and A(H5N8) genotypes, most of which had been previously identified in birds. All the A(H5N1) viruses associated with

the infections in fur farms in Spain (October 2022) and Finland (July–October 2023) belonged to the EA-2022-BB genotype (Agüero et al., 2023; Kareinen et al., 2024). A recent in vivo experimental study in ferrets showed that the virus responsible for the Spanish outbreak in American mink is capable of transmitting via direct contact to 75% of exposed ferrets, and airborne transmission was identified in 37.5% of contacts. This virus contains the adaptive mutation T271A in the PB2 protein. Reversing this mutation was demonstrated to reduce mortality and airborne transmission (Restori et al., 2024). No additional mutations associated with transmission were observed. Another study investigated the pathogenicity and transmissibility of this strain in swine (Kwon et al., 2024). Experimental infection demonstrated that the virus replicated in the lower respiratory tract, but no transmission to in-contact swine was observed. Of note, deep sequencing analyses identified the emergence of several mutations within subpopulations associated with mammalian adaptation (ie. PB2-E627K, PB2-E627V, PB2-K526R and HA-Q222L, and H5 numbering) in samples taken from the infected animals.

During the current epidemiological year and based on the data available so far, infections in wild animals have been caused by four different genotypes. In February and March 2024, the first infections in mammals associated with the genotypes EA-2021-I and EA-2023-DG were identified in two red foxes in Norway and Germany, respectively.

Approximately 44% of the A(H5Nx) viruses that have been characterised since October 2020 from mammals in Europe (n = 256) contain at least one of the adaptive markers associated with an increased virulence and replication in mammals in the PB2 protein (E627K, D701N, T271A or K526R) (Suttie et al., 2019). These mutations have rarely been identified in the A(H5) viruses of clade 2.3.4.4b collected in birds in Europe over the same time period (about 1%). This observation suggests that these mutations with potential public health implications have likely emerged upon transmission to mammals.

## **HPAI A(H5N1) outbreaks in non-human mammals in the Americas**

### *HPAI A(H5N1) outbreaks in cattle and other mammal species in the USA*

Genetic analyses of complete genome sequences of A(H5N1) viruses collected from dairy cows in nine states in the USA between March and April 2024 have been described (Nguyen et al., 2024). The viruses belong to clade 2.3.4.4b genotype B3.13, a genotype detected to date only in North America. It contains PA, HA, NA and M gene segments from Eurasian A(H5N1) virus, and PB2, PB1, NP and NS gene segments from LPAI wild bird viruses of the American lineage. Results from phylodynamic analyses indicate a single spillover event to cattle, likely from wild birds, which might have occurred several months prior to the first confirmation of HPAI virus infection in cattle by the USDA in March 2024. The tree topologies clearly indicate sustained virus transmission from cattle to cattle, from cattle to poultry and domestic animal species (i.e. domestic cats), as well as back to wild birds (Nguyen et al., 2024). Moreover, in May 2024, the same virus circulating in dairy cows was identified as the causative agent of infection in alpacas kept in an A(H5N1) virus-infected poultry establishment, suggesting a mammal-to-bird-to-mammal transmission. Multiple mutations associated with increased virulence or mammalian adaptation have been identified across the genome. In particular, the mammalian adaptive marker PB2-M631L (Zhang et al., 2017) has been detected in 99% of dairy cow sequences, but only sporadically in birds. Moreover, the NP gene that distinguishes B3.13 from all the other North American genotypes may have resulted in a phenotype change that has likely favoured its spread in this new species (Nguyen et al., 2024).



In early March 2024, A(H5N1) viruses were identified in goat kids with neurological signs on a farm in Minnesota, where A(H5N1) infection had recently been reported in poultry; genetic analyses showed that the viruses from goats were highly related to the viruses collected from poultry reared in the same farm (AVMA, online) and clustered separately from the viruses collected from dairy cattle.

### *HPAI A(H5N1) outbreaks in marine mammals in South America*

Since the end of 2022, multiple clade 2.3.4.4b A(H5N1) infections have been reported in marine mammals along the South American coasts (Plaza et al., 2024a), including an unprecedented mass mortality event in October 2023 in southern elephant seals in Península Valdés, Argentina (Uhart et al., 2024). Genetic analyses indicate that all the viruses from pinnipeds form a monophyletic group within the American genotype B3.2, thus suggesting multiple likely introductions of the same virus across these species followed by mammal-to-mammal transmission among populations of mammals spanning across borders. Further, occasional back transmission of this virus into some seabird species has been observed. Genotype B3.2 is a reassortant strain containing four segments from the Eurasian A(H5N1) virus (PA, HA, NA, and MP) and four segments from LPAI viruses of the North American lineage (PB2, PB1, NP and NS). However, during mammal-to-mammal transmission, this virus has acquired eight amino acid mutations (Q591K and D701N in PB2; L548F in PB1; A20T, M86I and M548I in PA; and R21Q and I226T in NS1) that had never been identified in viruses circulating in birds in South America (except for the back spillover events from mammals). Some of these mammalian clade specific mutations have been previously described as important mammalian adaptive markers (i.e. PB2-D701N and PB2- Q591K) (Uhart et al., 2024). Of note, the A(H5N1) virus strain from a human case in Chile, highly related to the A(H5N1) viruses collected from marine mammals and possessing the same set of mutations (except for the PB1-L548F), has been demonstrated to be transmissible by contact between co-housed ferrets, but did not exhibit any productive respiratory droplet transmission (Pulit-Penaloza et al., 2024).

## 2.3 Food safety aspects related to HPAI

Given the detections of HPAI viruses in dairy cattle in the USA, some countries are taking actions to ensure the safety of the meat and milk supply chain, to reaffirm consumer confidence and also to raise awareness regarding the risk posed by the consumption of food in the context of HPAI.

In the USA, where HPAI virus has been circulating in dairy cows, the US Food and Drug Administration (FDA), the USDA, the Food Safety and Inspection Service (FSIS), the APHIS and the Agricultural Research Service (ARS) conducted several studies to verify the safety of the meat and milk supply in the context of the A(H5N1) outbreak.

To verify whether any viral particles were present in beef, samples of ground beef obtained at retail in states where dairy cattle herds have tested positive for A(H5N1) virus were analysed by APHIS using PCR. Final results posted on 1 May 2024 showed that no viral particles were found to be present in ground beef (USDA-APHIS, online-d). In addition, final results of a ground beef cooking study, which were released on 16 May 2024, showed that the FSIS-recommended cooking temperatures are effective in inactivating A(H5N1) virus. ARS inoculated a very high concentration of an A(H5N1) virus into 300 grams of ground beef patties (burger patties are usually 113 grams). The burger patties were then cooked at three different temperatures (120, 145 and 160 degrees Fahrenheit,

corresponding to 49, 63 and 71°C), and virus presence was measured after cooking. There was no virus present in the burgers cooked at 145°F (medium) or 160°F (well done), which is FSIS' recommended cooking temperature, but infectious virus was present in the burgers cooked at 120°F (USDA-APHIS, online-d). The third study was conducted on beef muscle of cull dairy cows condemned for systemic disease. Muscle samples collected at selected FSIS-inspected slaughter facilities were analysed by APHIS using PCR to determine the presence of viral RNA. Testing completed on 28 May 2024 on all 109 muscle samples collected revealed the presence of viral RNA in tissue samples, including diaphragm muscle, from one cow (1/109) (USDA-APHIS, online-d). This finding should not be a concern, as no meat from these dairy cows entered the food supply.

FDA (in collaboration with USDA and ARS) also initiated a study to assess whether the virus could be detected in pasteurised retail dairy products and, if detected, to determine whether the virus was viable. From 18 to 22 April 2024, a total of 297 samples of Grade A pasteurised retail milk products (whole milk, 2% reduced fat milk, 1% low fat milk, skim milk, half and half, yogurt, cream, cottage cheese and sour cream) were collected from 17 US states, representing products from 132 processors in 38 states. The retail dairy product samples were first screened by RT-PCR to determine the presence of A(H5N1) viral RNA, and then the RT-PCR-positive samples were followed up with gold-standard egg inoculation testing to determine whether they contained live virus. Viral RNA was detected in 60 samples (20.2%) with titer equivalents of up to 5.4 log<sub>10</sub> 50% egg infectious doses (EID<sub>50</sub>) per mL, with a mean and median of 3.0 log<sub>10</sub>/mL and 2.9 log<sub>10</sub>/mL, respectively. No infectious virus was detected in any of the RT-PCR positive samples when inoculated in embryonated chicken eggs (FDA, online-a). In order to minimise additional exposure of humans and other animal species to A(H5N1) virus, and to reduce the potential for additional infections as well as the opportunity of the virus to adapt to new hosts, FDA issued a letter on 6 June 2024 (FDA, online-b) recommending the state regulatory partners to stop the intrastate sale of raw milk, which represents a potential route of consumer exposure to the virus. Furthermore, the FDA released on 28 June 2024 the results of the study on the detection and quantification of influenza A virus in bulk tank milk samples, and on the inactivation of HPAI virus by continuous flow pasteurisation. Researchers investigated first the level of virus in unpasteurised (raw) milk intended for commercial processing by using RT-PCR. Of the 275 raw milk samples obtained from multiple farms in four affected states, 158 were positive for viral RNA and, of those, 39 were found to have infectious virus with an average concentration of 3.5 log<sub>10</sub> EID<sub>50</sub> per mL, which is about 3,000 virus particles per mL. In the second phase, researchers used homogenised raw whole milk that was artificially contaminated with a higher concentration of virus than was found in any raw milk samples, an average concentration of 6.7 log<sub>10</sub> EID<sub>50</sub> per mL (or approximately 5 million virus particles per mL). Spiked milk samples were processed in a high temperature short time (HTST) continuous flow pasteurisation system at 161°F (72°C) for 15 seconds. In each of the nine repeated experiments, the virus was completely inactivated (FDA, online-a).

In Canada, the Canadian Food Inspection Agency (CFIA) has carried out commercial milk sampling and testing for HPAI virus fragments. Laboratories completed testing of 600 retail milk samples (as of 18 June 2024) from across Canada (Atlantic provinces, Ontario, Quebec and western provinces). All samples have been tested negative for HPAI fragments (GovCAN, online). In addition, under the supervision of Health Canada, CFIA laboratories carried out a study in May and June 2024 on the effectiveness of pasteurisation to inactivate HPAI virus in milk. The pasteurisation treatments tested were chosen to simulate

those used by the Canadian dairy industry, and results showed that they were effective at inactivating high concentrations of the virus that were added to raw milk (GovCAN, online).

In the United Kingdom, the UK Food Standards Agency released on 9 May 2024 the results of a rapid risk assessment regarding the overall risk to UK consumers from A(H5N1) virus (genotype B3.13) in imported milk, dairy products, colostrum and colostrum-based products originating from US dairy cattle. The overall probability that UK consumers will reach potentially infectious exposures to HPAI virus via imported US dairy products was assessed to be very low, due to the low amount of the USA's dairy products consumed in the United Kingdom, the high proportion of these imports undergoing processing methods that are considered highly likely to inactivate any infectious virus present, and the assumed low oral infectivity of influenza virus for humans (FSA, 2024).

The Food and Agriculture Organization of the United Nations (FAO) produced a preliminary rapid risk assessment of foodborne A(H5N1) virus with information/data as of 14 June 2024 and concluded that the risk of people acquiring A(H5N1) from food is negligible. This risk estimate of A(H5N1) foodborne disease is based on the fact that i) there is no epidemiological evidence of avian influenza A transmission to humans via food; ii) its presence in foods is limited to those derived from food-producing animals infected with the virus; iii) the presence of infectious virus can be readily reduced even further through routine control measures (cooking and pasteurisation) (FAO, 2024).

Some studies have investigated the potential infectivity of raw milk and the effect of physical treatments on the inactivation of HPAI virus in raw milk. There were reports of infection in domestic cats after consuming raw (unpasteurised) colostrum and milk from infected cows (Burrough et al., 2024) and also an experimental infection of mice after oral inoculation with A(H5N1) virus-positive milk (Guan et al., 2024). Guan et al. (2024) reported that A(H5N1) virus may remain infectious for several weeks (> 5 weeks) in raw milk kept at 4°C. A(H5N1) virus genetic materials could still be detected in pasteurised dairy products (Schafers et al., 2024; Spackman et al., 2024), while infectious avian influenza A(H5N1) virus has not been detected in retail pasteurised milk or dairy products (FDA, online-a; GovCAN, online). Most studies available have reported that pasteurisation temperatures could inactivate HPAI viruses in cows' milk (Schafers et al., 2024; FDA, online-a; GovCAN, online). However, two recent 'correspondences' (Guan et al., 2024; Kaiser et al., 2024) have reported the presence of viable virus after heat treatment at 72°C for 15 seconds, in experimental settings. These findings must be interpreted with caution based on uncertainty around 3 aspects:

- The lack of information on the likely viral load in naturally infected milk samples;
- Laboratory experimental conditions are not comparable to industrial-scale pasteurisation processes;
- The presence of small titers of viable virus does not equal to risk of human infection via the food chain, as to cause infection, a virus must be able to overwhelm or evade the host's defense mechanisms (e.g. stomach acidity and immune response) (FAO, 2024) and be able to enter and replicate within the hosts' cells. In humans, cells that express the preferential receptors for A(H5N1) and permit the virus to enter and replicate are not reported in the human digestive tract (FAO, 2024).

## 2.4 Avian influenza virus infections in humans

#### 2.4.1 Most recent human infections with avian influenza A(H3N8), A(H5N1), A(H5N6), A(H9N2) and A(H10N5) viruses

Since the last report and as of 20 June 2024, 14 new human cases with avian influenza infection have been reported from Vietnam (one case A(H5N1) and one A(H9N2)), Australia (with travel history to India, one A(H5N1)), USA (three cases A(H5N1)), China (two A(H5N6), three A(H9N2) and one A(H10N3)), India (one A(H9N2)) and Mexico (one fatal case A(H5N2)) (Table 4). Most of the cases reported exposure to poultry or live poultry markets prior to avian influenza virus detection or onset of illness. Three cases were related to dairy cattle with presumed or confirmed infection. One case had exposure to wild birds, and two cases had no known reported exposure. To date, no new cases have been detected among close contacts of the patients.

**Table 4:** Most recent human cases due to avian influenza viruses, by virus subtype

Subtype	New cases reported 13 March – 20 June 2024	Number of reports with disease onset or detection in 2024	Total cases (deaths)	Countries reporting human cases
A(H3N8)	-	-	3 (1) since 2022.	China
A(H5N1)	Five cases, including one death, in Vietnam, USA and Australia (ex India).	10	892 (463) since 2004.	A total of 24 countries reported cases. EU/EEA: Spain, with virus fragment detections in two poultry workers (considered to be contamination and not productive infections).
A(H5N6)	Two fatal cases in China.	2	92 (37) since 2014.	China (91), Laos (1)
A(H9N2)	Five cases in China, India and Vietnam.	7	137 (2) since 1998.	No EU/EEA country. China (122), Egypt (4), Bangladesh (3), Cambodia (2), India (2), Oman (1), Pakistan (1), Senegal (1), Vietnam (1)
A(H10N5)	-	-	1 (1) first reported in 2024.	China (1)
A(H10N3)	One case in China	1	3 since 2021.	China (3)
A(H5N2)	One fatal case in Mexico	1	1 (1) first reported in 2024.	Mexico (1)

Source: ECDC line list and WHO.

#### 2.4.2 Human A(H3N8) cases, summary

As of 20 June 2024, no new human infections had been reported since the previous report. During 2022 and 2023, a total of three infections were reported from China, with two in children (four and five years old) and one in an adult (56-year-old female) exposed to either infected backyard poultry or live poultry markets. The infections were mild in one case and more severe, or critical, in the other two, including one death (Bao et al., 2022; Sit et al., 2022). Human-to-human transmission has not been reported and all three cases were considered sporadic spillover events.

#### 2.4.3 Human A(H5N1) cases, summary

Since 13 March and as of 20 June 2024, five new human infections with avian influenza A(H5N1), including one death, have been reported in Vietnam (1), the USA (3) and Australia (ex India) (1).

Of the newly reported cases during this time period, one in Vietnam was a fatality, documented in a young man (21-year-old student) with no underlying conditions. He developed symptoms on 11 March 2024 (fever and cough), which became more severe over time, with persistent respiratory and gastrointestinal symptoms, followed by the development of severe pneumonia. The patient died on 23 March after a week of hospitalisation and ICU treatment from 15 March. He had exposure to wild birds from hunting a couple of weeks prior to onset of symptoms. There was no contact with dead or sick poultry reported, or contact with anyone exhibiting similar symptoms between the bird hunting and the onset of symptoms. No new cases have been detected among close contacts of the case (SGGP, online; WHO, online-b). This case represents the first A(H5N1) detection in humans in Vietnam since October 2022.

Following a multi-state outbreak of avian influenza A(H5N1) in dairy cattle in the USA, three human cases were reported by the US authorities in April–May 2024, all in adult farm workers with exposure to cattle presumed or confirmed to have been infected. The cases were detected as part of enhanced surveillance. The first case was reported on 1 April 2024 in Texas. The case appears to be the first human infection with influenza A(H5N1) virus associated with exposure to infected mammals (WHO, online-c). The patient reported conjunctivitis as the only symptom, which began on 27 March 2024 and later resolved following treatment with antivirals. The individual was told to isolate. No new cases were detected among close contacts of the individual. The virus isolated from this case belonged to the HA clade 2.3.4.4b of A(H5N1), genotype B3.13, and was closely related to the virus detected in dairy cattle in Texas. Genetic analysis revealed some changes in the virus sequence from the patient specimen compared to the viral sequences found in cattle. The virus sequence from the human case displayed the PB2 E627K mutation, which has been associated with viral adaptation to mammalian hosts. However, sequences remained avian-like (i.e. retaining their strong preference for avian rather than mammalian receptors). There were no markers identified that are known to be associated with resistance to influenza antiviral medications (Uyeki et al., 2024).

A second case was reported in Michigan on 22 May 2024. An adult individual who worked at a dairy farm reported conjunctivitis as the only symptom. The case was detected through enhanced monitoring because of work exposure to A(H5N1) virus-infected cattle. Of two samples collected, the sample taken from the nose tested negative for influenza, whereas a sample taken from the eye tested positive for A(H5). No new cases have been reported among contacts of this case (CDC, online-b). As per official reports, the case developed symptoms following a direct splash of infected milk to the eye. The person was not wearing full personal protective equipment (MDHHS, online). According to genetic analysis, the virus identified belonged to HA clade 2.3.4.4b, genotype B3.13. The genome of the virus was closely related to viruses found in dairy cattle, suggesting cow-to-human transmission. The E627K mutation observed in the PB2 segment of the virus from the Texas case was not present. The genome of the virus from the Michigan case did, however, have the PB2 M631L change, which is associated with viral adaptation to mammalian hosts and has been observed in 99% of virus sequences from dairy cows, but only occasionally in birds. No markers of antiviral resistance were detected in the virus sequences from the Michigan case and the virus was closely related to existing HPAI A(H5N1) candidate vaccines (CDC, online-c).

A third human case of HPAI A(H5) associated with the ongoing multi-state outbreak of A(H5N1) in dairy cattle in the USA was reported on 30 May 2024 in Michigan. The dairy

farm worker had exposure to infected cows, suggesting probable cow-to-human transmission. Unlike the previous two cases, the patient reported upper respiratory tract symptoms, including cough without fever, as well as eye discomfort with watery discharge. The patient received antiviral treatment (oseltamivir) and isolated at home. Household contacts and other workers at the farm were monitored, with no symptoms being reported. Household contacts were offered oseltamivir. There has been no indication of human-to-human transmission of A(H5N1) viruses at this time (ECDC, 2024a; MDHHS, online).

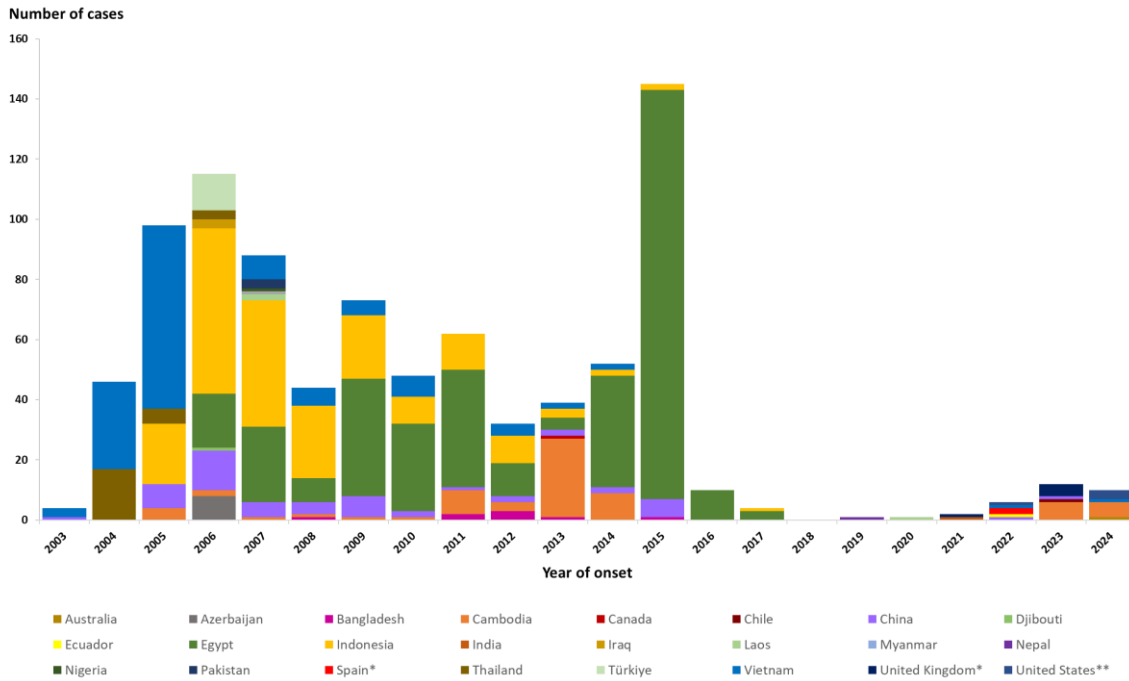
On 21 May 2024, Australian health authorities reported the first detection of a human infection with avian influenza A(H5N1) in Victoria state, Australia. The infection occurred in a child aged two and a half years, while visiting Kolkata, India, 12–29 February 2024. The child developed symptoms on 25 February 2024 (lower respiratory infection symptoms, loss of appetite, irritability and fever) and was hospitalised upon return to Australia on 2 March with severe symptoms. The patient was discharged after 2.5 weeks of hospitalisation. The patient did not travel outside of Kolkata and had no known exposure to live birds, animals or sick people during the trip. The virus was detected through enhanced surveillance for novel strains of influenza virus or strains causing concern. The virus identified from the patient belonged to clade 2.3.2.1a (GISAID Isolate ID: EPI\_ISL\_19156871). No new cases have been detected through contact tracing (ECDC, 2024b; WHO, online-d).

Overall, in 2023, four countries reported 12 cases/detections of A(H5N1): Cambodia (6, clade 2.3.2.1c), Chile (1), China (1) and the United Kingdom (4). As of 20 June 2024, so far this year, 10 cases have been reported by four countries: Cambodia (5), United States (3), Australia (1) and Vietnam (1).

Since 2003 and as of 20 June 2024, there have been 892 human cases, including 463 deaths (case fatality rate: 52%), of A(H5N1) infection notified to the World Health Organization (WHO) from 24 countries (Australia (ex India), Azerbaijan, Bangladesh, Cambodia, Canada, Chile, China, Djibouti, Ecuador, Egypt, Indonesia, India, Iraq, Laos, Myanmar, Nepal, Nigeria, Pakistan, Spain<sup>8</sup>, Thailand, Türkiye, Vietnam, United Kingdom and the USA (Figure 7).

---

<sup>8</sup> A(H5N1) virus detections in two Spanish poultry workers involved in culling activities are considered contaminations and not productive infections.



\*Includes detections due to suspected environmental contamination with no evidence of infection reported in 2022 from Spain (2) and the USA (1), and in 2023 from the United Kingdom (3, 1 inconclusive). A case in Australia was imported from India.

\*\*Three cases in the USA in 2024 were related to infected cattle.

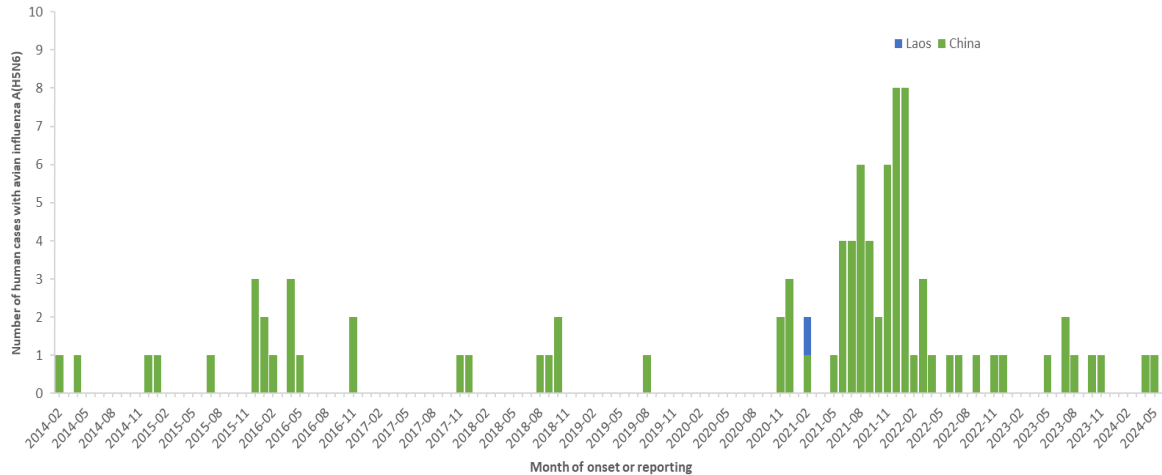
**Figure 7:** Distribution of confirmed human cases of A(H5N1) virus infection by year of onset and country, 2003–2024 (data as of 20 June 2024, n = 892)

#### 2.4.4 Human A(H5N6) cases, summary

Since the last report, two new fatal cases have been reported from Fujian province in China. Both cases had exposure to backyard poultry before onset of symptoms. The first case was a woman in her 50s with onset of symptoms on 13 April 2024. She was hospitalised on 22 April and diagnosed with avian influenza A(H5N6) infection two days later. The patient died on 30 April 2024. No new cases have been detected among close contacts of the case. Samples from close contacts, poultry and the environment tested negative (ECDC, 2024b). The second case was a man in his 40s, with onset of symptoms on 8 May 2024. The patient was hospitalised with severe pneumonia and confirmed positive for A(H5N6) on 14 May 2024. He subsequently passed away (ECDC, 2024c).

As of 20 June 2024, and since 2014, according to notifications made to WHO, China (91) and Laos (1) have reported a total of 92 human infections with A(H5N6) (Figure 8), including 37 with a fatal outcome (case fatality rate: 40%). Since 2021, the majority of A(H5N6) viruses identified in humans have belonged to clade 2.3.4.4b, although sequence information is not available for all viruses. After the modification of the H5 component in the vaccine used for poultry in China in January 2022, the number of human cases declined. However, with the information available, it is not possible to draw any further conclusions on whether the vaccination has caused the observed decline (Chen et al., 2022; Cui et al., 2022; Gu et al., 2022; Zhu et al., 2022).





**Figure 8:** Distribution of confirmed human cases of A(H5N6) virus infection by month and year of onset and country, 2014–2024 (data as of 20 June 2024, n = 92)

#### 2.4.5 Human A(H9N2) cases, summary

Since the last report and as of 20 June 2024, five new human cases with A(H9N2) infection have been reported by China (3), India (1) and Vietnam (1). All but one were children and all had exposure to backyard poultry or poultry markets. All five were hospitalised, and three of the patients developed severe symptoms (HCDC, online).

One case was a 3-year-old child from Guangxi province, China, with severe symptoms that developed on 2 February 2024. He was hospitalised three days later. He had exposure to a live poultry market. No new cases have been detected among close contacts of this case.

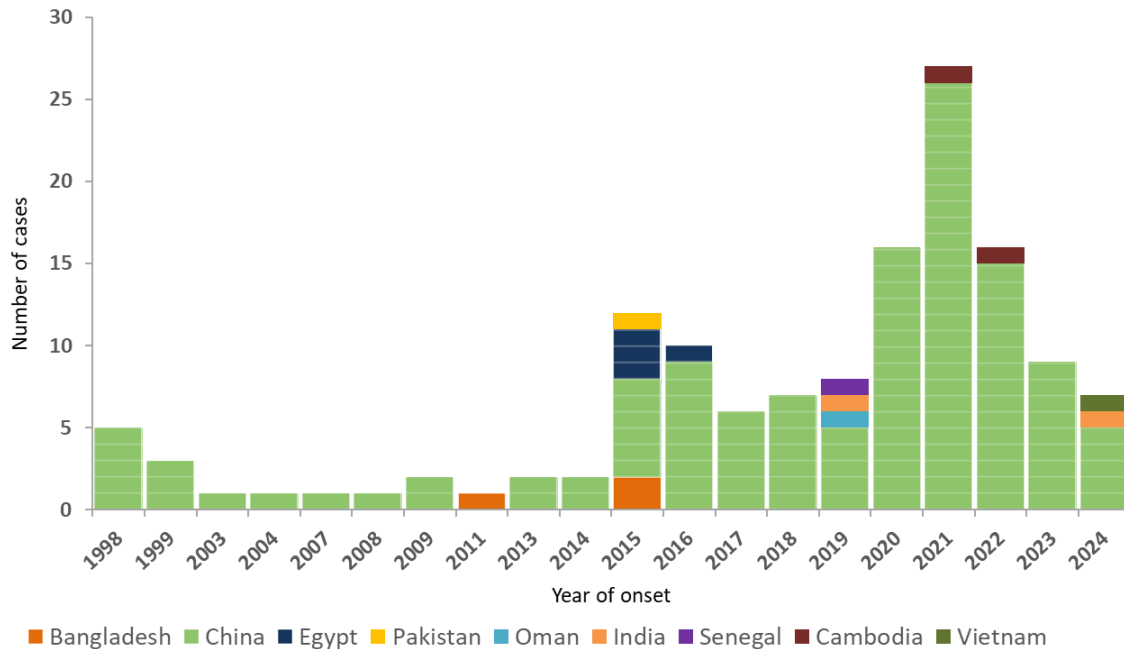
A second case was an 11-year-old boy from Jiangxi province, China, with a history of exposure to backyard poultry. He developed mild symptoms on 11 February and was admitted to hospital on 15 February 2024. No new cases have been reported among his contacts.

The third case was a three-year-old boy from Guangdong province, China. He developed mild symptoms on 17 February and was admitted to hospital on 19 February 2024. He had exposure to backyard poultry.

The fourth case was reported from Vietnam in a 37-year-old man, with underlying conditions, who developed severe symptoms on 10 March 2024 and was hospitalised on 16 March. He did not report direct exposure to poultry, but, according to reports, he lived in front of a live poultry market owned by his relatives (ECDC, 2024d). This is the first detection of A(H9N2) in Vietnam.

The fifth case was a child in West Bengal, India, who had previously been diagnosed with post-infectious bronchiolitis caused by viral pneumonia and tested positive for influenza B and adenovirus on 2 February 2024. On 3 March 2024, the patient was hospitalised due to recurrence of severe respiratory distress. Samples collected on 5 March tested positive for A(H9N2) and rhinovirus. The case had exposure to poultry at home and in the household surroundings. No other cases of respiratory illness have been reported among family members, neighbours, or healthcare workers at health facilities attended by the case (WHO, online-e).

As of 20 June 2024, and since 1998, a total of 137 laboratory-confirmed cases of human infection with avian influenza A(H9N2) viruses, including two deaths (both in patients with underlying conditions), have been reported in nine countries (Figure 9): China (122), Egypt (4), Bangladesh (3), Cambodia (2), Oman (1), Pakistan (1), India (2), Senegal (1) and Vietnam (1). Most of the cases were children with mild disease.



**Figure 9:** Distribution of confirmed human cases of A(H9N2) virus infection by month and year of onset and country, 1998–2024 (as of 20 June 2024, n = 137)

#### 2.4.6 Human A(H10N3) cases, summary

According to WHO and a pre-print publication on 10 April 2024, a new human infection with avian influenza A(H10N3) has been reported in China (ECDC, 2024d; Liu et al., 2024b). A man in his fifties from Kunming City, Yunnan province, had onset of symptoms on 28 February 2024 and was admitted to hospital on 6 March with severe pneumonia. Prior to disease onset, the patient, who is a farmer, had exposure to poultry and a poultry-related environment, involving dead poultry and ducks. No additional cases have been identified among family members of the patient. Samples from close contacts and environmental samples tested negative for A(H10N3) virus.

This is the third case of human infection with avian influenza A(H10N3) reported in China and globally; all three cases had severe illness. The first case was reported in Jiangsu Province, China, in 2021: a man in his forties developed symptoms on 23 April 2021 and eventually recovered; the second case, a man in his thirties from Zhejiang Province, developed severe symptoms on 11 June 2022 and has since recovered. No new cases have been reported among close contacts of the three cases.

#### 2.4.7 Human A(H5N2) cases, summary

On 23 May 2024, Mexican health authorities reported to the Pan American Health Organization (PAHO)/WHO a deceased case infected with avian influenza A(H5N2) virus, detected in Mexico. This is the first laboratory confirmed human case with A(H5N2) infection (WHO, online-a). Previous studies have found poultry workers seropositive for avian influenza A(H5N2) (Ogata et al., 2008; Yamazaki et al., 2009; Okoye et al., 2013).

Nevertheless, presence of A(H5N2)-neutralising antibodies was associated with an increasing age and previous seasonal influenza vaccination, suggesting potential presence of cross-reactive antibodies to A(H5N2) viruses (Ogata et al., 2008).

The patient was a 59-year-old male, with multiple underlying conditions, who developed respiratory infection on 17 April 2024, sought medical attention on 24 April and was hospitalised, but died from complications related to his comorbidities on the same day. The individual had no known history of exposure to poultry or other animals. The case had no reported travel and was bed-ridden in the three weeks prior to symptom onset.

A respiratory sample, taken on 24 April, was analysed on 8 May at the National Institute of Respiratory Diseases and on 20 May at the Institute of Epidemiological Diagnosis and Reference in Mexico using RT-PCR analysis and sequencing. The subtype was confirmed as A(H5N2). Genetic analysis found that the virus had 99% similarity to LPAI A(H5N2) strains from birds in Texcoco, state of Mexico (WHO, online-a).

No additional cases have been detected among close contacts of the case. These included household members (no reported illness, no sampling possible), healthcare workers (all asymptomatic, only sampled on 27 May) and twelve additional people from the vicinity of the case's residence (seven with and five without symptoms, test results as of 28 May).

Outbreaks of LPAI A(H5N2) have been observed in poultry in the state of Mexico in 2024. It has not been possible to establish an epidemiological link between the human case and the outbreak in poultry (WHO, online-a).

#### 2.4.8 Genetic characteristics of avian influenza viruses from humans

The GISAID's EpiFlu™ Database (Shu and McCauley, 2017) was accessed on 20 June 2024 and protein sequences from all available segments from human cases of avian influenza reported since 5 March 2024 were retrieved for five A(H5N1) (EPI\_ISL\_19031556/EPI\_ISL\_19000405, EPI\_ISL\_19027114, EPI\_ISL\_19156871, EPI\_ISL\_19162802 and EPI\_ISL\_19177746), one A(H5N2) (EPI\_ISL\_19186488/EPI\_ISL\_19186450), two A(H5N6) (EPI\_ISL\_19132453 and EPI\_ISL\_19145644), one H9N2 (EPI\_ISL\_19130558) and one A(H10N3) (EPI\_ISL\_19067870). The sequences were analysed using an in-house developed script to determine mutations of interest and these are referred to by H5 numbering, unless otherwise stated (Table ).

#### HPAI A(H5Nx)

One A(H5N1) virus, reported from Australia but with India as country of exposure, belonged to clade 2.3.2.1a, which has been mainly detected in South Asia and South-East Asia; two sequences available from the A(H5N1) case in Vietnam belonged to clade 2.3.2.1c, a clade mainly detected in South-East Asia; the remaining three human cases of A(H5N1) from the USA belonged to clade 2.3.4.4b and were closely related to viruses found in dairy cattle in the USA (genotype B3.13) (Nguyen et al., 2024; Xing et al., 2024). For virus A/Michigan/91/2024, most segments were missing and the deposited HA segment was partial, which limited the possibility of determining mutations. However, a high similarity to the virus sequences from US cattle could be confirmed.

The two A(H5N6) virus sequences belonged to clade 2.3.4.4h that has been detected in wild birds and poultry in South, South-East and East Asia (Turner et al., 2021).

The mutation analysis of the HA segment for the eight A(H5Nx) sequences revealed a previously reported profile (EFSA, ECDC and EURL, 2024a) in which seven out of eight carried both T108I, which in combination with S107R has been associated with increased virulence in chickens and mice, and increased pH of fusion (Wessels et al., 2018), and S133A, which is linked to increased pseudovirus binding to  $\alpha 2-6$  human-type receptors (Yang et al., 2007). Furthermore, all the A(H5Nx) viruses had a deletion at position 328 (a polybasic cleavage motif), which is seen in the vast majority of clade 2.3.2.1c, compared to A/Goose/Guangdong/1/96. Such deletion may lead to increased pathogenicity of avian influenza viruses (Suttie et al., 2019).

The D94N and S155N substitutions, both associated with increased virus binding to  $\alpha 2-6$  human-type receptors (Su et al., 2008; Wang et al., 2010) were present in five and three, respectively, of the eight A(H5Nx) viruses. The combination of K218Q and S223R that increases receptor binding to  $\alpha 2-3$  and  $\alpha 2-6$  receptors (Guo et al., 2017) was present in the five HPAI viruses (Table 5). The HA sequence of A/Victoria/149/2024 had V210I, which is associated with increased virus binding to  $\alpha 2-6$  (Watanabe et al., 2011). An NA deletion at approximately position 46–75 (stalk region) was previously found in all six human cases of A(H5N1) reported for the period December 2023 to March 2024. However, a deletion of this type only occurred in two of the A(H5N1) viruses analysed. The presence of PB2 mutations E627K in A/Texas/37/2024 (CDC, online-c), associated with increased virulence and replication in mammals, and M631L in A/Michigan/90/2024, was confirmed. In A(H10N7) viruses, these mutations have been linked to enhancement of virus replication and disease severity in mice (Zhang et al., 2017; Suttie et al., 2019). The E627K was also present in the viruses A/Vietnam/KhanhhoaRV1-005/2024 and A/Khanh\_Hoa/RV1-005/2024 from the human A(H5N1) case in Vietnam. For the two A(H5N6) viruses reported by China, a distinct PA and PB2 mutation profile was observed as the PA substitution A343S, which, with the E347D mutation, has been shown to have reduced viral polymerase activity and mouse virulence (Zhong et al., 2018), and the PB2 substitution I292V that is associated with increased polymerase activity in mammalian cell line and increased virulence in mice for A(H9N2) (Gao et al., 2019).

## **A(H5N2)**

The sequence available for the A(H5N2) case in Mexico belonged to an LPAI virus of the A(H5N2) subtype in the American lineage and its HA contained K218Q and S223R.

## **A(H9N2)**

One case of A(H9N2) from Vietnam (EPI\_ISL\_19130558) was retrieved and analysed. The HA segment had leucine at position 226 (H3 numbering), which is associated with increased virus binding to  $\alpha 2-6$ , enhanced replication in mammalian cells and ferrets, and enhanced contact transmission in ferrets (Wan and Perez, 2007; Wan et al., 2008). Further screening was also made for the HA amino acid substitutions T150A, R164Q, N166D and I220T (H9 numbering), which in various combinations are involved in antibody escape, increased viral replication in avian and mammalian cells, and enhanced viral replication in mice (Zhang et al., 2023b). The HA segment had only N166D where the other positions were wild type. For the other segments, the PB2 mutation A588V was detected, reported to increase polymerase activity and replication in mammalian and avian cell lines (Xiao et al., 2016) and the antiviral drug related mutation in S31N in M2 with a phenotype of increased resistance to amantadine and rimantadine (Suttie et al., 2019).

## A(H10N3)

Limited experimental data could be found for the subtype of the A(H10N3) virus reported from China. A pre-print on molecular characterisation has revealed the presence of Q226L in HA, D701N in PB2, S409N in PA and S31N M2 (Liu et al., 2024b). In our analysis, both I292V and A588V was present in PB2, which, for A(H10N8), promotes mammalian adaptations (Xiao et al., 2016). All segments were most related to avian sequences, with approximately 98% similarity based on the blastn function in GISAID. This suggest that no reassortment has occurred and that the segments are of avian origin.

**Table 5:** Mutation overview of human cases of avian influenza, reported 5 March–20 June 2024

Segment		HA							
Reference Position		D94N	T108I	S133A	S155N	V210I	K218Q	S223R	~326-329del
<b>Virus</b>	<b>Subtype</b>								
A/Victoria/149/2024	A(H5N1)	D94N	T108I	S133A	S155N	V210I			328del
A/Vietnam/KhanhhoaRV1-005/2024	A(H5N1)	D94N	T108I	S133A	S155N				327-328del
A/Texas/37/2024	A(H5N1)		T108I	S133A			K218Q	S223R	327-328del
A/Khanh_Hoa/RV1-005/2024	A(H5N1)	D94N	T108I	S133A	S155N				328del
A/Michigan/90/2024	A(H5N1)		T108I	S133A			K218Q	S223R	327-328del
A/Michigan/91/2024	A(H5N1)						K218Q	S223R	327-328del
A/Fujian/1/2024(H5N6)	A(H5N6)	D94N	T108I	S133A			K218Q	S223R	328del
A/Fujian/2/2024(H5N6)	A(H5N6)	D94N	T108I	S133A			K218Q		328del
A/State_of_Mexico/INER-INF645/2024	A(H5N2)						K218Q	S223R	
A/Yunnan/0110/2024	A(H10N3)								

Segment		NA	PB2				PA
Reference Position		~49-68del	I292V	A588V	E627K	M631L	A343S
<b>Virus</b>	<b>Subtype</b>						
A/Victoria/149/2024	A(H5N1)	36-70del	I292V				
A/Vietnam/KhanhhoaRV1-005/2024	A(H5N1)	46-75del			E627K		
A/Texas/37/2024	A(H5N1)				E627K		
A/Khanh_Hoa/RV1-005/2024	A(H5N1)	not determined			E627K		
A/Michigan/90/2024	A(H5N1)					M631L	
A/Michigan/91/2024	A(H5N1)						
A/Fujian/1/2024(H5N6)	A(H5N6)		I292V				A343S
A/Fujian/2/2024(H5N6)	A(H5N6)		I292V				A343S
A/State_of_Mexico/INER-INF645/2024	A(H5N2)	not determined					
A/Yunnan/0110/2024	A(H10N3)		I292V	A588V			A343S

### 2.4.9 Additional information relevant for public health and international risk assessments

Options for One Health mitigation measures to reduce the potential for transmission of avian influenza to humans are discussed in a technical report on drivers and critical steps

for a pandemic due to avian influenza, published jointly by ECDC and EFSA (EFSA and ECDC, 2024b). In order to protect human health, strong collaboration between the animal and human sectors is critical. ECDC has also recently published a technical report on strengthening surveillance to detect infections with avian influenza virus in the EU/EEA during the summer, between seasonal influenza periods (ECDC, 2024e). In this updated version of the document published in 2023 (ECDC, 2023a), surveillance in primary and secondary care settings and relevant aspects of wastewater surveillance have been included.

Experimental infection of ferrets with the A(H5N1) virus from the human case in Texas (A/Texas/37/2024) caused severe disease with 100% mortality in all six infected ferrets. Transmission between ferrets occurred following direct contact, but transmission was less efficient through respiratory droplets, with one of three ferrets (33%) housed in neighbouring enclosures becoming infected. Although the three human cases of A(H5N1) reported so far with previous exposure to infected cattle in the USA have been mild, the results of the study highlight that the A(H5N1) viruses being transmitted in poultry and dairy cattle could cause serious illness. Nevertheless, the study also suggests that additional genetic adaptations would be required for the current A(H5N1) viruses to transmit easily via respiratory droplets (CDC, online-a).

The US Centers for Disease Control and Prevention (US CDC) published an updated technical report on the situation and risk of avian influenza A(H5N1) in the USA and internationally, taking into consideration sporadic human cases and recent activity in animals, including the multi-state outbreak of A(H5N1) in cattle in the USA. Given that the majority of human cases of A(H5N1) reported since 2022 had exposure to poultry and no observed human-to-human transmission, and that most viruses currently circulating are unable to efficiently bind to receptors in the upper respiratory tract of humans, the US CDC considers that the overall risk of A(H5N1) viruses currently circulating in birds and cattle in the USA for the general public remains low. However, individuals with occupational or recreational exposure to infected animals are considered to be at greater risk of infection (CDC, 2024). The US CDC has issued interim recommendations for prevention of human exposure to A(H5N1), monitoring, public health investigations, and control measures. A framework for assessing the individual risk of infection with A(H5N1) based on exposure and setting is also provided, with those who have had direct and unprotected contact with infected animals or their environment, as well as exposure to contaminated raw milk from infected cows or products from contaminated raw cow's milk considered to be at highest risk of infection (CDC, online-d).

The UK Health Security Agency (UKHSA) updated their risk assessment of A(H5N1) clade 2.3.4.4b to human health, which on an updated scale of 6, now is assessed as level 3 (limited or facilitated mammalian transmission) with high confidence, but considers that it may have increased to level 4 (sustained and/or multi-species mammalian outbreaks, increasing zoonotic human cases or limited human-to-human transmission associated with zoonotic exposure) with low confidence (UKHSA, online-a). Based on the likelihood of exposure and impact of infection, UKHSA assessed the risk to human health from the A(H5N1) clade 2.3.4.4b genotype B3.13 associated with the outbreak in US cattle as very low for people in the United Kingdom (UKHSA, online-b).

Based on available information, WHO, FAO and WOAHA assessed the overall public health risk posed by A(H5N1) to be low, and for those exposed to infected animals or

contaminated environments, the risk of infection is considered low-to-moderate (FAO et al., 2024).

#### 2.4.10 ECDC risk assessment

Overall, ECDC assesses the risk of human infection with the HPAI A(H5) clade 2.3.4.4b viruses currently circulating in Europe as low for the general public in the EU/EEA and low-to-moderate for those occupationally or otherwise exposed to infected animals or contaminated environments. The assessment is based on available evidence relating to the transmission, prevalence, and characteristics of HPAI A(H5N1) viruses currently circulating in animals in Europe.

Although fewer virus detections have been reported in poultry and wild birds in Europe compared to the same time period last year, HPAI viruses continued to circulate at a very low level and have been geographically widespread. Given the extensive circulation of avian influenza in animal populations, with frequent opportunities for human exposure in recent years, transmission from infected animals to humans remains rare. So far, there have been no confirmed cases of A(H5N1) infection in humans in the EU/EEA.

Globally, sporadic cases of A(H5N1) infection have been reported in humans, most of which have had a history of unprotected exposure to poultry, contaminated environments, or more recently, dairy cattle. No sustained transmission between humans has been observed. Nevertheless, limited human-to-human transmission of A(H5N1) probably occurred on rare occasions following extended and close contact with symptomatic cases during the period 2004–2007 (CDC, 2024).

Clinical presentations of individuals infected with A(H5N1) have ranged from asymptomatic or mild, such as conjunctivitis and upper respiratory tract symptoms, to severe illness resulting in death, with an estimated case fatality rate of 52%. Sporadic infections with avian influenza in humans are likely to continue occurring in areas where the virus is prevalent and individuals have unprotected contact with animals infected with avian influenza viruses or their environment.

Although the virus continues to diversify, the A(H5N1) viruses currently circulating in European bird populations retain a binding preference for  $\alpha$ 2-3 avian-type receptors and are considered to be avian-like. However, mutations associated with mammalian adaptation of A(H5N1) have been identified in infected mammalian species and occasionally in birds. Further understanding of the implications of such mutations for mammalian adaptation, infection and transmission is required to assess any change in the associated risk to humans. However, there have been no identified mutations or reassortments of the virus that would make it human-adapted or enhance transmission between humans. In addition, the vast majority of the circulating A(H5N1) viruses in Europe remain susceptible to antivirals for seasonal influenza virus infection. There are also no indications that the A(H5N1) viruses currently circulating in the EU/EEA differ antigenically from proposed candidate vaccine viruses.

To date, there have been no reports of A(H5N1) infection in cattle in EU/EEA. Genetic sequences of samples from the human cases associated with the multi-state outbreak of A(H5N1) in cattle in the USA confirmed that the virus belonged to clade 2.3.4.4b, genotype B3.13 (Uyeki et al., 2024; CDC, online-c). At present, the genotype B3.13 identified in cattle and human cases in the USA has not been detected in Europe. Although mutations associated with viral adaptation to mammalian hosts were displayed in the virus sequences

available from the human cases, viruses from both cattle and humans remain avian-like. There were no markers of reduced antiviral susceptibility identified in the viruses from the human cases and they were antigenically similar to available candidate vaccine viruses. As a result, with the information currently available, the transmission of HPAI A(H5N1) in cattle in the USA does not change the overall assessment of the risk for the EU/EEA population.

Considering the widespread occurrence of A(H5N1) in birds and poultry as well as spillovers to mammals with suspected onward transmission in certain settings (Lindh et al., 2023; Plaza et al., 2024b; U. S. Department of Agriculture, 2024), viral evolution or reassortment may occur which could change the current assessment. As a result, the risk assessment is reviewed regularly by ECDC, taking into consideration any new developments or information becoming available.

## 3. Conclusions

### 3.1 Birds

- The trend observed in Europe since October 2023, with lower numbers of HPAI virus detections in both wild and domestic birds compared to the corresponding periods in the 2020–2021, 2021–2022 and 2022–2023 epidemiological years, continued between March and June 2024. Indeed, the total number of HPAI virus detections in Europe has not been as low as during the current epidemiological year since the 2019–2020 and 2018–2019 epidemiological years for wild and domestic birds, respectively. The low numbers of HPAI virus detections in wild birds may be partly due to some level of flock immunity acquired by previously affected wild bird species, the depletion of certain wild bird populations, lack of new HPAI virus introductions, characteristics of circulating HPAI virus genotypes, decreased detection of dead wild birds, and other reasons that need to be further investigated.
- The overall low number of HPAI outbreaks reported in poultry in Europe can be assumed to be associated with the lower number of HPAI virus detections reported in wild birds and thus a lower level of environmental contamination. Between-farm transmission, particularly the association with same farm ownership, remained an important factor for secondary spread and highlights the need for improved biosecurity and controls.
- The majority of the HPAI outbreaks in poultry in Europe were reported as primary, with indirect contact with wild birds being the most likely source of introduction, although in the affected countries the number of HPAI virus detections in wild birds was very limited, suggesting a possible underdetection of HPAI viruses in wild birds. This, together with the geographical extent of HPAI virus detections reported in wild birds in Europe, leads to believe that HPAI viruses are still circulating in wild birds throughout the summer months, albeit at very low levels. Seabirds have continued to be affected by the EA-2022-BB genotype, though in very low numbers in contrast to previous epidemiological years.
- It is expected that the number of HPAI virus detections in wild birds in Europe will remain low in the coming weeks, at least until the autumn migration of waterfowl gathers pace.



- The rate of HPAI virus detections in Europe in which wild birds were not identified to species increased again, particularly for Anatidae.
- A similar reduction in reported HPAI virus detections in wild and domestic birds as in Europe can be observed worldwide. Compared to the previous reporting period (EFSA, ECDC and EURL, 2024a), the number of HPAI virus detections in both domestic and wild birds decreased, and a lower number of countries reported to WOAH overall.
- Most of the HPAI outbreaks reported in poultry worldwide continued to be concentrated in North America, particularly in the USA.
- In Asia, the HPAI situation in domestic and wild birds intensified during this reporting period. Apart from previously affected countries such as Japan, Korea and Taiwan, now also India and Iraq officially notified to WOAH HPAI virus detections in domestic and wild birds, respectively. Of specific concern are the HPAI virus detections in wild birds in China due to the upcoming autumn migration to Europe.
- HPAI viruses are expected to continue to spread in the Antarctic region, although the impact thereof can only be assessed during the next breeding season, from about November 2024 onwards. Dependent on epidemiological developments in the Antarctic region, there is a risk of further spread of A(H5N1) virus to Oceania, including Australia and New Zealand.
- For the first time in many years, Australia has been affected by three different HPAI virus subtypes during the current reporting period, which likely represents a separate event from the rest of the world: A(H7N3), A(H7N8) and A(H7N9).
- Since October 2023, there has been an increase in the number of circulating genotypes originating from multiple reassortment events, likely due to the increased prevalence of HPAI virus circulation in wild Anseriformes. Most of these genotypes have never been detected in Europe before. It is not possible to assess whether these new genotypes originated from Europe or if they represent new introductions of the virus, given the limited data available from other countries outside Europe.
- HPAI virus subtype A(H5N5) continues to be detected in wild birds in the northern hemisphere, with detections in large-billed crows and European herring gulls in Japan, and an American crow in Canada, during the current reporting period. Based on the available genetic data, all the A(H5N5) viruses collected from Europe, Canada and Japan since 2023 belong to the same EA-2021-I genotype, indicating an intercontinental spread from Europe elsewhere. Multiple and independent emergence of the of mammalian adaptive mutations (PB2-E627K and PB2-D701N) have been identified in the viruses collected from the three continents.
- In the 2023–2024 epidemiological year, the detection of 16 A(H5) viruses in wild and domestic birds collected from eight different European countries containing markers of mammalian adaptation in the PB2 protein (E627K, K526R or D701N) indicates that viruses with an enhanced capacity to infect mammals can replicate and spread in birds. Of particular concern is the spread of A(H5N5), genotype EA-2021-I, viruses with PB2-E627K mutation, observed in wild bird populations in

multiple countries in northern Europe. This poses a threat for host jumps and reassortments with influenza A viruses circulating in mammals.

- Despite several mutations associated with increased zoonotic potential have been detected in the A(H5N1) viruses currently circulating in Europe, to date, no key mutations associated with the switch in the virus binding preference from avian- to human-type receptors were identified. However, viruses with such mutations are detected in other geographic regions (e.g. A(H10N3) in China). New incursions in Europe of LPAI or HPAI viruses with increased zoonotic/pandemic potential should be closely monitored.

### 3.2 Mammals

- During the current reporting period, the first natural HPAI virus detections were confirmed in the following mammal species: alpaca (USA), cattle (USA) and walrus (Norway).
- In Europe, primarily carnivorous or scavenging mammal species (i.e. cat, Eurasian otter, raccoon and red fox) continued to be affected in low numbers. The low number of HPAI virus detections in those species during the current period can be assumed to be associated with the low number of HPAI virus detections in wild birds and thus with a lower level of contact between carnivores and infected birds through feeding or scavenging.
- Outside Europe, all HPAI virus detections in mammals during this reporting period were reported from North America: > 5 different mammal species, including domestic and peri-domestic mammals in close contact with humans (alpaca, cat, cattle and house mouse). In most of these detections the new A(H5N1) virus genotype B3.13 was identified.
- Extensive spread of A(H5N1) virus genotype B3.13 has been observed among > 130 dairy farms in 12 US states. While within-herd transmission has been characterised to be primarily through milking equipment during the milking process, between-farm spread has likely been due to the movement of animals, people, vehicles, equipment and fomites. Further transmission from cattle to other species categories (i.e. domestic and wild mammals, domestic and wild birds, and humans) has been demonstrated.
- In cattle, the clinical manifestation of HPAI has been very different from other mammal species and is concentrated on the effects of virus replication in the mammary gland. Likewise, the highest viral concentrations are found in milk among all clinical samples from cattle tested. Infection of carnivorous mammal species ingesting milk from infected dairy cows has been shown.
- In response to the HPAI situation in dairy cattle in the USA, several European countries have initiated or are planning testing and/or surveillance of HPAI viruses in cattle and milk.
- Unlike the mammal infections reported in Europe during the summer months in 2023, mainly caused by the EA-2022-BB genotype that intensively circulated in colony-breeding seabirds before, the recent A(H5) viruses identified in wild mammals belonged to different A(H5N1) and A(H5N5) virus genotypes.

- The high percentage (about 44%) of European viruses collected from mammal species containing molecular markers of mammalian adaptation in the PB2 protein indicates that these mutations can be rapidly acquired by the virus during infection in mammalian species. Viruses containing such mutations may have a greater zoonotic potential.
- To date, no key mutations associated with the switch in the virus binding preference from avian- to human-type receptors were identified in the A(H5) viruses collected from mammalian species in Europe.

### 3.3 Food

- There is no evidence that people can become infected after ingesting food potentially contaminated with HPAI virus.
- There is no evidence of the presence of infectious HPAI virus in any commercially available food products (e.g. commercially pasteurised dairy products, meat and eggs).
- Industrial pasteurisation and recommended cooking temperatures play a significant role in inactivating HPAI virus in cows' milk, meat, eggs and products thereof.

### 3.4 Humans

- Sporadic cases of zoonotic avian influenza A(H5N1), A(H5N6) and A(H9N2) continued to be reported outside Europe during the period March to June 2024. In addition, there was a third human case of avian influenza A(H10N3) virus infection and the first ever laboratory-confirmed human infection with A(H5N2) virus was reported.
- The majority of human infections with avian influenza viruses have been associated with unprotected exposure to poultry, live poultry markets, or contaminated environments. In addition, three recent cases of A(H5N1) reported exposure to dairy cattle with presumed or confirmed infection. To date, there has been no sustained human-to-human transmission observed.
- Despite the widespread occurrence of A(H5N1) in wild birds, poultry and some mammals, with many possible human exposures since 2020, there have been no confirmed human cases detected in the EU/EEA.

With the extensive circulation of avian influenza viruses in bird populations globally, sporadic transmission to humans is likely to continue occurring in settings where people are exposed to infected animals or their environment without appropriate protective equipment.

## 4. Options for response

### 4.1 Birds

- Increased surveillance in wild birds in Europe is indicated in the coming months in anticipation of the upcoming autumn migration of wild birds from different parts of the world, especially from Asia.

- Active surveillance in wild birds, especially in those that silently maintain HPAI viruses in the wild (e.g. waterfowl), is indicated to improve knowledge on HPAI viruses circulating in wild bird populations, as well as to estimate viral prevalence and seroprevalence among different species for a better epidemiological understanding of these viruses. Serological studies, combined with mortality data, may also help infer whether some level of flock immunity has been reached in different species.
- For wild birds, general options for response include accurate and comprehensive recording of HPAI-associated mortality events (e.g. estimating the impact on wild bird populations), preventing disturbance of areas undergoing HPAI outbreaks to reduce virus spread, and, depending on the circumstances, removal of HPAI virus-affected carcasses from areas where wild birds congregate to reduce environmental contamination and further virus spread.
- Biosecurity remains an important factor to prevent HPAI virus introduction from wild birds into poultry establishments and further between-farm spread. Sharing farm equipment and personnel, particularly when farms have the same ownership, should be, if possible, avoided, or at least kept to a minimum. In case of shared equipment or personnel, strict biosecurity protocols should be followed.
- The geographic expansion of A(H5N5) viruses in wild birds in northern parts of Europe and worldwide should continue to be closely monitored.
- Timely generation and sharing of genome sequence data from avian influenza viruses is of utmost importance to promptly detect the possible emergence of viruses with mutations associated with increased zoonotic potential, resistance toward antiviral drugs or different antigenic properties, whose biological characteristics should be further evaluated. Genetic data are also instrumental to track the virus spread and identify novel incursions of viruses which may represent a threat for human or animal health.
- Reinforcement of genetic characterisation of viruses collected from birds also in areas where a high number of infections in mammalian species was identified is recommended to promptly detect possible mammal-to-avian transmission of viruses containing markers of virus adaptation to mammalian species, which may have a higher zoonotic potential.

## 4.2 Mammals

- Increased surveillance of HPAI viruses in wild (e.g. red foxes) and free-roaming domestic carnivores (e.g. cats and dogs) continues to be recommended to monitor both the level of virus infection in these species and the risk of emergence and transmission of mammalian-adapted viruses. Surveillance efforts should also focus on domestic and farmed mammals exposed to highly contaminated environments or in close contact with HPAI virus-infected poultry or wildlife. Research to investigate the role of mammals in maintaining HPAI viruses and driving their evolutionary dynamics is recommended.
- In light of the recent events in the USA and the first results of experimental infections with Eurasian A(H5N1) viruses in dairy cattle, testing of/surveillance in ruminants is recommended when a combination of factors is observed, such as the

manifestation of overt and unresolved clinical signs typically associated with HPAI virus infection in ruminants (e.g. undiagnosed severe decrease in milk production and presence of darker, thickened milk), but also the occurrence of HPAI virus infection in other domestic, peridomestic and wild animals in/around cattle farms. In addition, HPAI should be considered as a differential diagnosis in cases of undiagnosed or unresolved clinical signs during periods of HPAI virus circulation in the area where ruminants are kept.

- National reference laboratories should consider the procurement of tests and reagents to be prepared for carrying out virological and serological diagnostic activities targeting mammals, including ruminants, to allow for rapid escalation of testing capacity. Liaison with the EURL is recommended to ensure that appropriate virological and serological tests are used. Such activities should serve the purpose of increasing knowledge on HPAI and LPAI viruses posing a potential zoonotic risk.
- Disease dynamics associated with HPAI virus infection during mass mortality events in mammal species should be thoroughly investigated. Testing a sufficient number of animals and assuring a prompt generation and sharing of genome sequences are of utmost importance to shed light on the virus origin, evolution and possible transmission between individuals. The latter is also indicated to timely assess the pandemic risk.
- More accurate and timely reporting of HPAI virus detections in mammals is recommended in a way that reliable numbers of infected animals could be used as quantitative information for risk assessment.

### 4.3 Humans

- Measures should be taken to reduce human risk of exposure to avian influenza:
  - The general public should avoid contact with sick or dead birds and other animals susceptible to avian influenza and, if they find dead animals, inform relevant authorities to ensure safe removal and further investigation, if required.
  - Appropriate personal protective equipment should be used to reduce the risk of infection when in contact with potentially infected animals or highly contaminated environments.
  - Information should be provided to raise awareness among people at potential risk of exposure on how it can be mitigated. Guidance tailored to specific occupational groups, or people engaged in recreational activities where additional measures may be beneficial, should be provided.
- Countries should remain vigilant for potential human cases of avian influenza, especially in geographical areas where the virus is known to occur in poultry, wild birds, or other animals.
- Healthcare workers in primary care should be made aware of the epidemiological situation and range of symptoms associated with avian influenza infection in humans.

- In the summer months between seasonal influenza periods, people seeking medical care with respiratory symptoms or other symptoms compatible with zoonotic avian influenza should be asked about exposure to sick or dead animals within two weeks of symptom onset or, if not available, before admission. Additional details on the strengthening of surveillance in the influenza inter-seasonal period are provided in ECDC's report on enhanced influenza surveillance to detect avian influenza virus infections (ECDC, 2024e).
- People who have been exposed to animals with suspected or confirmed avian influenza virus infection while not wearing appropriate personal protective equipment should be monitored for symptoms for 10–14 days after the last exposure and tested if symptoms develop. Asymptomatic individuals exposed to animals with suspected or confirmed avian influenza virus infection where appropriate protective measures have not been taken should be assessed on a case-by-case basis and tested depending on the level of exposure. Given the uncertainty of potential mammal-to-mammal transmission and depending on the epidemiological situation, a low threshold can be considered for the testing of individuals exposed to potentially infected mammals. Further information on testing, follow-up and management of individuals with exposure and confirmed infection can be found in ECDC's guidance on testing and detection of zoonotic influenza virus infections in humans (ECDC, 2022) and ECDC's investigation protocol for human exposures and cases of avian influenza (ECDC, 2023b).
- Avian influenza viruses from humans should be sequenced and shared in public databases in a timely manner. Genetic changes in avian influenza viruses that may alter zoonotic potential or susceptibility to available antivirals should be monitored.
- Although there is no indication of an increased risk of avian influenza transmission to humans in the EU/EEA at present, based on available epidemiological and sequencing data, the risk assessment should be reviewed regularly, taking into consideration any new developments and information becoming available.
- Vaccination against seasonal influenza can be offered to individuals who are occupationally exposed to avian influenza to reduce the risk of reassortment between avian and human influenza viruses. Furthermore, vaccination against A(H5) virus can be considered to protect those at higher risk of exposure to A(H5N1), and possibly lower the risk of virus reassortment and human-adapted mutations, as a component of a wider, comprehensive approach to prevent human infections. Specific vaccination recommendations are under the remit of national authorities (EFSA and ECDC, 2024b).

## References

- Agüero M, Monne I, Sánchez A, Zecchin B, Fusaro A, Ruano MJ, Del Valle Arrojo M, Fernández-Antonio R, Souto AM, Tordable P, Cañas J, Bonfante F, Giussani E, Terregino C and Orejas JJ, 2023. Highly pathogenic avian influenza A(H5N1) virus infection in farmed minks, Spain, October 2022. *Eurosurveillance*, 28(3). doi: 10.2807/1560-7917.ES.2023.28.3.2300001
- Avian Flu Diary, online. Two Reports On HPAI H5N8 Infecting Marine Mammals (Denmark & Germany). Available online: <https://afludiary.blogspot.com/2022/02/two-reports-on-hpai-h5n8-infecting.html> [Accessed: 29 June 2022]
- AVMA (American Veterinary Medical Association), online. Goat in Minnesota tests positive for HPAI. Available online: <https://www.avma.org/news/goat-minnesota-tests-positive-hpai> [Accessed: 25 June 2024]
- Ärztblatt, online. Bird flu virus detected in dead seals. Available online: <https://www.aerzteblatt.de/nachrichten/127460/Vogelgrippevirus-bei-toten-Seehunden-nachgewiesen> [Accessed: 20 March 2024]
- Bao P, Liu Y, Zhang X, Fan H, Zhao J, Mu M, Li H, Wang Y, Ge H, Li S, Yang X, Cui Q, Chen R, Gao L, Sun Z, Gao L, Qiu S, Liu X, Horby PW, Li X, Fang L and Liu W, 2022. Human infection with a reassortment avian influenza A H3N8 virus: an epidemiological investigation study. *Nature Communications*, 13(6817). doi: 10.1038/s41467-022-34601-1
- Bennison A, Byrne AMP, Reid SM, Lynton-Jenkins JG, Mollett B, Silva DD, Peers-Dent J, Finlayson K, Hall R, Blockley F, Blyth M, Falchieri M, Fowler Z, Fitzcharles EM, Brown IH, James J and Banyard AC, 2023. Detection and spread of high pathogenicity avian influenza virus H5N1 in the Antarctic Region, Cold Spring Harbor Laboratory. *bioRxiv*. Unpublished document. doi: 10.1101/2023.11.23.568045
- Bordes L, Gerhards NM, Peters S, Van Oort S, Roose M, Dresken R, Venema S, Vrieling M, Engelsma M, Van Der Poel WHM and De Swart RL, 2024. H5N1 clade 2.3.4.4b avian influenza viruses replicate in differentiated bovine airway epithelial cells cultured at air-liquid interface. *Journal of General Virology*, 105(6). doi: 10.1099/jgv.0.002007
- Brown JD, Black A, Haman KH, Diel DG, Ramirez VE, Ziejka RS, Fenelon HT, Rabinowitz PM, Stevens L, Poulson R and Stallknecht DE, 2024. Antibodies to Influenza A(H5N1) Virus in Hunting Dogs Retrieving Wild Fowl, Washington, USA. *Emerging Infectious Diseases*, 30, 1271–1274. doi: 10.3201/eid3006.231459
- Burrough ER, Magstadt DR, Petersen B, Timmermans SJ, Gauger PC, Zhang J, Siepker C, Mainenti M, Li G, Thompson AC, Gorden PJ, Plummer PJ and Main R, 2024. Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus Infection in Domestic Dairy Cattle and Cats, United States, 2024. *Emerging Infectious Diseases*, 30, 1335–1343. doi: 10.3201/eid3007.240508
- BusinessDay, online. Chile scientists warn of Humboldt penguin extinction risk. Available online: <https://www.businesslive.co.za/bd/world/americas/2024-06-11-chile-scientists-warn-of-humboldt-penguin-extinction-risk/> [Accessed: 27 June 2024]
- Campagna C, Uhart M, Falabella V, Campagna J, Zavattieri V, Vanstreels RET and Lewis MN, 2024. Catastrophic mortality of southern elephant seals caused by H5N1 avian influenza. *Marine Mammal Science*, 40(1), 322–325. doi: 10.1111/mms.13101
- Caserta LC, Frye EA, Butt SL, Laverack MA, Nooruzzaman M, Covalenda LM, Thompson A, Prarat Koscielny M, Cronk B, Johnson A, Kleinhenz K, Edwards EE, Gomez G, Hitchener GR, Martins M, Kapczynski DR, Suarez DL, Alexander Morris ER, Hensley T, Beeby JS, Lejeune M, Swinford A, Elvinger F, Dimitrov KM and Diel DG, 2024. From birds to mammals: spillover of highly pathogenic avian influenza H5N1 virus to dairy cattle led to efficient intra- and interspecies transmission, Cold Spring Harbor Laboratory. *bioRxiv*. Unpublished document. doi: 10.1101/2024.05.22.595317

- Castillo A, Fasce R, Parra B, Andrade W, Covarrubias P, Hueche A, Campano C, Tambly C, Rojas M, Araya M, Hernandez F, Bustos P and Fernandez J, 2023. The first case of human infection with H5N1 avian Influenza A virus in Chile. *Journal of Travel Medicine*, 30(5). doi: 10.1093/jtm/taad083
- CDC (Centers for Disease Control and Prevention), 2024. Technical Report: June 2024 Highly Pathogenic Avian Influenza A(H5N1) Viruses. Available online: <https://www.cdc.gov/bird-flu/php/technical-report/h5n1-06052024.html>
- CDC (Centers for Disease Control and Prevention), online-a. CDC Reports A(H5N1) Ferret Study Results. Available online: <https://www.cdc.gov/bird-flu/spotlights/ferret-study-results.html#:~:text=The%20study%2C%20completed%20on%20Friday,conduct%20in%20the%20past%20year> [Accessed: 25 June]
- CDC (Centers for Disease Control and Prevention), online-b. CDC Reports Second Human Case of H5 Bird Flu Tied to Dairy Cow Outbreak. Available online: <https://www.cdc.gov/media/releases/2024/s0522-human-case-h5.html#:~:text=CDC%20Newsroom%20Home,CDC%20Reports%20Second%20Human%20Case%20of%20H5,Tied%20to%20Dairy%20Cow%20Outbreak&text=May%202022%2C%202024%20%E2%80%93%20A%20human,in%20the%20state%20of%20Michigan> [Accessed: 20 June 2024]
- CDC (Centers for Disease Control and Prevention), online-c. Technical Update: Summary Analysis of the Genetic Sequence of a Highly Pathogenic Avian Influenza A(H5N1) Virus Identified in a Human in Michigan. Available online: [https://www.cdc.gov/bird-flu/spotlights/h5n1-technical-update-052524.html?CDC\\_AAref\\_Val=https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-technical-update-may-24-2024.html](https://www.cdc.gov/bird-flu/spotlights/h5n1-technical-update-052524.html?CDC_AAref_Val=https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-technical-update-may-24-2024.html) [Accessed: 20 June 2024]
- CDC (Centers for Disease Control and Prevention), online-d. Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations. Available online: [https://www.cdc.gov/bird-flu/prevention/hpai-interimrecommendations.html#cdc\\_generic\\_section\\_12-appendix-risk-by-exposure-table](https://www.cdc.gov/bird-flu/prevention/hpai-interimrecommendations.html#cdc_generic_section_12-appendix-risk-by-exposure-table) [Accessed: 15 June 2024]
- CFIA, online. High pathogenicity avian influenza in wildlife. Available online: <https://cfia-ncr.maps.arcgis.com/apps/dashboards/89c779e98cdf492c899df23e1c38fdb> [Accessed: 20 June 2024]
- Chen J, Xu L, Liu T, Xie S, Li K, Li X, Zhang M, Wu Y, Wang X, Wang J, Shi K, Niu B, Liao M and Jia W, 2022. Novel Reassortant Avian Influenza A(H5N6) Virus, China, 2021. *Emerging Infectious Diseases*, 28, 1703–1707. doi: 10.3201/eid2808.212241
- CIDRAP, online-a. Officials warn of H5N1 avian flu reassortant circulating in parts of Asia. Available online: <https://www.cidrap.umn.edu/avian-influenza-bird-flu/officials-warn-h5n1-avian-flu-reassortant-circulating-parts-asia> [Accessed: 27 June 2024]
- CIDRAP, online-b. Scientists expand H5N1 testing in dairy products, launch human serology study. Available online: <https://www.cidrap.umn.edu/avian-influenza-bird-flu/scientists-expand-h5n1-testing-dairy-products-launch-human-serology-study> [Accessed: 01 July 2024]
- Cui P, Shi J, Wang C, Zhang Y, Xing X, Kong H, Yan C, Zeng X, Liu L, Tian G, Li C, Deng G and Chen H, 2022. Global dissemination of H5N1 influenza viruses bearing the clade 2.3.4.4b HA gene and biologic analysis of the ones detected in China. *Emerging Microbes and Infections*, 11, 1693–1704. doi: 10.1080/22221751.2022.2088407
- Des Moines Register, online. Second bird flu outbreak in 6 days infects 103K turkeys at northwest Iowa commercial facility. Available online: <https://eu.desmoinesregister.com/story/money/agriculture/2024/06/02/bird-flu-outbreak-infects-103000-turkeys-at-cherokee-county-facility/73950436007/> [Accessed: 10 July 2024]
- Du W, Dai M, Li Z, Boons GJ, Peeters B, van Kuppeveld FJM, de Vries E and de Haan CAM, 2018. Substrate Binding by the Second Sialic Acid-Binding Site of Influenza



- A Virus N1 Neuraminidase Contributes to Enzymatic Activity. *Journal of Virology*, 92(20). doi: 10.1128/JVI.01243-18
- ECDC (European Centre for Disease Prevention and Control), 2022. Testing and detection of zoonotic influenza virus infections in humans in the EU/EEA, and occupational safety and health measures for those exposed at work. ECDC, Stockholm. 32 pp. Available online: [https://www.ecdc.europa.eu/sites/default/files/documents/zoonotic-influenza-virus-infections-testing-detection\\_0.pdf](https://www.ecdc.europa.eu/sites/default/files/documents/zoonotic-influenza-virus-infections-testing-detection_0.pdf)
- ECDC (European Centre for Disease Prevention and Control), 2023a. Enhanced surveillance of severe avian influenza virus infections in hospital settings in the EU/EEA – 26 June 2023. ECDC, Stockholm. 5 pp. Available online: [https://www.ecdc.europa.eu/sites/default/files/documents/severe-avian-influenza-enhanced-surveillance-hospital-settings\\_0.pdf](https://www.ecdc.europa.eu/sites/default/files/documents/severe-avian-influenza-enhanced-surveillance-hospital-settings_0.pdf)
- ECDC (European Centre for Disease Prevention and Control), 2023b. Investigation protocol for human exposures and cases of avian influenza in the EU/EEA. ECDC, Stockholm. 46 pp. Available online: <https://www.ecdc.europa.eu/sites/default/files/documents/Investigation-protocol-human-exposures-cases-avian-influenza.pdf>
- ECDC (European Centre for Disease Prevention and Control), 2024a. Communicable disease threats report, 25-31 May 2024, week 22. ECDC, Stockholm. 17 pp. Available online: <https://www.ecdc.europa.eu/sites/default/files/documents/Communicable-disease-threats-report-week-22-2024.pdf>
- ECDC (European Centre for Disease Prevention and Control), 2024b. Communicable disease threats report, 18-25 May 2024, week 21. ECDC, Stockholm. 14 pp. Available online: [https://www.ecdc.europa.eu/sites/default/files/documents/Communicable-disease-threats-report-week-21-2024\\_0.pdf](https://www.ecdc.europa.eu/sites/default/files/documents/Communicable-disease-threats-report-week-21-2024_0.pdf)
- ECDC (European Centre for Disease Prevention and Control), 2024c. Communicable disease threats report, 15-21 June 2024, week 25. ECDC, Stockholm. 7 pp. Available online: <https://www.ecdc.europa.eu/sites/default/files/documents/Communicable-disease-threats-report-week-25-2024.pdf>
- ECDC (European Centre for Disease Prevention and Control), 2024d. Communicable disease threats report, 7 - 13 April 2024, week 15. ECDC, Stockholm. 16 pp. Available online: <https://www.ecdc.europa.eu/sites/default/files/documents/Communicable-disease-threats-report-week-15-2024.pdf>
- ECDC (European Centre for Disease Prevention and Control), 2024e. Enhanced influenza surveillance to detect avian influenza virus infections in the EU/EEA during the inter-seasonal period – 20 June 2024. ECDC, Stockholm. 7 pp. Available online: <https://www.ecdc.europa.eu/en/publications-data/enhanced-influenza-surveillance-detect-avian-influenza-virus-infections-eueea>
- ECDC (European Centre for Disease Prevention and Control), online. Risk assessment H5N1 clade 2.3.4.4b viruses. Available online: <https://www.ecdc.europa.eu/en/infectious-disease-topics/z-disease-list/avian-influenza/threats-and-outbreaks/risk-assessment-h5> [Accessed: 15 June 2024]
- EFSA (European Food Safety Authority), ECDC (European Centre for Disease Prevention and Control), EURL (European Reference Laboratory), Brown I, Kuiken T, Mulatti P, Smietanka K, Staubach C, Stroud D, Therkildsen OR, Willeberg P, Baldinelli F, Verdonck F and Adlhoch C, 2017. Avian influenza overview September – November 2017. *EFSA Journal* 2017;15(12):5141, 70 pp. doi:10.2903/j.efsa.2017.5141
- EFSA (European Food Safety Authority), ECDC (European Centre for Disease Prevention and Control), EURL (European Reference Laboratory for Avian Influenza), Adlhoch C, Fusaro A, Gonzales JL, Kuiken T, Marangon S, Niqueux É, Staubach C, Terregino C, Lima E, Muñoz Guajardo I and Baldinelli F, 2021. Scientific report:

- Avian influenza overview December 2020 – February 2021. EFSA Journal 2021;19(3):6497, 74 pp. doi:10.2903/j.efsa.2021.649710.2903/j.efsa.2021.6497
- EFSA (European Food Safety Authority), ECDC (European Centre for Disease Prevention and Control), EURL (European Reference Laboratory), Adlhoch C, Fusaro A, Gonzales JL, Kuiken T, Melidou A, Mirinavičiūtė G, Niqueux É, Ståhl K, Staubach C, Terregino C, Baldinelli F, Broglia A and Kohnle, 2023. Scientific report: Avian influenza overview April – June 2023. EFSA Journal 2023;21(7):8191, 54 pp. <https://doi.org/10.2903/j.efsa.2023.8191>
- EFSA (European Food Safety Authority), ECDC (European Centre for Disease Prevention and Control), EURL (European Union Reference Laboratory for Avian Influenza), Fusaro A, Gonzales JL, Kuiken T, Mirinavičiūtė G, Niqueux É, Ståhl K, Staubach C, Svartström O, Terregino C, Willgert K, Baldinelli F, Delacourt R, Georganas A and Kohnle L, 2024a. Scientific report: Avian influenza overview December 2023–March 2024. EFSA Journal 2024;22(3):8754, 69 pp. <https://doi.org/10.2903/j.efsa.2024.8754>
- EFSA (European Food Safety Authority), ECDC (European Centre for Disease Prevention and Control), Melidou A, Enkirch T, Willgert K, Adlhoch C, Alm E, Lamb F, Marangon S, Monne I, Stegeman JA, Delacourt R, Baldinelli F and Broglia A, 2024b. Drivers for a pandemic due to avian influenza and options for One Health mitigation measures. EFSA Journal;22(4);e8735, 24 pp. <https://doi.org/10.2903/j.efsa.2024.8735>
- EFSA (European Food Safety Authority), online. Avian influenza. Available online: <https://www.efsa.europa.eu/en/topics/topic/avian-influenza> [Accessed: 10 June 2024].
- European Commission, online. PAFF committees. Available online: [https://food.ec.europa.eu/horizontal-topics/committees/paff-committees\\_en](https://food.ec.europa.eu/horizontal-topics/committees/paff-committees_en) [Accessed: 10 June 2024]
- Falchieri M, Reid SM, Dastderji A, Cracknell J, Warren CJ, Mollett BC, Peers-Dent J, Schlachter A-LD, McGinn N, Hepple R, Thomas S, Ridout S, Quayle J, Pizzi R, Núñez A, Byrne AMP, James J and Banyard AC, 2024. Rapid mortality in captive bush dogs (*Speothos venaticus*) caused by influenza A of avian origin (H5N1) at a wildlife collection in the United Kingdom. bioRxiv. Unpublished document. doi: 10.1101/2024.04.18.590032
- FAO (Food and Agriculture Organization of the United Nations), 2024. Preliminary rapid risk assessment of foodborne avian influenza A (H5N1) virus. FAO, Rome. 2pp. Available online: <https://openknowledge.fao.org/items/abf49022-5302-4a70-900e-f22b540e08c2>
- FAO (Food and Agriculture Organization of the United Nations), WOA (World Organisation for Animal Health) and WHO (World Health Organization), 2024. Joint FAO/WHO/WOA preliminary assessment of recent influenza A(H5N1) viruses. 8pp. Available online: [https://cdn.who.int/media/docs/default-source/global-influenza-programme/2024\\_04\\_23\\_fao-woah-who\\_h5n1\\_assessment.pdf?sfvrsn%20=3ca3dba6\\_2&download=true](https://cdn.who.int/media/docs/default-source/global-influenza-programme/2024_04_23_fao-woah-who_h5n1_assessment.pdf?sfvrsn%20=3ca3dba6_2&download=true)
- FDA (Food and Drug Administration), online-a. Updates on Highly Pathogenic Avian Influenza (HPAI). Available online: <https://www.fda.gov/food/alerts-advisories-safety-information/updates-highly-pathogenic-avian-influenza-hpai#testing> [Accessed: 26 June 2024]
- FDA (Food and Drug Administration), online-b. Open letter to state regulatory partners regarding HPAIV and intrastate raw milk recommendations Available online: <https://www.fda.gov/media/179194/download?attachment> [Accessed: 28 June 2024]
- FLI (Friedrich-Loeffler-Institut), online-a. Avian influenza: No evidence of H5N1 infection in dairy cows outside the USA. Available online: <https://www.fli.de/en/news/short-messages/short-message/gefluegelpest-keine-hinweise-auf-h5n1-infektionen-bei-milchkuehen-ausserhalb-der-usa/> [Accessed: 20 June 2024]

- FLI (Friedrich-Loeffler-Institut), 2024. International team of scientists determine further spread of High Pathogenicity Avian Influenza (HPAI) in the Antarctic Peninsula Region. Place Friedrich-Loeffler-Institut, Friedrich-Loeffler-Institut. Available online: <https://www.fli.de/en/press/press-releases/press-singleview/international-team-of-scientists-determine-further-spread-of-high-pathogenicity-avian-influenza-hpai-in-the-antarctic-peninsula-region/>
- Floyd T, Banyard AC, Lean FZX, Byrne AMP, Fullick E, Whittard E, Mollett BC, Bexton S, Swinson V, Macrelli M, Lewis NS, Reid SM, Núñez A, Duff JP, Hansen R and Brown IH, 2021. Systemic infection with highly pathogenic H5N8 of avian origin produces encephalitis and mortality in wild mammals at a UK rehabilitation centre. bioRxiv:2021.2005.2026.445666. doi: 10.1101/2021.05.26.445666
- FSA (Food Standards Agency), 2024. Rapid Risk Assessment: Risk to UK consumers from Highly Pathogenic Avian Influenza (HPAI) H5N1 B3.13 in US dairy products. 13 pp. Available online: <https://www.food.gov.uk/print/pdf/node/23191>
- Fusaro A, Zecchin B, Giussani E, Palumbo E, Agüero-Garcia M, Bachofen C, Balint A, Banihashem F, Banyard AC, Beerens N, Bourg M, Briand FX, Brojer C, Brown IH, Brugger B, Byrne AMP, Cana A, Christodoulou V, Dirbakova Z, Fagulha T, Fouchier RAM, Garza-Cuartero L, Georgiades G, Gjerset B, Grasland B, Groza O, Harder T, Henriques AM, Hjulsager CK, Ivanova E, Janeliunas Z, Krivko L, Lemon K, Liang Y, Lika A, Malik P, McMenamy MJ, Nagy A, Nurmoja I, Onita I, Pohlmann A, Revilla-Fernandez S, Sanchez-Sanchez A, Savic V, Slavec B, Smietanka K, Snoeck CJ, Steensels M, Svansson V, Swieton E, Tammiranta N, Tinak M, Van Borm S, Zohari S, Adlhoch C, Baldinelli F, Terregino C and Monne I, 2024. High pathogenic avian influenza A(H5) viruses of clade 2.3.4.4b in Europe-Why trends of virus evolution are more difficult to predict. *Virus Evolution*, 10(1). doi: 10.1093/ve/veae027
- Gao W, Zu Z, Liu J, Song J, Wang X, Wang C, Liu L, Tong Q, Wang M, Sun H, Sun Y, Liu J, Chang K-C and Pu J, 2019. Prevailing I292V PB2 mutation in avian influenza H9N2 virus increases viral polymerase function and attenuates IFN- $\beta$  induction in human cells. *Journal of General Virology*, 100(9), 1273–1281. doi: 10.1099/jgv.0.001294
- GISAID, online. Available online: <https://gisaid.org/>
- Github izsvenezie-virology, online-a. FlutMut. Available online: <https://github.com/izsvenezie-virology/FluMut> [Accessed: 3 July 2024]
- Github izsvenezie-virology, online-b. FlutMutDB with v5.0 mutations. Available online: <https://github.com/izsvenezie-virology/FluMutGUI/releases/tag/v.3.0.0> [Accessed: 28 June 2024]
- UNMC (University of Nebraska Medical Center), online-a. Two chickens test positive for bird flu at San Francisco live bird market. Available online: <https://www.unmc.edu/healthsecurity/transmission/2024/06/04/two-chickens-test-positive-for-bird-flu-at-san-francisco-live-bird-market/#:~:text=The%20bird%20flu%20virus%20was,Francisco%20Director%20of%20Health%20Dr> [Accessed: 15 June 2024]
- UNMC (University of Nebraska Medical Center), online-b. Svalbard, Norway: Walrus dies from bird flu on Arctic island. Available online: <https://www.unmc.edu/healthsecurity/transmission/2024/04/30/svalbard-norway-walrus-dies-from-bird-flu-on-arctic-island/> [Accessed: 27 June 2024]
- GovMEX (Government of Mexico), online. Senasica confirms case of AH5N2 avian influenza in backyard flock in Michoacán. Available online: <https://www.gob.mx/senasica/articulos/confirmacion-senasica-caso-de-influenza-aviar-ah5n2-en-traspasio-de-michoacan?idiom=es> [Accessed: June 27 2024]
- Golke A, Jańczak D, Szaluś-Jordanow O, Dzieciatkowski T, Sapieryński R, Moroz-Fik A, Mickiewicz M and Frymus T, 2024. Natural Infection with Highly Pathogenic Avian Influenza A/H5N1 Virus in Pet Ferrets. *Viruses*, 16(931). doi: 10.3390/v16060931
- Good MR, Ji W, Fernández-Quintero ML, Ward AB and Guthmiller JJ, 2024. A single mutation in dairy cow-associated H5N1 viruses increases receptor binding breadth. bioRxiv. Unpublished document. doi: 10.1101/2024.06.22.600211

- GovAU (Government of Australia), online. Avian influenza - Detection in Australia. Available online: [https://www.outbreak.gov.au/current-outbreaks/avian-influenza#toc\\_0](https://www.outbreak.gov.au/current-outbreaks/avian-influenza#toc_0) [Accessed: 27 June 2024]
- GovCan (Government of Canada), online. Commercial milk sampling and testing for highly pathogenic avian influenza (HPAI) viral fragments in Canada. Available online: <https://inspection.canada.ca/en/animal-health/terrestrial-animals/diseases/reportable/avian-influenza/latest-bird-flu-situation/commercial-milk-sampling-and-testing-hpai-vira> [Accessed: 25 June 2024]
- Grant M, 2024. SVA (Swedish Veterinary Agency). July 2024. Personal communication by e-mail
- Gu W, Shi J, Cui P, Yan C, Zhang Y, Wang C, Zhang Y, Xing X, Zeng X, Liu L, Tian G, Suzuki Y, Li C, Deng G and Chen H, 2022. Novel H5N6 reassortants bearing the clade 2.3.4.4b HA gene of H5N8 virus have been detected in poultry and caused multiple human infections in China. *Emerging Microbes and Infections*, 11, 1174–1185. doi: 10.1080/22221751.2022.2063076
- Guan L, Einfeld AJ, Pattinson D, Gu C, Biswas A, Maemura T, Trifkovic S, Babujee L, Presler R, Dahn R, Halfmann PJ, Barnhardt T, Neumann G, Thompson A, Swinford AK, Dimitrov KM, Poulsen K, Kawaoka Y, 2024. Cow's Milk Containing Avian Influenza A(H5N1) Virus — Heat Inactivation and Infectivity in Mice. *New England Journal of Medicine*, 391, 87–90. doi: 10.1056/NEJMc2405495
- Guo H, De Vries E, McBride R, Dekkers J, Peng W, Bouwman KM, Nycholat C, Verheije MH, Paulson JC, Van Kuppeveld FJM and De Haan CAM, 2017. Highly Pathogenic Influenza A(H5Nx) Viruses with Altered H5 Receptor-Binding Specificity. *Emerging Infectious Diseases*, 23, 220–231. doi: 10.3201/eid2302.161072
- HCDC, online. Ho Chi Minh City: first human case of avian influenza A(H9N2) recorded in the country. Available online: <https://hcdc.vn/tphcm-ghi-nhan-ca-mac-cum-gia-cam-ah9n2-tren-nguoi-dau-tien-cua-ca-nuoc-8EcfhD.html> [Accessed: 22 June 2024]
- Herve S, Schmitz A, Briand F-X, Gorin S, Queguiner S, Niqueux É, Paboeuf F, Scoizec A, Le Bouquin-Leneveu S, Eterradosi N and Simon G, 2021. Serological Evidence of Backyard Pig Exposure to Highly Pathogenic Avian Influenza H5N8 Virus during 2016-2017 Epizootic in France. *Pathogens*, 10. doi: 10.3390/pathogens10050621
- Hindustan Times, online. Bird flu outbreak in Kerala's Alappuzha: Should you be concerned? Symptoms, prevention tips of H5N1 flu. Available online: <https://www.hindustantimes.com/lifestyle/health/bird-flu-outbreak-in-keralas-alappuzha-should-you-be-concerned-symptoms-prevention-tips-of-h5n1-flu-101713429108016.html> [Accessed: 27 June 2024]
- Kaiser F, Morris DH, Wickenhagen A, Mukesh R, Gallogly S, Yinda KC, De Wit E, Lloyd-Smith JO and Munster VJ, 2024. Inactivation of Avian Influenza A(H5N1) Virus in Raw Milk at 63°C and 72°C. *New England Journal of Medicine*, 391, 90–92. doi: 10.1056/nejmc2405488
- Kareinen L, Tammiranta N, Kauppinen A, Zecchin B, Pastori A, Monne I, Terregino C, Giussani E, Kaarto R, Karkamo V, Lahteinen T, Lounela H, Kantala T, Laamanen I, Nokireki T, London L, Helve O, Kaariainen S, Ikonen N, Jalava J, Kalin-Manttari L, Katz A, Savolainen-Kopra C, Lindh E, Sironen T, Korhonen EM, Aaltonen K, Galiano M, Fusaro A and Gadd T, 2024. Highly pathogenic avian influenza A(H5N1) virus infections on fur farms connected to mass mortalities of black-headed gulls, Finland, July to October 2023. *EuroSurveillance*, 29(25). doi: 10.2807/1560-7917.ES.2024.29.25.2400063
- Kristensen C, Jensen HE, Trebbien R, Webby RJ and Larsen LE, 2024. The avian and human influenza A virus receptors sialic acid (SA)- $\alpha$ 2,3 and SA- $\alpha$ 2,6 are widely expressed in the bovine mammary gland. *bioRxiv*. Unpublished document. doi: 10.1101/2024.05.03.592326
- Kwon T, Trujillo JD, Carossino M, Lyoo EL, McDowell CD, Cool K, Matias-Ferreira FS, Jeevan T, Morozov I, Gaudreault NN, Balasuriya UBR, Webby RJ, Osterrieder N and Richt JA, 2024. Pigs are highly susceptible to but do not transmit mink-

- derived highly pathogenic avian influenza virus H5N1 clade 2.3.4.4b. *Emerging Microbes and Infections*, 13(1). doi: 10.1080/22221751.2024.2353292
- Le Sage V, Campbell AJ, Reed D, Duprex WP and Lakdawala S, 2024. Influenza H5N1 and H1N1 viruses remain infectious in unpasteurized milk on milking machinery surfaces. medRxiv. Unpublished document. doi: 10.1101/2024.05.22.24307745
- Lee EK, Lee YN, Kye SJ, Lewis NS, Brown IH, Sagong M, Heo GB, Kang YM, Cho HK, Kang HM, Cheon SH, Lee M, Park BK, Kim YJ and Lee YJ, 2018. Characterization of a novel reassortant H5N6 highly pathogenic avian influenza virus clade 2.3.4.4 in Korea, 2017. *Emerging Microbes and Infections*, 7(103). doi: 10.1038/s41426-018-0104-3
- Leguia M, Garcia-Glaessner A, Muñoz-Saavedra B, Juarez D, Barrera P, Calvo-Mac C, Jara J, Silva W, Ploog K, Amaro L, Colchao-Claux P, Johnson CK, Uhart MM, Nelson MI and Lescano J, 2023. Highly pathogenic avian influenza A (H5N1) in marine mammals and seabirds in Peru. *Nature Communications*, 14, 5489. doi: 10.1038/s41467-023-41182-0
- León F, Le Bohec C, J. Pizarro E, Baille L, Cristofari R, Houstin A, P. Zitterbart D, Barriga G, Poulin E and A. Vianna J, 2024. Highly Pathogenic Avian Influenza A (H5N1) Suspected in penguins and shags on the 2 Antarctic Peninsula and West Antarctic Coast. bioRxiv. 18 May 2024. Unpublished document. doi: 10.1101/2024.03.16.58536
- Lindh E, Lounela H, Ikonen N, Kantala T, Savolainen-Kopra C, Kauppinen A, Österlund P, Kareinen L, Katz A, Nokireki T, Jalava J, London L, Pitkäpaasi M, Vuolle J, Punto-Luoma AL, Kaarto R, Voutilainen L, Holopainen R, Kalin-Mänttari L, Laaksonen T, Kiviranta H, Pennanen A, Helve O, Laamanen I, Melin M, Tammiranta N, Rimhanen-Finne R, Gadd T and Salminen M, 2023. Highly pathogenic avian influenza A(H5N1) virus infection on multiple fur farms in the South and Central Ostrobothnia regions of Finland, July 2023. *Eurosurveillance*, 28(31), pii=2300400. doi: 10.2807/1560-7917.ES.2023.28.31.2300400
- Liu K, Qi X, Bao C, Wang X and Liu X, 2024a. Novel H10N3 avian influenza viruses: a potential threat to public health. *The Lancet Microbe*, 5(1), doi: 10.1016/S2666-5247(23)00409-3
- Liu G, Dai J, Zhao J, Xia J, Zhang P, Ding Y, Li Q, Hou M, Xiong X, Jian Q and Liu Y, 2024b. First human case of avian influenza A (H10N3) in Southwest China. Research Square. Unpublished document. doi: 10.21203/rs.3.rs-4181286/v1
- Mattilsynet, online. To private practicing veterinarians about avian influenza in mammals. Available online: <https://www.mattilsynet.no/dyr/dyresykdommer/fugleinfluensa/informasjon-til-privatpraktiserende-veterinaerer-om-fugleinfluensa-hos-pattedyr> [Accessed: 25 June 2024]
- MDHHS (The Michigan Department of Health and Human Services), online. Additional influenza A(H5) case detected in Michigan. Available online: <https://www.michigan.gov/mdhhs/inside-mdhhs/newsroom/2024/05/30/h5n1-updates> [Accessed: 20 June 2024]
- Muñoz G, Mendieta V, Ulloa M, Agüero B, Torres CG, Kruger L and Neira V, 2024a. Lack of Highly Pathogenic Avian Influenza H5N1 in the South Shetland Islands in Antarctica, Early 2023. *Animals*, 14(7). doi: 10.3390/ani14071008
- Muñoz G, Ulloa M, Alegria R, Quezada B, Bennett B, Enciso N, Atavales J, Johow M, Aguayo C, Araya H and Neira V, 2024b. Stranding and mass mortality in humboldt penguins (*Spheniscus humboldti*), associated to HPAIV H5N1 outbreak in Chile. *Preventive Veterinary Medicine*, 227. doi: 10.1016/j.prevetmed.2024.106206
- Nébih, online. The Nébih confirmed a bird flu infection in a cat. Available online: <https://portal.nebih.gov.hu/-/madarinfluenza-fertozest-igazolt-egy-macskanal-a-nebih> [Accessed: 27 June 2024]
- Nelli RK, Harm TA, Siepker C, Groeltz-Thrush JM, Jones B, Twu N-C, Nenninger AS, Magstadt DR, Burrough ER, Piñeyro PE, Mainenti M, Carnaccini S, Plummer PJ and Bell TM, 2024. Sialic Acid Receptor Specificity in Mammary Gland of Dairy Cattle

- Infected with Highly Pathogenic Avian Influenza A(H5N1) Virus. *Emerging Infectious Diseases*, 30(7). doi: 10.3201/eid3007.240689
- Nguyen T-Q, Hutter C, Markin A, Thomas M, Lantz K, Killian ML, Janzen GM, Vijendran S, Wagle S, Inderski B, Magstadt DR, Li G, Diel DG, Frye EA, Dimitrov KM, Swinford AK, Thompson AC, Snevik KR, Suarez DL, Spackman E, Lakin SM, Ahola SC, Johnson KR, Baker AL, Robbe-Austerman S, Torchetti MK and Anderson TK, 2024. Emergence and interstate spread of highly pathogenic avian influenza A(H5N1) in dairy cattle. *bioRxiv*. Unpublished document. doi: 10.1101/2024.05.01.591751
- Noticias Agrícolas, online. Philippines reports H5N1 bird flu outbreak on poultry farms. Available online: <https://www.noticiasagricolas.com.br/noticias/granjeiros/373823-filipinas-relata-surto-de-gripe-aviaria-h-5-n-1-em-granjas-avicolas.html> [Accessed: 26 June 2024]
- Ogata T, Yamazaki Y, Okabe N, Nakamura Y, Tashiro M, Nagata N, Itamura S, Yasui Y, Nakashima K, Doi M, Izumi Y, Fujieda T, Yamato SI and Kawada Y, 2008. Human H5N2 Avian Influenza Infection in Japan and the Factors Associated with High H5N2-Neutralizing Antibody Titer. *Journal of Epidemiology*, 18(4), 160–166. doi: 10.2188/jea.je2007446
- Okoye J, Eze D, Krueger WS, Heil GL, Friary JA and Gray GC, 2013. Serologic evidence of avian influenza virus infections among Nigerian agricultural workers. *Journal of Medical Virology*, 85(4), 670–676. doi: 10.1002/jmv.23520
- Outbreak News, online. Denmark reports 1st highly pathogenic avian influenza case in harbor seal. Available online: <http://outbreaknewstoday.com/denmark-reports-1st-highly-pathogenic-avian-influenza-case-in-harbor-seal-89870/> [Accessed: 29 June 2022]
- Pardo-Roa C, Nelson MI, Ariyama N, Aguayo C, Almonacid LI, Muñoz G, Navarro C, Avila C, Ulloa M, Reyes R, Luppichini EF, Mathieu C, Vergara R, Gonzalez A, Gonzalez CG, Araya H, Fernandez J, Fasce R, Johow M, Medina RA and Neira V, 2023. Cross-species transmission and PB2 mammalian adaptations of highly pathogenic avian influenza A/H5N1 viruses in Chile. *bioRxiv*. Unpublished document. doi: 10.1101/2023.06.30.547205
- Pinto RM, Bakshi S, Lytras S, Zakaria MK, Swingler S, Worrell JC, Herder V, Hargrave KE, Varjak M, Cameron-Ruiz N, Collados Rodriguez M, Varela M, Wickenhagen A, Loney C, Pei Y, Hughes J, Valette E, Turnbull ML, Furnon W, Gu Q, Orr L, Taggart A, Diebold O, Davis C, Boutell C, Grey F, Hutchinson E, Digard P, Monne I, Wootton SK, MacLeod MKL, Wilson SJ and Palmarini M, 2023. BTN3A3 evasion promotes the zoonotic potential of influenza A viruses. *Nature*, 619, 338–347. doi: 10.1038/s41586-023-06261-8
- Plaza PI, Gamarra-Toledo V, Rodriguez Eugui J, Rosciano N and Lambertucci SA, 2024a. Pacific and Atlantic sea lion mortality caused by highly pathogenic Avian Influenza A(H5N1) in South America. *Travel Medicine and Infectious Diseases*, 59, 102712. doi: 10.1016/j.tmaid.2024.102712
- Plaza PI, Gamarra-Toledo V, Eugui JR and Lambertucci SA, 2024b. Recent Changes in Patterns of Mammal Infection with Highly Pathogenic Avian Influenza A(H5N1) Virus Worldwide. *Emerging Infectious Diseases*, 30, 444–452. doi: 10.3201/eid3003.231098
- Pulit-Penalosa JA, Brock N, Belser JA, Sun X, Pappas C, Kieran TJ, Basu Thakur P, Zeng H, Cui D, Frederick J, Fasce R, Tumpey TM and Maines TR, 2024. Highly pathogenic avian influenza A(H5N1) virus of clade 2.3.4.4b isolated from a human case in Chile causes fatal disease and transmits between co-housed ferrets. *Emerging Microbes and Infections*, 13(1). doi: 10.1080/22221751.2024.2332667
- Rabalski L, Milewska A, Pohlmann A, Gackowska K, Lepionka T, Szczepaniak K, Swiatalska A, Sieminska I, Arent Z, Beer M, Koopmans M, Grzybek M and Pyrc K, 2023. Emergence and potential transmission route of avian influenza A (H5N1) virus in domestic cats in Poland, June 2023. *Eurosurveillance*, 28(31). doi: 10.2807/1560-7917.es.2023.28.31.2300390

- Restori KH, Septer KM, Field CJ, Patel DR, VanInsberghe D, Raghunathan V, Lowen AC and Sutton TC, 2024. Risk assessment of a highly pathogenic H5N1 influenza virus from mink. *Nature Communications*, 15(1). doi: 10.1038/s41467-024-48475-y
- Reuters, online-a. Scientists investigate thousands of dead Antarctic penguins for bird flu. Available online: <https://www.reuters.com/business/healthcare-pharmaceuticals/scientists-investigate-thousands-dead-antarctic-penguins-bird-flu-2024-04-04/> [Accessed: 27 June 2024]
- Reuters, online-b. Cows infected with bird flu have died in five US states. Available online: <https://www.reuters.com/world/us/cows-infected-with-bird-flu-have-died-five-us-states-2024-06-06/> [Accessed: 25 June 2024]
- Rimondi A, Vanstreels RET, Olivera V, Donini A, Lauriente MM and Uhart MM, 2024. Highly Pathogenic Avian Influenza A(H5N1) Viruses from Multispecies Outbreak, Argentina, August 2023. *Emerging Infectious Diseases*, 30. doi: 10.3201/eid3004.231725
- Ríos Carrasco M, Gröne A, Van Den Brand JMA and De Vries RP, 2024. The mammary glands of cows abundantly display receptors for circulating avian H5 viruses, Cold Spring Harbor Laboratory. *bioRxiv*. Unpublished document. doi: 10.1101/2024.05.24.595667
- Rosone F, Bonfante F, Sala MG, Maniero S, Cersini A, Ricci I, Garofalo L, Caciolo D, Denisi A, Napolitan A, Parente M, Zecchin B, Terregino C and Scicluna MT, 2023. Seroconversion of a Swine Herd in a Free-Range Rural Multi-Species Farm against HPAI H5N1 2.3.4.4b Clade Virus. *Microorganisms*, 11(5), 1162. doi: 10.3390/microorganisms11051162
- Revilla-Fernández S, Höflechner-Pörtl A, Zimpernik I and Vogelgesang J, 2024. AGES (Austrian Agency for Health and Food Safety GmbH). June 2024. Personal communication by e-mail
- SCAR (Scientific Committee on Antarctic Research), online. Sub-Antarctic and Antarctic Highly Pathogenic Avian Influenza H5N1 monitoring project Available online: <https://scar.org/library-data/avian-flu#database> [Accessed: 27 June 2024]
- Schafers J, Warren CJ, Yang J, Zhang J, Cole SJ, Cooper J, Drewek K, Kolli BR, McGinn N, Qureshi M, Reid SM, Peacock TP, Brown I, James J, Banyard AC, Iqbal M, Digard P and Hutchinson E, 2024. Pasteurisation temperatures effectively inactivate influenza A viruses in milk. *medRxiv*. Unpublished document. doi: 10.1101/2024.05.30.24308212
- Schüleïn A, Ritzmann M, Christian J, Schneider K and Neubauer-Juric A, 2021. Exposure of wild boar to Influenza A viruses in Bavaria: Analysis of seroprevalences and antibody subtype specificity before and after the panzootic of highly pathogenic avian influenza viruses A (H5N8). *Zoonoses and Public Health*, 68(5), 503–515. doi: <https://doi.org/10.1111/zph.12841>
- Scott A, Hernandez-Jover M, Groves P and Toribio J-A, 2020. An overview of avian influenza in the context of the Australian commercial poultry industry. *One Health*, 10. doi: 10.1016/j.onehlt.2020.100139
- SGGP, online. New case of H5N1 human infection reported in Khanh Hoa. Available online: <https://en.sggp.org.vn/new-case-of-h5n1-human-infection-reported-in-khanh-hoa-post108915.html> [Accessed: 20 June 2024]
- Shin DL, Siebert U, Lakemeyer J, Grilo M, Pawliczka I, Wu NH, Valentin-Weigand P, Haas L and Herrler G, 2019. Highly Pathogenic Avian Influenza A(H5N8) Virus in Gray Seals, Baltic Sea. *Emerging Infectious Diseases*, 25(12), 2295–2298. doi: 10.3201/eid2512.181472
- Shu Y and McCauley J, 2017. GISAID: Global initiative on sharing all influenza data – from vision to reality. *Eurosurveillance*, 22(13). doi: 10.2807/1560-7917.es.2017.22.13.30494
- Sit THC, Sun W, Tse ACN, Brackman CJ, Cheng SMS, Tang AWY, Cheung JTL, Peiris M and Poon LLM, 2022. Novel Zoonotic Avian Influenza A(H3N8) Virus in Chicken, Hong Kong, China. *Emerging Infectious Diseases*, 28(10), 2009–2015. doi: 10.3201/eid2810.221067

- Smith GJ, Donis RO, WHO (World Health Organization), WOA (World Organisation for Animal Health) and FAO (Food and Agriculture Organization of the United Nations), 2015. Nomenclature updates resulting from the evolution of avian influenza A(H5) virus clades 2.1.3.2a, 2.2.1, and 2.3.4 during 2013–2014. *Influenza and Other Respiratory Viruses*, 9(5), 271–276. doi: 10.1111/irv.12324
- Spackman E, Jones DR, McCoig AM, Colonius TJ, Goraichuk I and Suarez DL, 2024. Characterization of highly pathogenic avian influenza virus in retail dairy products in the US. medRxiv. Unpublished document. doi: 10.1101/2024.05.21.24307706
- Stech O, Veits J, Abdelwhab E-SM, Wessels U, Mettenleiter TC and Stech J, 2015. The Neuraminidase Stalk Deletion Serves as Major Virulence Determinant of H5N1 Highly Pathogenic Avian Influenza Viruses in Chicken. *Scientific Reports*, 5, 13493. doi: 10.1038/srep13493
- Su Y, Yang HY, Zhang BJ, Jia HL and Tien P, 2008. Analysis of a point mutation in H5N1 avian influenza virus hemagglutinin in relation to virus entry into live mammalian cells. *Archives of Virology*, 153(12), 2253–2261. doi: 10.1007/s00705-008-0255-y
- Suttie A, Deng YM, Greenhill AR, Dussart P, Horwood PF and Karlsson EA, 2019. Inventory of molecular markers affecting biological characteristics of avian influenza A viruses. *Virus Genes*, 55(6), 739–768. doi: 10.1007/s11262-019-01700-z
- Szaluś-Jordanow O, Golke A, Dzieciatkowski T, Czopowicz M, Kardas M, Mickiewicz M, Moroz-Fik A, Łobaczewski A, Markowska-Daniel I and Frymus T, 2024. Upper Respiratory Tract Disease in a Dog Infected by a Highly Pathogenic Avian A/H5N1 Virus. *Microorganisms*, 12(4). doi: 10.3390/microorganisms12040689
- Terregino C, 2024. EURL for Avian Influenza and Newcastle Disease. July 2024. Personal communication by e-mail
- Thanawongnuwech R, Amonsin A, Tantilertcharoen R, Damrongwatanapokin S, Theamboonlers A, Payungporn S, Nanthapornphiphat K, Ratanamunghanon S, Tunak E, Songserm T, Vivatthanavanich V, Lekdumrongsak T, Kesdangakonwut S, Tunhikorn S and Poovorawan Y, 2005. Probable Tiger-to-Tiger Transmission of Avian Influenza H5N1. *Emerging Infectious Diseases*, 11(5), 699–701. doi: 10.3201/eid1105.050007
- The Guardian, online-a. Bird flu detected at egg farm in Sydney’s Hawkesbury. Available online: <https://www.theguardian.com/australia-news/article/2024/jun/19/bird-flu-detected-egg-farm-hawkesbury-sydney-nsw> [Accessed: 25 June 2024]
- The Guardian, online-b. First case of walrus dying from bird flu recorded in Arctic. Available online: <https://www.theguardian.com/world/2024/apr/30/first-walrus-bird-flu-death-arctic-islands> [Accessed: 27 June 2024]
- The Hindu, online. Avian flu confirmed at nine more places in Alappuzha. Available online: <https://www.thehindu.com/news/national/kerala/avian-flu-confirmed-at-nine-more-places-in-alappuzha/article68304828.ece> [Accessed: 26 June 2024]
- The Poultry Site, online. Bird flu spreads to seventh Australian poultry farm. Available online: <https://www.thepoultrysite.com/news/2024/06/bird-flu-spreads-to-seventh-australian-poultry-farm> [Accessed: 27 June 2024]
- Tomás G, Marandino A, Panzera Y, Rodriguez S, Wallau GL, Dezordi FZ, Perez R, Bassetti L, Negro R, Williman J, Uriarte V, Grazioli F, Leizagoyen C, Riveron S, Coronel J, Bello S, Paez E, Lima M, Mendez V and Perez R, 2024. Highly pathogenic avian influenza H5N1 virus infections in pinnipeds and seabirds in Uruguay: Implications for bird-mammal transmission in South America. *Virus Evolution*, 10(1). doi: 10.1093/ve/veae031
- Turner JCM, Barman S, Feeroz MM, Hasan MK, Akhtar S, Jeevan T, Walker D, Franks J, Seiler P, Mukherjee N, Kercher L, McKenzie P, Lam T, El-Shesheny R and Webby RJ, 2021. Highly Pathogenic Avian Influenza A(H5N6) Virus Clade 2.3.4.4h in Wild Birds and Live Poultry Markets, Bangladesh. *Emerging Infectious Diseases*, 27(8), 2492–2494. doi: 10.3201/eid2709.210819
- Uhart M, Vanstreels RET, Nelson MI, Olivera V, Campagna J, Zavattieri V, Lemey P, Campagna C, Falabella V and Rimondi A, 2024. Massive outbreak of Influenza A



- H5N1 in elephant seals at Península Valdés, Argentina: increased evidence for mammal-to-mammal transmission. bioRxiv. Unpublished document. doi: 10.1101/2024.05.31.596774
- UKHSA (United Kingdom Health Agency), online-a. Influenza A(H5N1) 2.3.4.4b B3.13: US cattle outbreak Human health risk assessment ratified 13 May. Available online: [https://assets.publishing.service.gov.uk/media/6655f2f2d470e3279dd332dc/influenza-A\\_H5N1\\_human-health-risk-assessment-23-May-2024.pdf](https://assets.publishing.service.gov.uk/media/6655f2f2d470e3279dd332dc/influenza-A_H5N1_human-health-risk-assessment-23-May-2024.pdf) [Accessed: 20 June 2024]
- UKHSA (United Kingdom Health Agency), online-b. HAIRS risk statement: Avian influenza A(H5N1) in livestock. Available online: <https://www.gov.uk/government/publications/hairs-risk-statement-avian-influenza-ah5n1-in-livestock/hairs-risk-statement-avian-influenza-ah5n1-in-livestock> [Accessed: 10 June 2024]
- USDA (United States Department of Agriculture), online-a. Detections of Highly Pathogenic Avian Influenza in Wild Birds. Available online: <https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/wild-birds#:~:text=Detections%20of%20Highly%20Pathogenic%20Avian%20Influenza%20in%20Wild%20Birds,-Last%20Modified%3A%20May&text=Wild%20birds%20can%20be%20infected,domestic%20poultry%20to%20the%20virus> [Accessed 26 June 2024]
- USDA (United States Department of Agriculture), online-b. Highly Pathogenic Avian Influenza (H5N1) - Michigan Dairy Herd and Poultry Flock Summary. Epidemiological Investigations of HPAI H5N1 Genotype B3.13 in Michigan Dairy Herds and Poultry Flocks. Available online: <https://www.aphis.usda.gov/sites/default/files/hpai-h5n1-dairy-cattle-mi-epi-invest.pdf> [Accessed 25 June 2024]
- USDA (United States Department of Agriculture), online-c. Highly Pathogenic Avian Influenza H5N1 Genotype B3.13 in Dairy Cattle: National Epidemiologic Brief. Place U.S. Department of Agriculture, U.S. Department of Agriculture. Available online: <https://www.aphis.usda.gov/sites/default/files/hpai-dairy-national-epi-brief.pdf> [Accessed 26 June 2024]
- USDA (United States Department of Agriculture), online-d. USDA Actions to Protect Livestock Health From Highly Pathogenic H5N1 Avian Influenza. Available online: <https://www.usda.gov/media/press-releases/2024/04/24/usda-actions-protect-livestock-health-highly-pathogenic-h5n1-avian> Available online: [25 June 2024]
- USDA (United States Department of Agriculture), online-e. USDA Announces \$824 Million in New Funding to Protect Livestock Health; Launches Voluntary H5N1 Dairy Herd Status Pilot Program. Available online: <https://www.usda.gov/media/press-releases/2024/05/30/usda-announces-824-million-new-funding-protect-livestock-health> [Accessed: 25 June 2024]
- USDA (United States Department of Agriculture), online-f. Detections of Highly Pathogenic Avian Influenza in Mammals. Available online: <https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/mammals> [Accessed: 25 June 2024]
- USDA (United States Department of Agriculture), online-g. Highly Pathogenic Avian Influenza (HPAI) H5N1 Detections in Alpacas. Available online: <https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/mammals/highly-pathogenic-avian> [Accessed: 25 June 2024]
- USDA-APHIS (United States Department of Agriculture Animal and Plant Health Inspection Service), online-a. Federal and State Veterinary, Public Health Agencies Share Update on HPAI Detection in Kansas, Texas Dairy Herds. Available online: <https://www.aphis.usda.gov/news/agency-announcements/federal-state-veterinary-public-health-agencies-share-update-hpai> [Accessed 2 July 2024]
- USDA-APHIS (United States Department of Agriculture Animal and Plant Health Inspection Service), online-b. HPAI Confirmed Cases in Livestock. Available

- online: <https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/hpai-confirmed-cases-livestock> [Accessed: 3 July 2024]
- USDA-APHIS (United States Department of Agriculture Animal and Plant Health Inspection Service), online-c. Federal Order Requiring Testing for and Reporting of Highly Pathogenic Avian Influenza (HPAI) in Livestock. Available online: <https://www.aphis.usda.gov/sites/default/files/dairy-federal-order.pdf> [Accessed 28 June 2024]
- USDA-APHIS (United States Department of Agriculture Animal and Plant Health Inspection Service), online-d. Updates on H5N1 Beef Safety Studies. Available online: <https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/livestock/h5n1-beef-safety-studies#:~:text=On%20May%2028%2C%202024%2C%20testing,diaphragm%20muscle%2C%20from%20one%20cow> [Accessed: 25 June 2024]
- Uyeki TM, Milton S, Abdul Hamid C, Reinoso Webb C, Presley SM, Shetty V, Rollo SN, Martinez DL, Rai S, Gonzales ER, Kniss KL, Jang Y, Frederick JC, De La Cruz JA, Liddell J, Di H, Kirby MK, Barnes JR and Davis CT, 2024. Highly Pathogenic Avian Influenza A(H5N1) Virus Infection in a Dairy Farm Worker. *New England Journal of Medicine*, 390(21), 2028–2029. doi: 10.1056/nejmc2405371
- Wan H and Perez DR, 2007. Amino acid 226 in the hemagglutinin of H9N2 influenza viruses determines cell tropism and replication in human airway epithelial cells. *Journal of Virology*, 81(10), 5181–5191. doi: 10.1128/JVI.02827-06
- Wan H, Sorrell EM, Song H, Hossain MJ, Ramirez-Nieto G, Monne I, Stevens J, Cattoli G, Capua I, Chen LM, Donis RO, Busch J, Paulson JC, Brockwell C, Webby R, Blanco J, Al-Natour MQ and Perez DR, 2008. Replication and transmission of H9N2 influenza viruses in ferrets: evaluation of pandemic potential. *PLoS One*, 3(8), e2923. doi: 10.1371/journal.pone.0002923
- Wang W, Lu B, Zhou H, Suguitan AL, Jr., Cheng X, Subbarao K, Kemble G and Jin H, 2010. Glycosylation at 158N of the hemagglutinin protein and receptor binding specificity synergistically affect the antigenicity and immunogenicity of a live attenuated H5N1 A/Vietnam/1203/2004 vaccine virus in ferrets. *Journal of Virology*, 84(13), 6570–6577. doi: 10.1128/JVI.00221-10
- Watanabe Y, Ibrahim MS, Ellakany HF, Kawashita N, Mizuike R, Hiramatsu H, Sriwilaijaroen N, Takagi T, Suzuki Y and Ikuta K, 2011. Acquisition of Human-Type Receptor Binding Specificity by New H5N1 Influenza Virus Sublineages during Their Emergence in Birds in Egypt. *PLoS Pathogens*, 7(5), e1002068. doi: 10.1371/journal.ppat.1002068
- Wessels U, Abdelwhab EM, Veits J, Hoffmann D, Mamerow S, Stech O, Hellert J, Beer M, Mettenleiter TC and Stech J, 2018. A Dual Motif in the Hemagglutinin of H5N1 Goose/Guangdong-Like Highly Pathogenic Avian Influenza Virus Strains Is Conserved from Their Early Evolution and Increases both Membrane Fusion pH and Virulence. *Journal of Virology*, 92(17), JVI.00778-00718. doi: 10.1128/jvi.00778-18
- WHO (World Health Organization), 2023. Genetic and antigenic characteristics of zoonotic influenza A viruses and development of candidate vaccine viruses for pandemic preparedness. Geneva. 12 pp. Available online: [https://cdn.who.int/media/docs/default-source/influenza/who-influenza-recommendations/vcm-northern-hemisphere-recommendation-2023-2024/20230224\\_zoonotic\\_recommendations.pdf?sfvrsn=38c739fa\\_4](https://cdn.who.int/media/docs/default-source/influenza/who-influenza-recommendations/vcm-northern-hemisphere-recommendation-2023-2024/20230224_zoonotic_recommendations.pdf?sfvrsn=38c739fa_4)
- WHO (World Health Organization), online-a. Avian Influenza A(H5N2) - Mexico. Available online: <https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON524> [Accessed: 20 June 2024]
- WHO (World Health Organization), online-b. Avian Influenza A(H5N1) - Viet Nam. Available online: <https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON511> [Accessed: 20 June 2024]
- WHO (World Health Organization), online-c. Avian Influenza A(H5N1) - United States of America. Available online: <https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON512> [Accessed: 20 June 2024]

- WHO (World Health Organization), online-d. Avian Influenza A (H5N1) - Australia. Available online: <https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON519#:~:text=On%2017%20May%202024%2C%20the%20case%20on%2018%20May%202024> [Accessed: 7 June 2024]
- WHO (World Health Organization), online-e. Avian Influenza A (H9N2) - India. Available online: <https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON523> [Accessed: 21 June 2024]
- WOAH (World Organisation for Animal Health), online. Canada - Highly Pathogenic Influenza A (other than poultry, including wild birds) (2017-) - Monitoring Report 5. Available online: <https://wahis.woah.org/#/in-review/5065> [Accessed: 27 June 2024]
- Xiao C, Ma W, Sun N, Huang L, Li Y, Zeng Z, Wen Y, Zhang Z, Li H, Li Q, Yu Y, Zheng Y, Liu S, Hu P, Zhang X, Ning Z, Qi W and Liao M, 2016. PB2-588 V promotes the mammalian adaptation of H10N8, H7N9 and H9N2 avian influenza viruses. *Scientific Reports*, 19(6), 19474. doi: 10.1038/srep19474
- Xing X, Shi J, Cui P, Yan C, Zhang Y, Zhang Y, Wang C, Chen Y, Zeng X, Tian G, Liu L, Guan Y, Li C, Suzuki Y, Deng G and Chen H, 2024. Evolution and biological characterization of H5N1 influenza viruses bearing the clade 2.3.2.1 hemagglutinin gene. *Emerging Microbes and Infections*, 13(1). doi: 10.1080/22221751.2023.2284294
- Yamazaki Y, Doy M, Okabe N, Yasui Y, Nakashima K, Fujieda T, Yamato S-I, Kawata Y and Ogata T, 2009. Serological survey of avian H5N2-subtype influenza virus infections in human populations. *Archives of Virology*, 154, 421–427. doi: 10.1007/s00705-009-0319-7
- Yao XY, Lian CY, Lv ZH, Zhang XL and Shao JW, 2023. Emergence of a novel reassortant H5N6 subtype highly pathogenic avian influenza virus in farmed dogs in China. *Journal of Infection*, 87(4), e70–e72. doi: 10.1016/j.jinf.2023.07.013
- Yang ZY, Wei CJ, Kong WP, Wu L, Xu L, Smith DF and Nabel GJ, 2007. Immunization by avian H5 influenza hemagglutinin mutants with altered receptor binding specificity. *Science*, 317(5839), 825–828. doi: 10.1126/science.1135165
- Zhang X, Xu G, Wang C, Jiang M, Gao W, Wang M, Sun H, Sun Y, Chang K-C, Liu J and Pu J, 2017. Enhanced pathogenicity and neurotropism of mouse-adapted H10N7 influenza virus are mediated by novel PB2 and NA mutations. *Journal of General Virology*, 98(6), 1185–1195. doi: 10.1099/jgv.0.000770
- Zhang Y, Shi J, Cui P, Zhang Y, Chen Y, Hou Y, Liu L, Jiang Y, Guan Y, Chen H, Kong H and Deng G, 2023a. Genetic analysis and biological characterization of H10N3 influenza A viruses isolated in China from 2014 to 2021. *Journal of Medical Virology*, 95(2), e28476. doi: 10.1002/jmv.28476
- Zhang J, Wang X, Chen Y, Ye H, Ding S, Zhang T, Liu Y, Li H, Huang L, Qi W and Liao M, 2023b. Mutational antigenic landscape of prevailing H9N2 influenza virus hemagglutinin spectrum. *Cell Reports*, 42(11), 113409. doi: 10.1016/j.celrep.2023.113409
- Zhong G, Le MQ, Lopes TJS, Halfmann P, Hatta M, Fan S, Neumann G and Kawaoka Y, 2018. Mutations in the PA Protein of Avian H5N1 Influenza Viruses Affect Polymerase Activity and Mouse Virulence. *Journal of Virology*, 92(4). doi: 10.1128/JVI.01557-17
- Zhu W, Li X, Dong J, Bo H, Liu J, Yang J, Zhang Y, Wei H, Huang W, Zhao X, Chen T, Yang J, Li Z, Zeng X, Li C, Tang J, Xin L, Gao R, Liu L, Tan M, Shu Y, Yang L and Wang D, 2022. Epidemiologic, Clinical, and Genetic Characteristics of Human Infections with Influenza A(H5N6) Viruses, China. *Emerging Infectious Diseases*, 28(7), 1332–1344. doi: 10.3201/eid2807.212482

## Appendix A – Terms of Reference

### A.1. Background and Terms of Reference as provided by the requestor

Avian influenza is an infectious viral disease in birds, including domestic poultry. Infections with avian influenza viruses in poultry cause two main forms of that disease that are distinguished by their virulence. The low pathogenic (LPAI) form generally only causes mild symptoms, while the highly pathogenic (HPAI) form results in very high mortality rates in most poultry species. That disease may have a severe impact on the profitability of poultry farming.

Avian influenza is mainly found in birds, but under certain circumstances infections can also occur in humans even though the risk is generally very low.

More than a decade ago, it was discovered that virus acquired the capability to be carried by wild birds over long distances. This occurred for the HPAI of the subtype A(H5N1) from South East and Far East Asia to other parts of Asia, Europe and Africa as well as to North America. In the current epidemic the extent of the wild bird involvement in the epidemiology of the disease is exceptional.

The evolution of the HPAI epidemiological situation with high number of birds and new mammalian species affected is prompting response by both animal health and public health authorities in EU Member States and indicates the need for enhanced preparedness and prevention. Given the mammalian adaptation mutations detected in certain circulating viruses, the infection of mammals in fur farms, as well as an outbreak amongst cats extending the animal/human interface along with the suspicion of events of mammal-to-mammal transmission, animal health and public health authorities are currently working on addressing these challenges. In that context, they are developing or adapting their tools for epidemiological investigations, strengthening their collaboration issuing new emergency national legislations as well as adapting their surveillance guidance and programmes in the light of the upcoming seasonal flu season. The situation and actions above have been taken in reaction to:

- ECDC's current risk assessment (ECDC, online) that focuses on the immediate risk of avian influenza for human health fulfilling ECDC's new mandate and the Regulation (EU) 2022/2371<sup>9</sup> aiming to prevent and prepare for cross-border health threats, including epidemics; and
- EFSA's latest scientific opinions and reports (EFSA, online) coupled by measures taken (i.e., surveillance, prevention and control measures) under the Animal Health Law (i.e., Commission Delegated Regulation (EU) 2020/689<sup>10</sup> and Commission Delegated Regulation (EU) 2020/687<sup>11</sup>).

<sup>9</sup> Regulation (EU) 2022/2371 of the European Parliament and of the Council of 23 November 2022 on serious cross-border threats to health and repealing Decision No 1082/2013/EU. OJ L 314, 6.12.2022, p. 26–63.

<sup>10</sup> Commission Delegated Regulation (EU) 2020/689 of 17 December 2019 supplementing Regulation (EU) 2016/429 of the European Parliament and of the Council as regards rules for surveillance, eradication programmes, and disease-free status for certain listed and emerging diseases. OJ L 174, 3.6.2020, p. 211–340.

<sup>11</sup> Commission Delegated Regulation (EU) 2020/687 of 17 December 2019 supplementing Regulation (EU) 2016/429 of the European Parliament and the Council, as regards rules for the prevention and control of certain listed diseases. OJ L 174, 3.6.2020, p. 64–139.

In view of the One Health nature of this subject, and pursuant to Article 3 of Regulation (EU) 2022/2370<sup>12</sup> and Articles 29 and 31 of Regulation (EC) No 178/2002<sup>13</sup>, the European Centre for Disease Prevention and Control (ECDC) and the European Food Safety Authority (EFSA) are requested to carry out the following task:

To provide regular quarterly scientific reports, updating on the avian influenza situation within the Union and worldwide, to the Commission by:

- 1) Analysing the epidemiological data on HPAI and LPAI from Member States and describe the evolution of virus spread from certain regions towards the EU and in case of significant changes in the epidemiology of avian influenza;
- 2) Analysing the temporal and spatial pattern of HPAI and LPAI, as appropriate, in poultry, captive and wild birds, kept and wild mammals, as well the risk factors involved in the occurrence, spread and persistence in the EU of the avian influenza virus in and at the interface of these animal populations with specific attention to zoonotic risks;
- 3) Describing the options for adapting preparedness, prevention, and control measures, based on the finding from point 1) and 2).

## A.2 Interpretation of the Terms of Reference

In reply to the TORs above, this Scientific Report gives an overview of the HPAI virus detections in poultry, captive and wild birds, as well as in mammals, in Europe and worldwide between 16 March and 14 June (24 June for mammals) 2024, as reported by Member States and third countries via ADIS or WOA-H-WAHIS. Also LPAI virus detections of specific relevance are included, and possible actions for preparedness in the EU are discussed based on the situation worldwide. Member States and other European countries where HPAI outbreaks have occurred in poultry submitted additional epidemiological data to EFSA, which have been used to analyse the characteristics of the affected poultry establishments.

It was not possible to collect data for a comprehensive risk factor analysis on the occurrence and persistence of HPAI viruses within the EU. Risk factor analysis requires not only case-related information but also data on the susceptible population (e.g. location of establishments and population structure), which should be collected in a harmonised manner across the EU. Limitations in data collection, reporting and analysis were explained in the first avian influenza overview report (EFSA, ECDC and EURL, 2017).

This report mainly describes information that has become available since the publication of the EFSA report for the period December 2023 to March 2024 (EFSA, ECDC and EURL, 2024a) and that might affect the interpretation of risks related to avian influenza introduction and/or spread in Europe.

<sup>12</sup> Regulation (EU) 2022/2370 of the European Parliament and of the Council of 23 November 2022 amending Regulation (EC) No 853/2004 establishing a European centre for disease prevention and control. OJ L 314, 6.12.2022, p. 1–25.

<sup>13</sup> Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–24.

## Appendix B – Data and Methodologies

### B.1 Data on animals

#### B.1.1 Overview of avian influenza outbreaks in Europe

Data on HPAI outbreaks occurred in Europe between 16 March and 14 June 2024, and submitted by Member States or other European countries via ADIS, were taken into account for this report. Data extraction was carried on 14 June 2024. WOAH-WAHIS was consulted to complement the information for European countries not reporting HPAI notifications to ADIS. In addition, HPAI-affected countries were asked to provide more detailed epidemiological information on HPAI outbreaks occurred in poultry directly to EFSA. This information included details on the poultry species and production systems affected by HPAI, which were supplied in form of additional variables to complement the data reported via ADIS. All details are provided in Annex B. In addition, the information EU countries affected by HPAI and LPAI presented to the Standing Committee on Plants, Animals, Food and Feed (SCOPAFF), and the evidence on HPAI and LPAI outbreaks provided in the info notes from the affected countries to EC, were consulted to extract relevant information that is reported in Section 2.1.1. The presentations delivered at the SCOPAFF meetings are available on the EC website (European Commission, online).

Wild bird species have been categorised according to Table A.2 in Annex A, and the common and scientific names of wild bird species described in this report for Europe are reported in Table A.3 in Annex A. The public GISAID's EpiFlu™ database was accessed to download newly released avian influenza virus sequences.

The annexes to this Scientific Report are available here: <https://www.efsa.europa.eu/sites/default/files/2024-07/Annexes-a-b-c-AI-report.zip>

#### B.1.2 Overview of avian influenza outbreaks in other countries not reporting via ADIS

Data from WOAH-WAHIS on HPAI A(H5) and A(H7) in domestic and wild birds were used to describe and map the geographic distribution of avian influenza virus detections in domestic and wild birds in all regions of the world based on the observation dates. Data were retrieved on 14 June 2024 and extracted by EFSA. They were used and reproduced with permission. WOAH bears no responsibility for the integrity or accuracy of the data contained herein, but not limited to, any deletion, manipulation, or reformatting of data that may have occurred beyond its control.

#### B.1.3 Genetic characterisation of avian influenza viruses: description of the nomenclature of the HPAI A(H5) viruses used in the document

The HA gene of clade 2.3.4.4 A(H5) viruses has rapidly evolved since the most recent official update of the nomenclature of the A/goose/Guangdong/1/1996-lineage H5Nx virus (Smith et al., 2015). This clade emerged in China in 2008 and since then it has acquired various neuraminidase subtypes, including N1, N2, N3, N4, N5, N6 and N8, by reassortments with other avian influenza viruses from different regions, and has evolved into several subgroups. While a revised nomenclature of clade 2.3.4.4 viruses is pending, in previous reports we used the genetic clustering described in 2018 by Lee and co-authors, who recognised four groups (a–d) within clade 2.3.4.4 (Lee et al., 2018). Recently, an update to the unified nomenclature for clade 2.3.4.4 A(H5) viruses has been proposed by the WHO and eight genetic groups (a–h) have been recognised. To align the nomenclature system between international organisations, this classification has been adopted for this

report. Based on this proposed clustering, A(H5) viruses of clades 2.3.4.4a and d–h have mainly been circulating in poultry in Asia, while clades 2.3.4.4b and 2.3.4.4c have spread globally through wild bird migrations during 2014–2015 (2.3.4.4c) and from 2016 to the present day (2.3.4.4b). A list with the distribution of the different genetic clades reported by countries globally from birds, humans and the environment has been published by WHO in February 2023 (WHO, 2023).

## B.2 Data on humans

The number of human cases caused by infection with avian influenza viruses was collected by ECDC. As part of epidemic intelligence activities at ECDC, multiple sources are scanned regularly to collect information on laboratory-confirmed human cases. Data were extracted and line lists developed to collect case-based information on virus type, date of disease onset, country of reporting, country of exposure, sex, age, exposure, clinical information (hospitalisation, severity) and outcome. All cases included in the line list and mentioned in the document have been laboratory-confirmed. Data are continuously checked for double entries and validity. The data on human cases cover the full period since the first human case was reported. Therefore, data on human cases refer to different time periods and are included, irrespective of whether there have been any new human cases during the reporting period. Relevant information on human infections, risk factors, and the results from studies on infection and transmission in mammals with relevance for human health are included. Literature is searched using different search terms for the respective virus subtypes and assessed for relevance before being included.

## **Annex A – Data on Birds**

Annex A is available here: <https://www.efsa.europa.eu/sites/default/files/2024-07/Annexes-a-b-c-AI-report.zip>

## **Annex B – Data on poultry outbreaks**

Annex B is available here: <https://www.efsa.europa.eu/sites/default/files/2024-07/Annexes-a-b-c-AI-report.zip>

## **Annex C – Acknowledgements**

Annex C is available here: <https://www.efsa.europa.eu/sites/default/files/2024-07/Annexes-a-b-c-AI-report.zip>