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# Avian influenza overview December 2022 – March 2023

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## Abstract

Between 3 December 2022 and 1 March 2023 highly pathogenic avian influenza (HPAI) A(H5N1) virus, clade 2.3.4.4b, was reported in Europe in domestic (522) and wild (1,138) birds over 24 countries. An unexpected number of HPAI virus detections in sea birds were observed, mainly in gull species and particularly in black-headed gulls (large mortality events were observed in France, Belgium, the Netherlands, and Italy). The close genetic relationship among viruses collected from black-headed gulls suggests a southward spread of the virus. Moreover, the genetic analyses indicate that the virus persisted in Europe in residential wild birds during and after the summer months. Although the virus retained a preferential binding for avian-like receptors, several mutations associated to increased zoonotic potential were detected. The risk of HPAI virus infection for poultry due to the virus circulating in black-headed gulls and other gull species might increase during the coming months, as breeding bird colonies move inland with possible overlap with poultry production areas. Worldwide, HPAI A(H5N1) virus continued to spread southward in the Americas, from Mexico to southern Chile. The Peruvian pelican was the most frequently reported infected species with thousands of deaths being reported. The reporting of HPAI A(H5N1) in mammals also continued probably linked to feeding on infected wild birds. In Peru, a mass mortality event of sea lions was observed in January and February 2022. Since October 2022, six A(H5N1) detections in humans were reported from Cambodia (a family cluster with 2 people, clade 2.3.2.1c), China (2, clade 2.3.4.4b), Ecuador (1, clade 2.3.4.4b), and Vietnam (1, clade 2.3.4.4b), as well as two A(H5N6) human infections from China. The risk of infection with currently circulating avian H5 influenza viruses of clade 2.3.4.4b in Europe is assessed as low for the general population in the EU/EEA, and low to moderate for occupationally or otherwise exposed people.

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# 1 Background

Since the latest EFSA, ECDC and EURL avian influenza overview report (EFSA et al., 2022) published in December 2022, the epidemiological situation of avian influenza has largely evolved. In Europe, highly pathogenic avian influenza (HPAI) cases continued to be reported in domestic and in wild birds, particularly in gull species; the Eurasian lineage of HPAI A(H5N1) virus introduced in the Americas continued to spread southward affecting poultry, wild bird species and wild mammals being also associated to mass mortality events; additional avian influenza detection were reported in humans, and mutations associated with genetic adaptation to mammals were detected in some of the circulating viruses in mammals and also birds. This evolving situation triggered the European Commission to request EFSA, ECDC and the EURL to issue a targeted overview report on avian influenza considering the new epidemiological and scientific data available.

The aim of this report is to provide technical and scientific assistance to the Commission by providing an overview of HPAI virus detections in birds and mammals as well as human infections due to avian influenza virus that occurred in and outside Europe between 3 December and 1 March 2023.

# 2 Results

## 2.1 HPAI detections in birds

### 2.1.1 HPAI detections in birds in Europe

Figure 1 shows the HPAI outbreaks in birds that were reported in Europe via ADIS or WOAH-WAHIS for the epidemiological years[1] 2016–2017, 2017–2018, 2018–2019, 2019–2020, 2020–2021, 2021–2022 and 2022–2023 by month of suspicion. For the current epidemiological year 2022–2023 that starts on 1 October 2022, data reported are truncated on 1 March 2023.

The HPAI epidemic observed in the 2021–2022 epidemiological year was so far the largest observed in Europe, with a total of 6,615 HPAI virus detections in 37 countries. Unexpectedly, the epidemic continued along the summer months with an extensive spread of the virus to colony-breeding seabirds, a group of species that were very rarely reported as HPAI affected before (Figure 4). In July and August 2022, the HPAI virus detections in wild birds predominantly affected the order of Suliformes (primarily northern gannets) and were reported along the coasts, whereas from September to December 2022 waterfowl replaced colony-breeding seabirds as the main wild birds in which most HPAI virus detection was reported (Figure 4). As a result, there was not a clear start of the HPAI epidemic season in October in the epidemiological year 2022–2023, neither in wild nor in domestic birds due to the persistence of the virus in wild birds (Figure 1). In the epidemiological years 2022-2023 up to 1 March 2023, a total of 2,701 HPAI virus detections were reported, 1,649 in wild birds and 1,052 in domestic birds over 28 European countries (Table A.7).

Considering the current reporting period, from 3 December 2022 to 1 March 2023, 1,660 HPAI virus detections were reported in poultry (403), captive (119) and wild birds (1,138) (Figure 2, Table A.7).

HPAI outbreaks in poultry were reported in France (191), Poland (88), Hungary (31), Czechia (26), Germany (20), United Kingdom (19), Belgium (6), Austria (3), Denmark (3), the Netherlands (3), Romania (3), Slovakia (3), Italy (2), Spain (2), Bulgaria (1), Moldova (1), Slovenia (1) (Figure 2, Table B1). Out of those 403 outbreaks, 78 were reported to be secondary outbreaks in France (33/191), Hungary (27/31), Poland (14/88), Romania (2/3), Belgium (1/6), Czechia (1/26). In the current reporting period, the number of poultry outbreaks

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[1] In this document an 'epidemiological year' refers to the period starting on week 40 (the beginning of October) and ending on 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.

continued to decrease from its higher point in November 2022 (Figure 3). Poultry outbreaks in France concentrated in Pays-de-la- Loire during the first half of the reporting period (124/191) and occurred primarily in domestic duck. With the exception of Hungary, most outbreaks have not been attributed to secondary spread. The most likely source of infection reported by countries seems to be indirect contact with wild birds or unknown. The information on the poultry species affected in the outbreaks were collected too close to the publication of the presents report, therefore these aspects will be analysed and fully described in the following EFSA, ECDC, EURL scientific report.

HPAI detections in captive birds were reported in Germany (52), France (27), United Kingdom (15), Belgium (11), Austria (4), the Netherlands (4), Hungary (1), Luxemburg (1), Poland (1), Slovakia (1), Slovenia (1) and Sweden (1) (Figure 2, Table B1). Out of those 119 outbreaks in captive birds 28 were reported as secondary outbreaks in Germany (27) and France (1).

During this reporting period, the vast majority of the wild bird detections were reported in sea birds, particularly in Laridae species, with the black-headed gull being the most affected gull species, followed by the herring gull (Figure 4).

In the period 3 December 2022 to 1 March 2023, there was a peak of HPAI virus detections in wild birds and poultry in January 2023 that was about one-third lower than that in January 2022, but slightly higher than in January 2021 (Figure 1). On wild birds, the number of HPAI virus detections in wild birds in the January 2023 peak was similar to that in January 2022 with an important difference: in the January 2023 peak, nearly all the wild birds were in the category 'colony-breeding seabirds', compared to mainly waterbirds in the January 2022 peak (Figure 4a). Within the category 'colony-breeding seabirds', nearly all wild birds found infected in January 2023 belonged to the family Laridae (gulls, terns and skimmers) and were predominantly black-headed gulls (*Chroicocephalus ridibundus* or *Larus ridibundus*), with fewer European herring gulls (*Larus argentatus*) (Figure 4b and 4c). The complete list of wild bird species found as HPAI virus infected from 3 December 2022 to 1 March 2023 is reported in Figure A.1 in Annex A. In January 2023, the weekly reported HPAI virus detections in black-headed gulls ranged from 14 to 50, which is substantially higher than that in the period October 2020 to December 2022 (1 to 8) (Figure 4c).

Those HPAI virus detections concentrated inland in Belgium, France, the Netherlands, Germany, Austria, Italy, northern Spain and increased from the end of January 2023 (Figures 5 and 6). The geographical distribution of HPAI virus detections between wild bird categories differed in this period. HPAI virus detections in waterbirds (mainly swans, geese, and mallards) were reported mainly from northern and eastern Europe, and those in seabirds (mainly black-headed gulls) mainly from southern and western Europe (Figures 5 and 6). It remains to be seen whether this pattern will change as black-headed gulls move north during spring migration and return to their breeding colony sites.

During this reporting period, mortality events affecting different wild bird species, particularly gull species, were observed in several countries. In France, during January 2023, increased mortality of wild birds was reported in the Île-de-France and Centre-Val-de-Loire regions around Paris: close to Chartres (Eure-et-Loir), 150 carcasses of gulls were found on a pontoon of a private pond (Franceinfo, online). Several other hotspots of abnormal black-headed gull mortality were also reported, accounting for over 1,900 dead birds in Essonne and Seine-et-Marne (close to Paris) during January and early February 2023, more than 100 dead birds in Moselle and Meurthe-et-Moselle (eastern France, close to Luxembourg and Germany) during the last week of January 2023, and around 50 dead birds in Maine-et-Loire (western France) in February 2023. Carcasses of a few bird-eating raptors, subsequently confirmed as being infected with A(H5N1) HPAI virus, were also found in some of these hotspots (Personal communication: LoÎc Palumbo and Anne van de Wiele, Office Français de la Biodiversité). In Belgium, in the second half of February 2023, increased numbers of carcasses of black-headed gulls, that had died from HPAI, were found washed ashore along the river Meuse in the province of Limburg, Belgium (nws, online). In the Netherlands, on 12 February 2023, a wild bird rehabilitation centre in Rotterdam reported increased numbers of black-headed gulls with neurological signs in the area, confirmed to be due to HPAI in recent weeks (Vogelklas, online). On 20 February, 30 dead black-headed gulls were found dead due to HPAI in a grassland area managed for meadowbirds 'Landje van Geijsel' bij Ouderkerk, the Netherlands (Trouw, online). On 3 March, 33 dead black-headed gulls were reported from a roosting site in Veenoordskolk, Deventer municipality, the Netherlands[2]. On 3 March, Dutch animal ambulance personnel reported high numbers of dead and sick black-headed gulls, including with neurological signs, in the areas around Weert, Den Bosch, Schaijk, Eindhoven, and Eersel[3] In northern Italy, mainly in the area of the Garda lake, an unprecedented increase in mortality in black-headed gulls was observed in the first months of 2023. Hundreds of animals were found dead or seriously ill (Brescia oggi, online). The exact number of gulls involved in these events is not known because in many cases the carcasses were eliminated by the competent authorities without being counted and/or sent to diagnostic laboratories. The characterised viruses from more than 50 birds tested since the beginning of February were all closely related and belong to the clade 2.3.4.4b, genotype H5N1-A/Herring_gull/France/22P015977/2022-like. Events of mortality in gulls was also reported in Switzerland, Diagnostic tests on these samples are ongoing.

Additional data available for the Netherlands from AI-Impact, DWHC, SOVON, and waarneming.nl on gull mortality observed monthly from December to February in the epidemiological years 2021-2022 and 2022-2023 reported a markable increase in the mortality of black headed gulls in February 2023 compared to the previous year (Table A.1).

The black-headed gull breeds across Europe and Asia between the latitudes of about 40 and 70 degrees north, with small breeding populations in Iceland, Greenland and the east coast of North America. Within this breeding range, northern populations are migratory, and populations further south are partially migratory, with a wintering range extending to Africa and southern Asia up to about the equator, mainly along the coast. The global population of black-headed gulls is about 2 to 3 million breeding pairs.

The European wintering population of black-headed gulls is over 4 million birds. Inland wintering, associated with human activities, has increased since 1960. Spring migration in Central Europe starts in early February and peaks in late March-early April for adults, with less pronounced migration of first-year birds into mid-May. Breeding sites are occupied in March. There are often large flocks in areas around breeding sites before re-occupation. Departure from breeding sites starts from early July, with dispersal of first-year birds in different directions. Autumn migration in Europe starts around late May and extends to early January, depending on latitude and age category (in sequence of timing: immatures, non-breeding adults, breeding adults and juveniles).

Black-headed gulls breed in dense colonies often of several thousands, but rarely >10,000 pairs, mostly in lakes surrounded by reedbeds with small islands; also coastal sand islands, bogs, and artificial ponds. In Europe, black-headed gulls breed in most countries, with higher numbers in the north. Historical capture-recapture data from ringing activities from EURING[4] and real time bird distribution data by EuroBird Portal[5] on the expected movements of black gulls in the coming weeks/months indicate a general east and north east movement from places where the H5N1 virus has been detected in this species (France, Belgium, the Netherlands, Italy), with large numbers still being observed particularly in Belgium and the Netherlands in the next months (Tables A.2 – A.5). Those data can be consulted in the Migration Mapping Tool developed by EFSA, EURING, Euro Bird Portal available online[6].

Although categorized under 'colony-breeding seabirds' in EFSA reports, black-headed gulls occur both along sea coasts and inland. They feed in open areas such as farmland and towns,

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[2] https://twitter.com/ErikMensonides/status/1631640351550107648?s=20

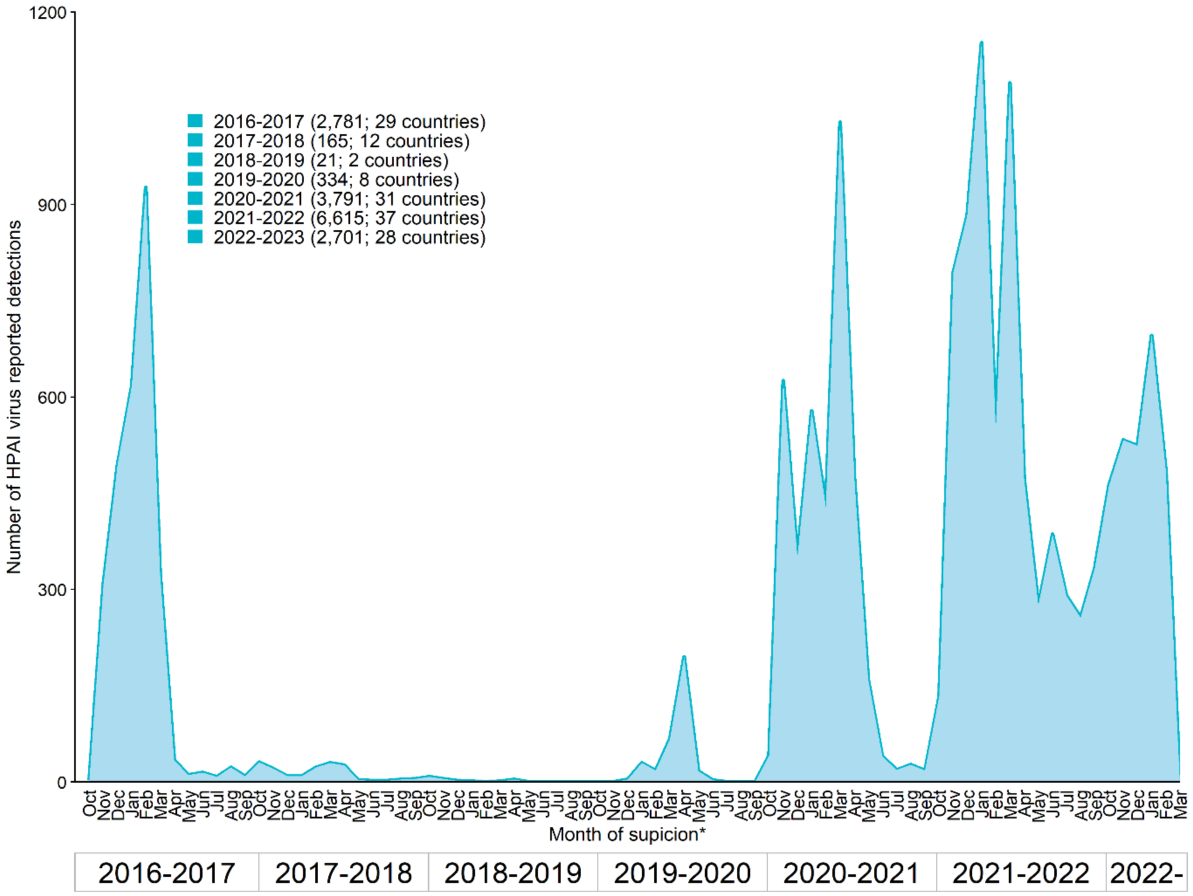
[3] https://twitter.com/MariskaKolk/status/1631734895557898240?s=20

[4] https://euring.org/data-and-codes/euring-databank

[5] https://eurobirdportal.org/ebp/en/#home/HIRRUS/r52weeks/CUCCAN/r52weeks/

[6] https://euring.org/research/migration-mapping

and are abundant near human settlements. In towns and garbage dumps they feed on refuse, and elsewhere on crabs, fish, earthworms and insects.



*When the date of suspicion is not available then the date of confirmation is used to assign the week of suspicion. United Kingdom data are from ADNS up to 31 December 2020. From 1 January 2021 onwards, the data source was the World Animal Health Information System (WOAH-WAHIS) for United Kingdom (excluding Northern Ireland), and ADNS/ADIS for the United Kingdom (Northern Ireland)[7].
Source: ADIS and WOAH (data extraction carried out on 1 March 2023).

**Figure 1:** Distribution of the number of HPAI virus detections in domestic and wild birds reported in Europe in the epidemiological years 2016–2017, 2017–2018, 2018–2019, 2019–2020, 2020–2021, and 2021-2022 by month of suspicion, from 1 October 2016 to 10 March 2023 (16,408)

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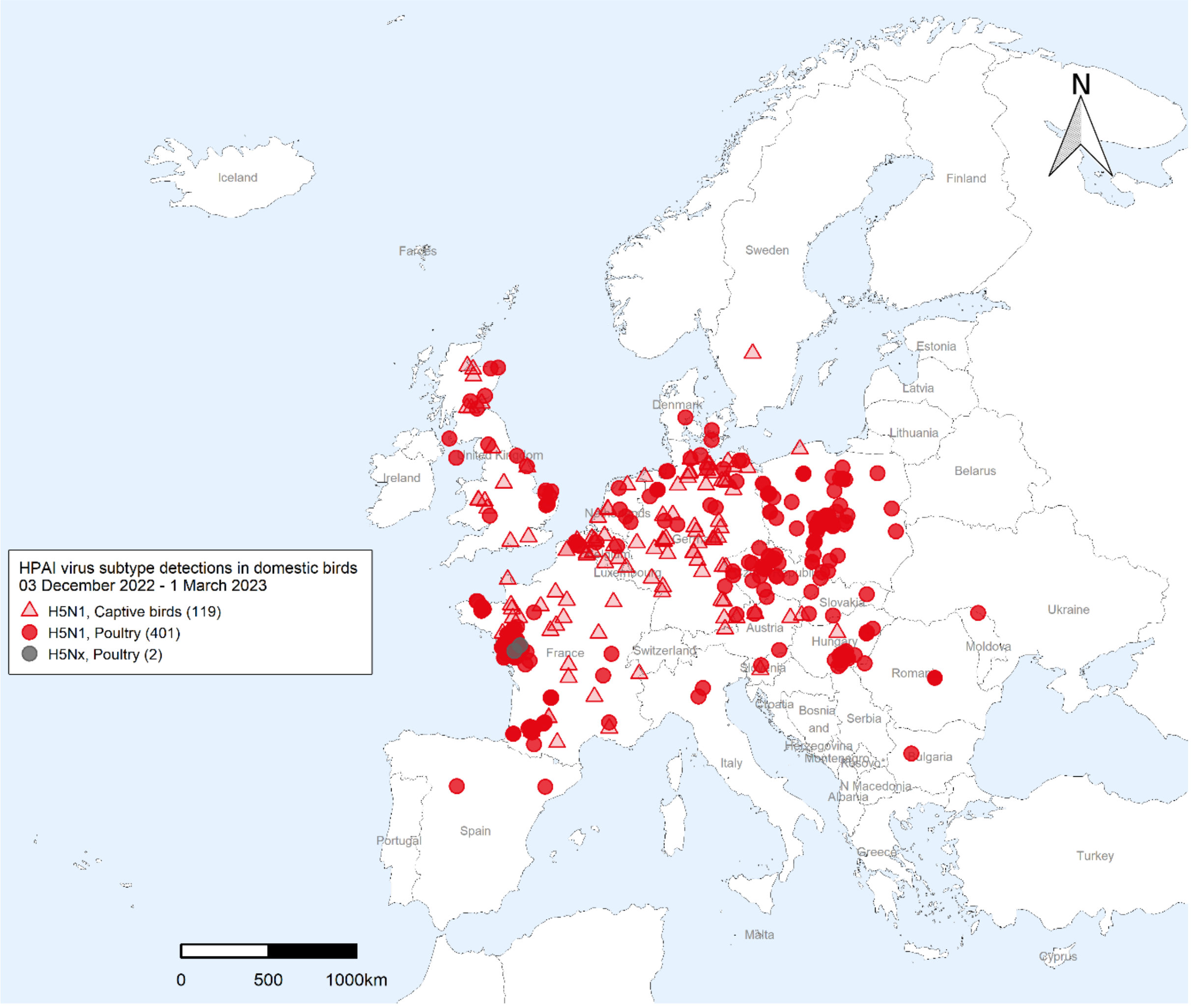
[7] In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and in particular with the Protocol on IE/NI, the EU requirements on data sampling are also applicable to the United Kingdom (Northern Ireland).



Author: EFSA
Data sources: ADIS, WOAH
Date updated: 01/03/2023

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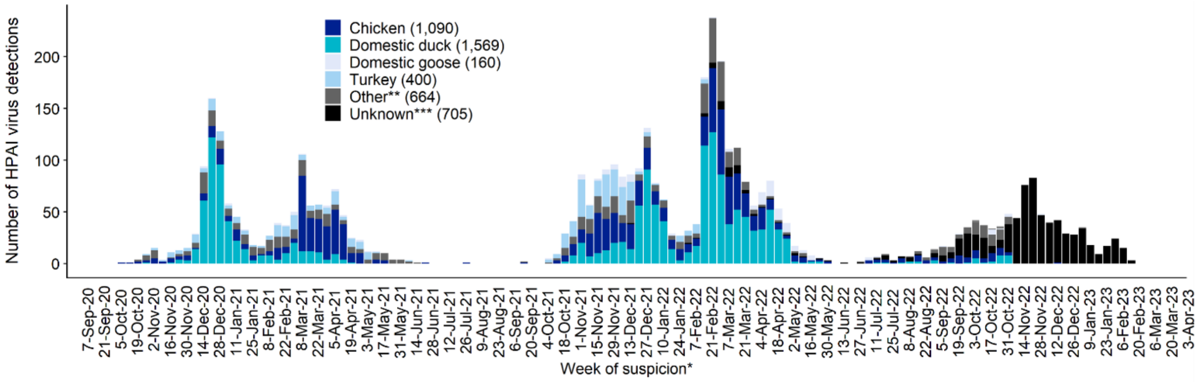
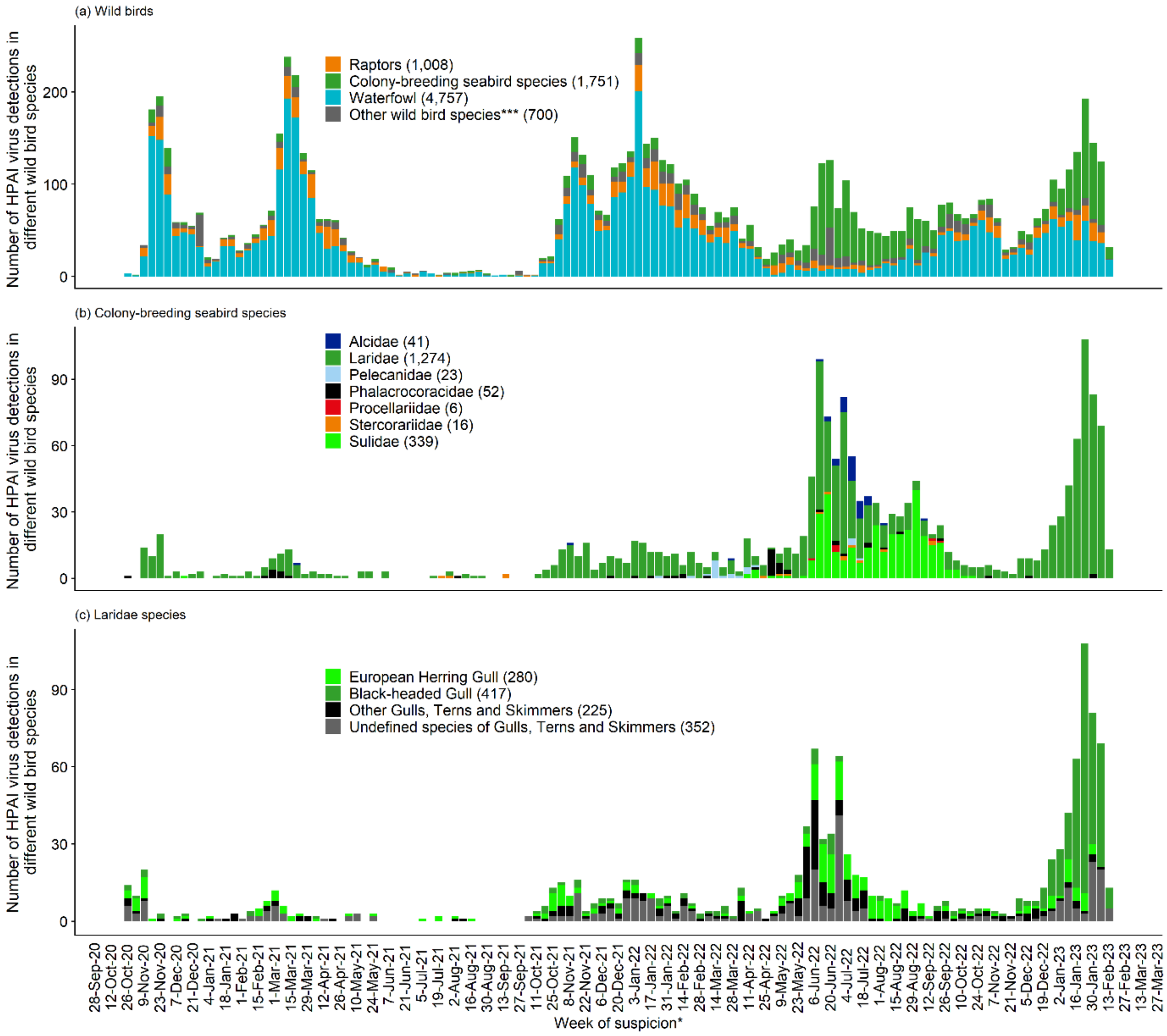
* This designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244 and the International Court of Justice Opinion on the Kosovo Declaration of Independence.
United Kingdom data are from ADNS up to 31 December 2020. From 1 January 2021 onwards, the data source was the World Animal Health Information System (WOAH-WAHIS) for United Kingdom (excluding Northern Ireland), and ADNS/ADIS for United Kingdom (Northern Ireland)[7].
Source: EFSA, ADIS and WOAH (data extraction carried out on 1 March 2023).

**Figure 2:** Geographical distribution, based on available geocoordinates, of highly pathogenic avian influenza virus outbreaks in poultry and captive birds (522) reported by virus subtype in Europe from 3 December 2022 to 1 March 2023



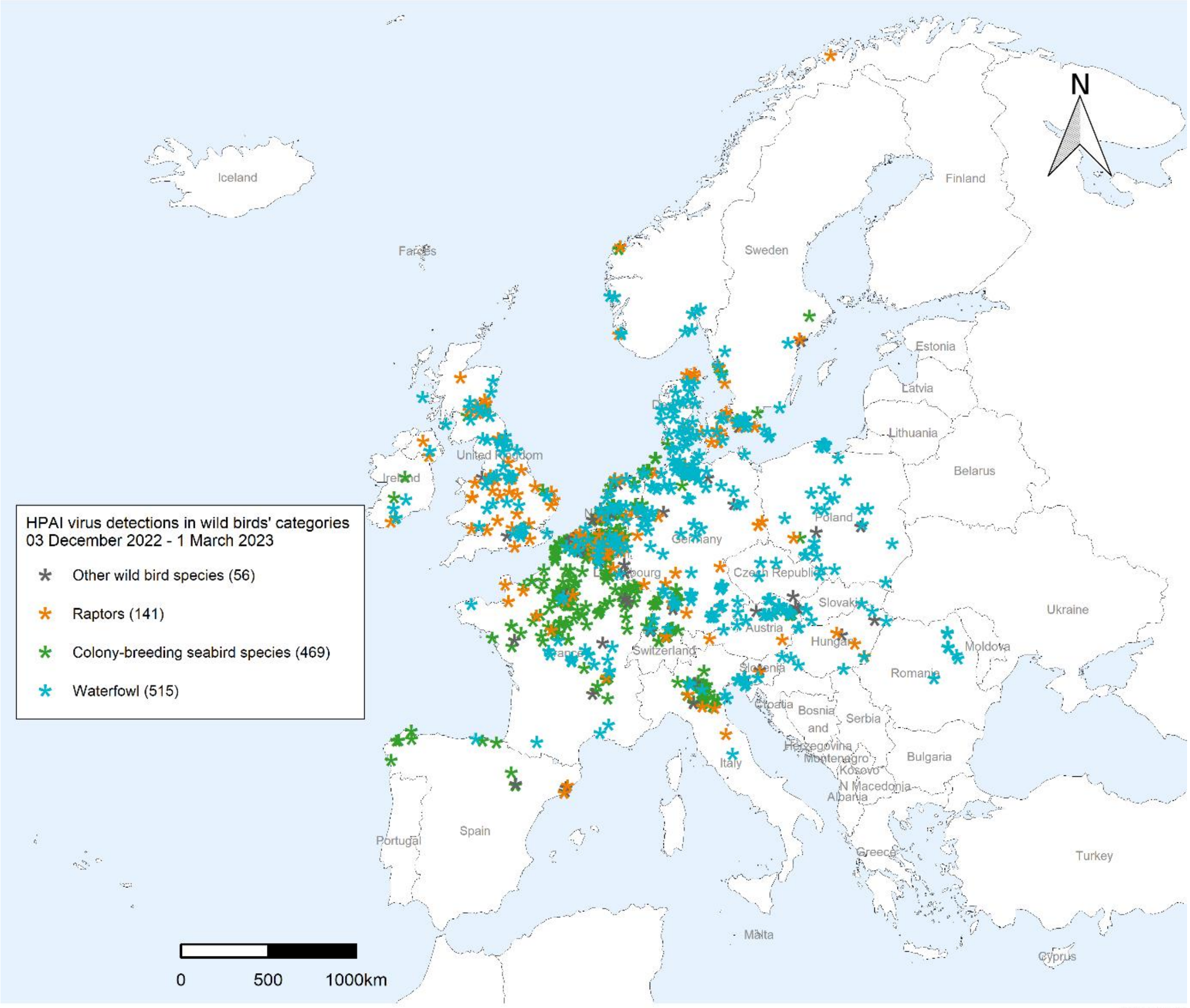
United Kingdom data are from ADNS up to 31 December 2020. From 1 January 2021 onwards, the data source was the World Animal Health Information System (WOAH-WAHIS) for United Kingdom (excluding Northern Ireland), and ADNS/ADIS for the United Kingdom (Northern Ireland)[7].
Source: EFSA, ADIS and WOAH (data extraction carried out on 1 March 2023).
* When the date of suspicion is not available then the date of confirmation is used to assign the week of suspicion.
** ‘Other’ groups all other affected countries that are not indicated in the legend
*** The information on poultry species affected from middle of November 2022 were collected too close to the publication of this report to be here analysed and reported; therefore, it will be fully described in the next EFSA, ECDC, EURL scientific report.

**Figure 3:** Distribution of the highly pathogenic avian influenza virus detections in poultry (522) in Europe by week of suspicion, from October 2020 to 1 March 2023



*When the date of suspicion is not available then the date of confirmation is used to assign the week of suspicion.
**'Other wild species' category contains unknown bird species, or categories different from those displayed. The complete list of species by each wild bird category is reported in Table A.8 in Annex A.
United Kingdom data are from ADNS up to 31 December 2020. From 1 January 2021 onwards, the data source was the World Animal Health Information System (WOAH-WAHIS) for United Kingdom (excluding Northern Ireland), and ADNS/ADIS for the United Kingdom (Northern Ireland)[7].
Source: ADNS, ADIS and WOAH (data extraction carried out on 1 March 2023), EFSA.
Note that the scale of the vertical axes is specific to each category and that the unit reported is the number of HPAI detections in different wild bird species and not the number of HPAI detections in wild birds (as more than one species can be involved in one single HPAI reported detection).

**Figure 4:** Distribution of total number of HPAI virus detections reported in Europe by week of suspicion (dates indicate the first day of the week) and (a) affected wild bird categories (8,216), (b) affected colony-breeding seabird families (1,751), (c) affected Laridae species (1,274), from October 2020 to 1 March 2023



Author: EFSA
Data sources: ADIS, WOAH
Date updated: 01/03/2023

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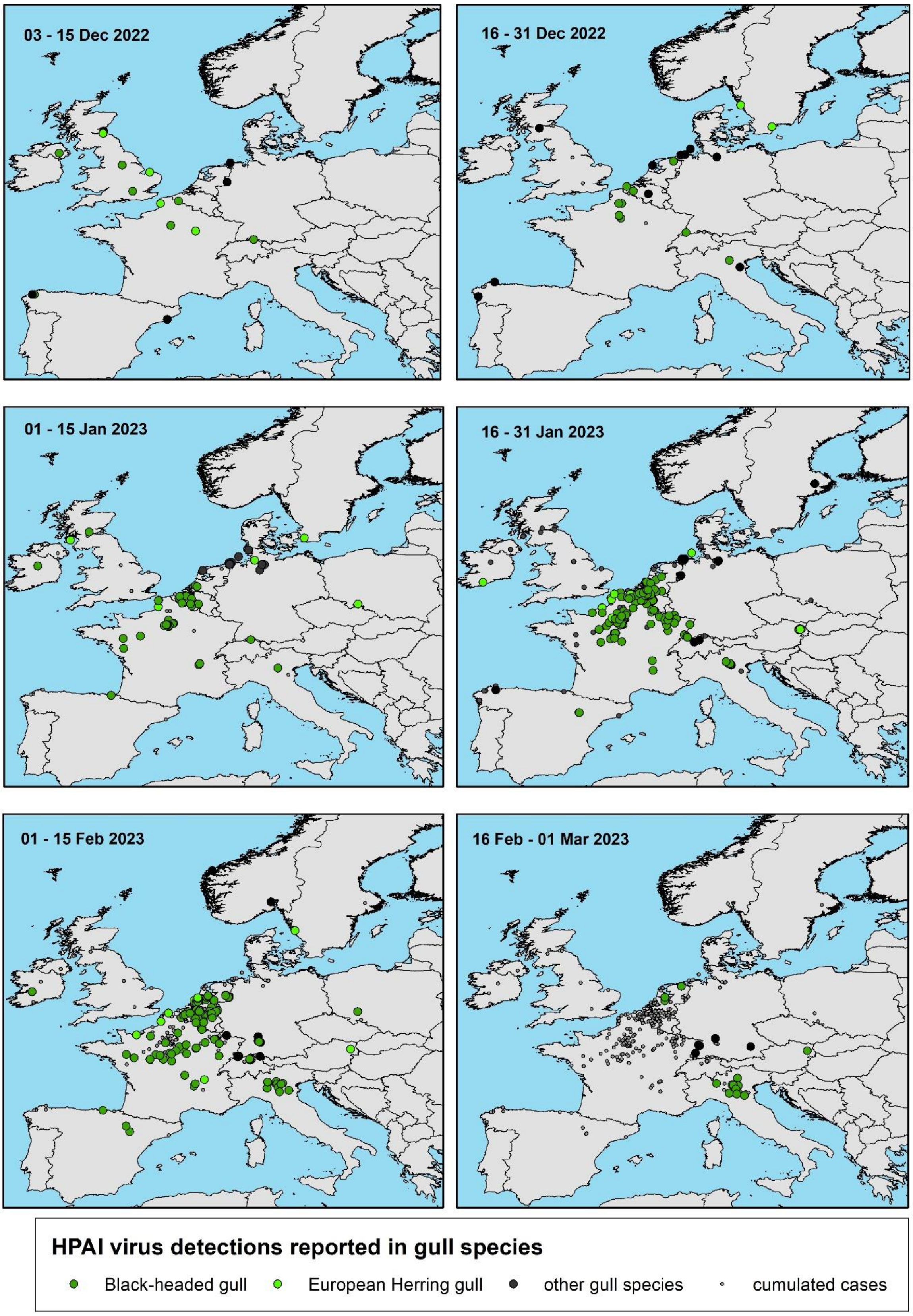
Source: EFSA, ADIS and WOAH (data extraction carried out on 1 March 2023). Note that in one single detection more than one wild bird species might be involved and each wild bird categories detected as HPAI infected is presented in the map.

**Figure 5:** Geographical distribution, based on available geocoordinates, of highly pathogenic avian influenza detections in wild birds’ categories in Europe, by species category, from 3 December 2022 to 1 March 2023



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Source: ADIS and WOAH (data extraction carried out on 1 March 2023). Note that in one single detection more than one wild bird species might be involved and each wild bird categories detected as HPAI infected is presented in the map

**Figure 6:** Geographical distribution, based on available geocoordinates, of highly pathogenic avian influenza detections in gull species in Europe at bi-weekly intervals, from 3 December 2022 to 1 March 2023

### 2.1.2 The avian influenza situation in other countries not reporting via ADIS, 3 December 2022 to 1 March 2023

An overview of the HPAI virus detections in birds notified from other countries not reporting via ADIS but via the WOAH from 3 December 2022 to 1 March 2023 is presented in Table 1 and Figure 7. Please note that the actual situation in South America is continuing evolving with new HPAI virus detections in wild, domestic birds and mammal species being reported to the public via different means, e.g. this is the case of more poultry outbreaks than those displayed in Table 1 reported by Argentina on 6 March 2023 (SENASA, 2023). However, in the tables and figures of the current report only the data extracted from WOAH on 1 March are presented; information available from other sources has not been systematically retrieved and is only described in the text.

Since its introduction in Central/South America in October 2022, HPAI A(H5N1) rapidly spread across South America. Worldwide, HPAI A(H5) virus continued to be detected in poultry during the current reporting period with a comparable level of reported outbreaks as in the previous reporting period from 10 September to 2 December 2022 (EFSA et al., 2022b). The number of notifications increased in Asia by approximately four times (55 vs 195) and three more countries (Kazakhstan, Nepal, Philippines and Turkey) have been reporting outbreaks to WOAH. Canada and the USA reported the vast majority of outbreaks from the Americas, with the reported number of outbreaks slightly more than halved compared to the previous reporting period. However, HPAI A(H5N1) virus has continued to spread in Central and South America, doubling the number of countries affected since the last report (6 vs 13). Since 3 December 2022, HPAI A(H5) virus has also been detected on poultry farms of different sizes in Argentina, Bolivia, Chile, Costa Rica, Honduras, Panama, Peru and Uruguay; Cuba reported an HPAI virus outbreak in a zoo

The list of wild bird species that have been reported to WOAH WAHIS as HPAI infected from South America since 3 December 2022 is presented in Table A.6. Additional information about HPAI virus detections in wild birds, not reported in WAHIS, was retrieved from different media sources and is reported below.

In Central America (Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica, Panama), mortality of brown pelicans (*Pelecanus occidentalis*) was reported in association with HPAI A(H5N1) virus detections in Panama (25 December, 1 dead), Honduras (5 January, 41 dead), Costa Rica (25 January, 3 dead, as well as 1 peregrine falcon), and Guatemala (14 February, unknown number). On 7 February, HPAI A(H5N1) also was reported in captive wild birds belonging to the Zoological Garden of Havana, Cuba.

Along the Pacific coast of South America (Colombia, Ecuador, Peru, Chile), corresponding to the Pacific Americas flyway and partially separated from the rest of South America by the physical barrier of the Andes Mountains, there was extensive mortality of wild birds and wild mammals associated to HPAI A(H5N1) virus detections in the reporting period. The first report was a mortality event of 200 Peruvian pelicans (*Pelecanus thagus*) in Peru due to HPAI A(H5N1) on 10 November 2022. The infection spread rapidly, and by the end of 2022 over 50,000 seabirds along the coast of Peru were reported dead, including 16,890 Peruvian pelicans (endangered in Peru), 4,324 brown boobies (*Sula leucogaster*) (endangered in Peru), 630 blue-footed boobies (*Sula nebouxii*), 168 guanay cormorants (*Leucocarbo bougainvillii*) (near threatened in Peru) (Gamarra-Toledo et al., 2023). In addition, the virus spread to marine mammals in Peru, with 634 South American sea lions (*Otaria flavescens*), 4 South American fur seals (*Arctocephalus australis*) and a dolphin (*Tursiops truncates*) according to Gamarra-Toledo et al. (2023) or *Delphinus delphis* according to Leguia et al. (2023) reported dead on Peruvian coasts during January and the first days of February 2023 in association to HPAI A(H5N1) virus detections (Gamarra-Toledo et al., 2023). On 4 March, the agriculture ministry reported at least 3,487 South American sea lions had been found dead in Peru in association with the HPAI A(H5N1) outbreak. This represents about 3.3% of the total population in the country[8].

Southwards from Peru, HPAI A(H5N1) virus was first reported in Peruvian pelicans in the administrative regions of Tarapacá and Antofagasta, northern Chile at a latitude of about 20 degrees South, on 8 December 2022. By 13 February 2023, it had reached southwards to Ancud in Los Lagos, the third southernmost administrative region of Chile at about 42 degrees South, where HPAI A(H5N1) was detected in a kelp gull (*Larus dominicanus*). By 1 January 2023, 3,247 wild seabirds killed by the virus between Arica and Valparaíso had been buried, but the actual mortality was undoubtedly many times higher. The virus was detected in many wild bird species in Chile (Table A.6); those with high mortality included Peruvian pelicans, kelp gulls, Belcher's gulls (*Larus belcheri*), gray gulls (*Leucophaeus modestus*), guanay cormorants, Peruvian boobies, elegant terns (*Thalasseus elegans*), and turkey vultures (*Cathartes aura*). In addition, HPAI A(H5N1) virus was detected in two South American sea lions along the Chilean coast, both in the administrative region Antofagasta. On 7 March, a marine otter (*Lontra felina*) in Arica, Chile, was reported infected with HPAI (H5N1) virus (El Diario de la Araicania, online).On the east side of the Andes Mountains (Ecuador, Colombia, Venezuela, Guyana, Surinam, French Guiana, Brazil, Bolivia, Paraguay, Uruguay, Argentina), there was far less mortality of wild birds compared to the west side, and none of wild mammals, reported in the period 3 December 2022 to 1 March 2023. The highest reported wildlife mortality was a die-off of 172 Peruvian pelicans from HPAI A(H5N1) on the coast of Venezuela, reported on 10 December 2022. This location corresponds both with the Mississippi and the Atlantic Americas Flyways.

Although HPAI A(H5N1) virus in poultry was reported in Colombia, there were no reported detections in wild birds. HPAI A(H5N1) virus was reported in blue-and-white swallow (*Pygochelidon cyanoleuca*) in Bolivia (nearby an affected poultry farm), and in 5 black-necked swans (*Cygnus melancoryphus*) on the coast of Uruguay on 16 February 2023. The black-necked swan is resident in Argentina, Brazil, Chile, Uruguay, and the Falkland Islands, not a migratory species from further north. Therefore, the black-necked swan cases in coastal Uruguay suggest that HPAI A(H5N1) virus may have spread south with wild bird migration along the Atlantic Americas Flyway.

HPAI A(H5N1) virus was reported in Andean geese (*Chloephaga melanoptera*) in Jujuy, Argentina, on 16 February 2023, and in a red-gartered coot (*Fulica armillata*) in Neuquén, Argentina, on 22 February 2023. At a latitude of about 40 degrees South, this is the furthest south that HPAI A(H5N1) virus detection has been reported east of the Andes Mountains. Since both Jujuy and Neuquén are located on the eastern slope of the Andean Mountains, bordering Chile, it cannot be excluded that virus incursion came across the mountains from Chile, where the virus already was present.

There were very few HPAI virus detections reported from African countries (e.g. Egypt) and China to WOAH WAHIS, although some HPAI viral sequences from birds have been deposited in GISAID. The very scarce information available raise uncertainty about possible circulation of HPAI virus in those areas.

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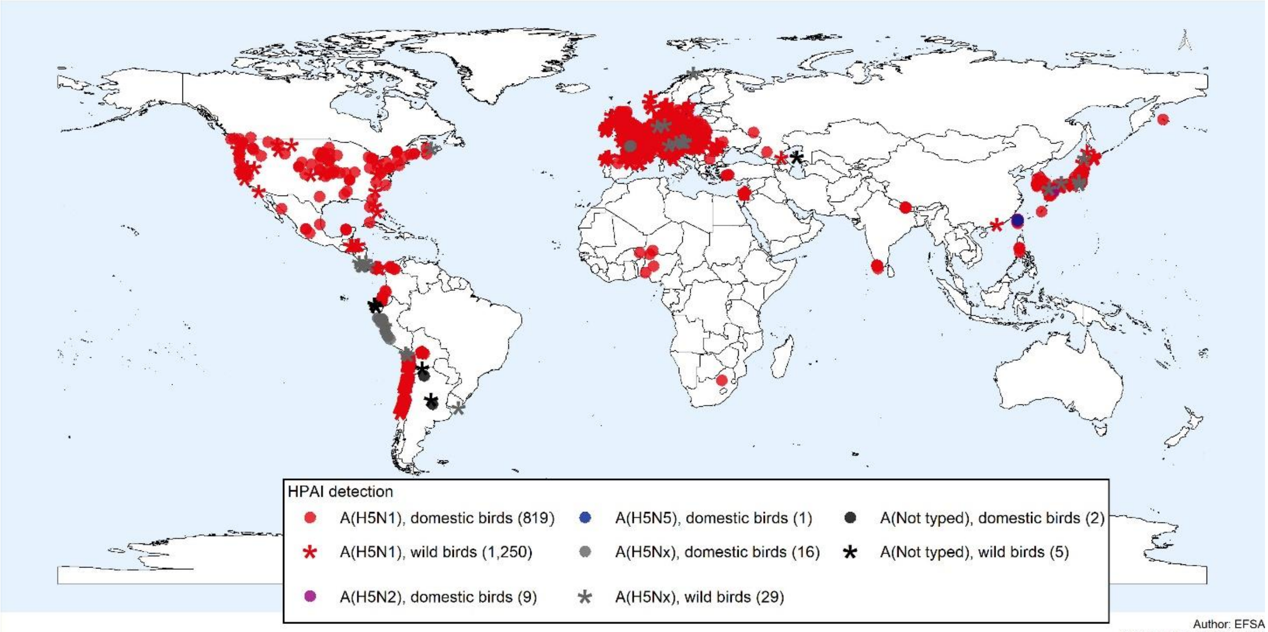
[8] https://twitter.com/BNOFeed/status/1631491427413680128

**Table 1:** Number of HPAI virus detections in non-European countries, by virus subtype and country, from 3 December to 1 March 2023

| Region | Country | Domestic birds | | | | | Wild birds | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | | A(H5N1) | A(H5N2) | A(H5N5) | A(H5Nx) | A(Not typed) | A(H5N1) | A(H5Nx) | A(Not typed) | |
| Africa (6) | Niger | 2 | | | | | | | | **2** |
| | Nigeria | 3 | | | | | | | | **3** |
| | South Africa | 1 | | | | | | | | **1** |
| Americas (265) | Argentina | | | | | 2 | | | 2 | **4** |
| | Bolivia | 15 | | | | | 1 | | | **16** |
| | Canada | 17 | | | | | | 1 | | **18** |
| | Chile | 1 | | | | | 53 | | | **54** |
| | Colombia | 9 | | | | | | | | **9** |
| | Costa Rica | | | | 1 | | | 5 | | **6** |
| | Cuba | 1 | | | | | | | | **1** |
| | Ecuador | 13 | | | | | | | 2 | **15** |
| | Guatemala | | | | | | 1 | | | **1** |
| | Honduras | | | | | | 3 | | | **3** |
| | Mexico | 8 | | | | | | | | **8** |
| | Panama | 2 | | | | | 5 | | | **7** |
| | Peru | | | | 13 | | | 3 | | **16** |
| | United States of America | 89 | | | | | 17 | | | **106** |
| | Uruguay | | | | | | | 1 | | **1** |
| Asia (195) | Taiwan | 26 | 8 | 1 | | | | | | **35** |
| | Hong Kong | | | | | | 1 | | | **1** |
| | India | 10 | | | | | | | | **10** |
| | Israel | 9 | | | | | 2 | | | **11** |
| | Japan | 52 | 1 | | | | 39 | 8 | | **100** |
| | Kazakhstan | | | | | | | | 1 | **1** |
| | Korea | 25 | | | | | | | | **25** |
| | Nepal | 7 | | | | | | | | **7** |
| | Philippines | 3 | | | | | | | | **3** |
| | Turkey | 2 | | | | | | | | **2** |
| Europe (5) | Russia | 4 | | | | | 1 | | | **5** |
| **Total** | | **299** | **9** | **1** | **14** | **2** | **123** | **18** | **5** | **471** |

Source: WOAH-WAHIS (data extraction carried out on 1 March 2023).



Author: EFSA
Data sources: ADIS, WOAH
Date updated: 01/03/2023

Disclaimer: The designations employed and the presentation of material on this map 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.

**Figure 7:** Geographical distribution, based on available geocoordinates, of highly pathogenic avian influenza virus detections reported in domestic birds (847) and wild birds (1,284) by virus type, from 3 December 2022 to 1 March 2023

## 2.2 HPAI detections in mammals

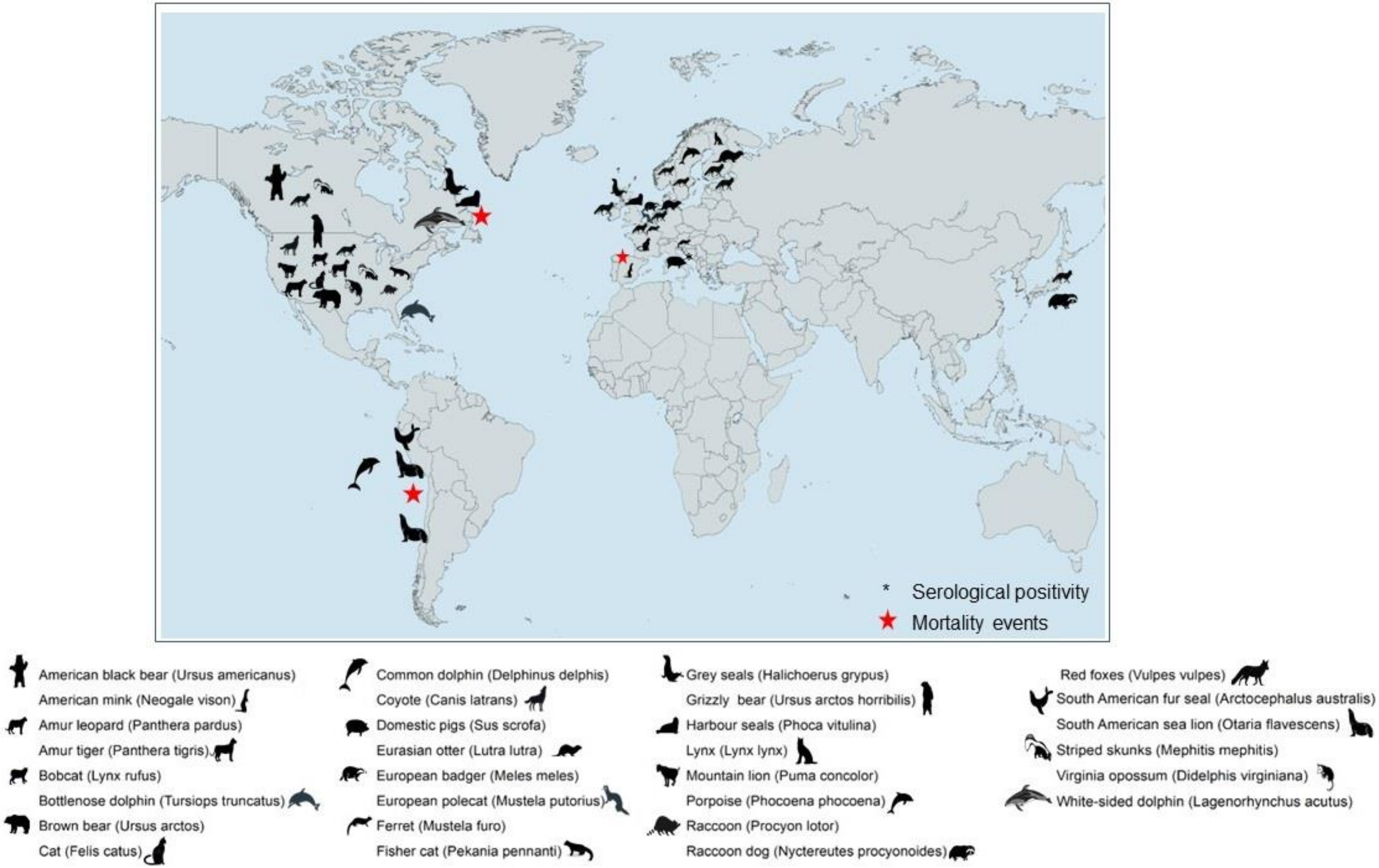
During the period from 3 December 2022 to 1 March 2023, HPAI A(H5N1) viruses were reported in several mammal species in Europe and Americas: in cats and red foxes in France and the USA, in ferrets in Belgium, in lynx, skunk, raccoon, mountain lion, brown bear and American black bear in USA and in sea lions in Peru and in Chile (Table 2).

The geographical distribution of HPAI A(H5) viruses, clade 2.3.4.4b, that have been reported since October 2020 are presented in Figure 8. These reports involve 24 species of carnivores, 4 species of cetaceans, as well as domestic pigs and wild boar (artiodactyls) and Virginia opossums (marsupials). The mammal species involved are mainly those that hunt wild birds, feed on dead wild birds, or both. The species in which HPAI A(H5N1) virus was reported most frequently is the red fox, which lives all across Europe, north Africa, most of Asia apart from the extreme southeast, and North America except southwest USA and Mexico (GBIF, online; IUCN, online). The frequent detection of HPAI A(H5N1) virus in red foxes is likely a consequence of its wide distribution, which largely overlaps the geographical spread of the HPAI A(H5N1) outbreaks, and its diet, which partly includes both hunted and scavenged wild birds.

While most of the reports of HPAI (H5N1) virus in mammals consist of single or at most a few animals, there were three mass mortality events of mammals associated with HPAI A(H5N1) virus detections in 2022 (USA and Spain) and 2023 (Peru) and possible mammal-to-mammal transmission (Figure 8). The first was an unusual mortality event of seals, including harbour seals, on the coast of Maine, USA, in the summer of 2022, which coincided with an outbreak of HPAI A(H5N1) virus in wild birds in the region (Puryear et al., 2022). The majority of stranded seals were found dead. Of those that stranded live, symptoms included respiratory signs with a subset of neurologic cases. Of the seals examined between 21 June and 13 July, a total of 15 of 25 harbour seals and 2 of 4 grey seals tested positive for HPAI A(H5N1) virus (details of genetics in section 2.3.3). The source of the virus was likely infected wild birds. However, the authors of the preprint report considered it unlikely that multiple seals acquired virus through predation or scavenging of an infected source, as birds are not a typical food source for harbour or grey seals. Instead, transmission likely occurred through either environmental transmission or direct contact between seals, though the data did not allow to distinguish between these two possible routes.

The second involved a farm of 52,000 American minks, housed in 30 partially open barns in Galícia, northwest Spain (Aguero et al., 2023). These animals showed an increased mortality rate in the first week of October 2022 (0.8% vs 0.2%). Mortality peaked at 4.3% (>2,200 mink) in mid-October. Clinical signs of infection in minks included loss of appetite, hypersalivation, depression, bloody snout and neurological manifestations such as ataxia and tremors. Out of 15 minks tested, 14 were positive for HPAI A(H5N1) virus (details on genetics in section 2.3.3). The feed of the minks included raw poultry by-products, but there had been no HPAI A(H5N1) virus outbreaks in the region from where these by-products were obtained, whereas several HPAI A(H5N1) cases in yellow-legged gulls and northern gannets were detected in that region. Given that the open housing system of mink farming is known to allow the access to wildlife including wild birds into the farms, and that direct contact with mink is possible (European Food Safety et al., 2021; Sikkema et al., 2022), the mink may have been in contact with infected wild birds that were attracted to the mink feed. However, it is difficult to explain all the infections of mink by bird-to-mink contact. Instead, the authors of the report state that their findings indicate onward transmission to other mink, based on increasing number of infected animals and progression of the infection from the initially affected area to the entire holding.

The third HPAI A(H5N1) outbreak in mammals involved two species of sea lions in Peru (Gamarra-Toledo et al., 2023). This sea lion die-off coincided with an outbreak of HPAI A(H5N1) in seabirds in Peru, associated with the mortality of >50,000 birds by the end of 2022, particularly Peruvian pelicans and Peruvian boobies. In the first 5 weeks of 2023, 630 South American sea lions and 4 South American fur seals were found dead on the coast of Peru, with up to 100 carcasses floating together at sea. The clinical symptoms of dying individuals were mainly neurological, such as tremors, convulsions and paralysis. They also showed respiratory signs such as dyspnea, tachypnea, nasal and buccal secretions and pulmonary edema. Of 12 sea lions tested, 9 were positive for HPAI A(H5N1) (details on genetics below). The source of the virus affecting these sea lions was very probably the large number of infected birds on the Peruvian coastline. Sea lions may have been infected by close contact or consumption of these birds or their carcasses. However, since many animals died simultaneously in groups, the authors could not exclude direct transmission among sea lions due to their colonial breeding, and because.



Disclaimer: The designations employed and the presentation of material on this map 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.

**Figure 8:** Geographical distribution of detections of HPAI in mammals since 2016 (based on Table 2)

**Table 2:** Avian influenza A(H5Nx) virus detections in mammal species other than humans related to circulating viruses worldwide, 2016–2022

| Virus | Animal (order, family, species) | | | Country | Epidemic season | Reference |
|---|---|---|---|---|---|---|
| **A(H5N8) clade 2.3.4.4b** | Artiodactyla | *Suidae* | Domestic pigs (*Sus scrofa*), serological detection | France | December 2016 | (Herve et al., 2021) |
| | | | Wild boar, serological detection | Germany | 2017 | (Schülein et al., 2021) |
| | Carnivora | *Phocidae* | Grey seals (*Halichoerus grypus*) | Poland, United Kingdom, Sweden | November 2016;<br>2020-2021 | (Shin et al., 2019; Floyd et al., 2021; SVA, online-b); personal communication by Siamak Zohari, SVA) |
| | | | Harbour seals (*Phoca vitulina*) | Germany, United Kingdom; Denmark | December 2020 | (Floyd et al., 2021; Ärzteblatt, online; Avian Flu Diary, online-b; Outbreak News, online; SSI, online) |
| | | *Canidae* | Red foxes (*Vulpes vulpes*) | United Kingdom, | December 2020 | (Floyd et al., 2021) |
| **A(H5N1) clade 2.3.4.4b** | Carnivora | *Canidae* | Red foxes (*Vulpes vulpes*) | Sweden; Netherlands; Finland; France, Estonia; Ireland; Belgium; Norway; Japan; USA; Canada | 2020-2021<br>2021-2022<br>2022-2023 | (SVA, online-b; WOAH, online-a, b;USDA, online); personal communication by Siamak Zohari, SVA; Irish National Reference Laboratory for Avian Influenza, personal communication) |
| | | | Common raccoon dog (*Nyctereutes procyonoides*) | Japan | 2021-2022 | (WOAH, online-b) |
| | | | Coyote (*Canis latrans*) | USA | 2021-2022 | (WOAH, online-b) |
| | | *Mustelidae* | Eurasian otter (*Lutra lutra*) | Netherlands; Finland | 2021-2022 | (WUR, online) |
| | | | European badger (*Meles meles)* | Netherlands | 2021-2022 | (WUR, online) |
| | | | European polecat (*Mustela putorius*) | Netherlands | 2021-2022 | (WUR, online) |
| | | | Ferret (*Mustela furo*) | Slovenia, Belgium | 2021-2022<br>2022-2023 | (Slovenian National Reference Laboratory for Avian Influenza, personal communication; European Commission, online) |
| | | | American mink (*Neovison vison*) | Canada, Spain | 2021-2022<br>2022-2023 | (Galicia, online; WOAH, online-b) |
| | | *Felidae* | Lynx (*Lynx lynx*) | Finland | 2021-2022 | (FFA, online) |
| | | | Bobcat (*Lynx rufus*) | USA | 2021-2022<br>2022-2023 | (WOAH, online-b) |
| | | | Fisher cat (*Pekania pennanti*) | USA | 2021-2022 | (WOAH, online-b) |
| | | | Amur leopard (*Panthera pardus*) | USA | 2021-2022 | (USDA, online) |
| | | | Amur tiger (*Panthera tigris*)(b) | USA | 2022-2023 | (WOAH, online-b) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | Mountain lion (*Puma concolor*) | USA | 2022-2023 | (WOAH, online-b) |
| | | | Cat (*Felis catus*) | France, USA | 2022-2023 | (WOAH, online-b) |
| | | *Procyonidae* | Raccoon (*Procyon lotor*) | USA | 2021-2022<br>2022-2023 | (WOAH, online-b) |
| | | *Mephitidae* | Skunks (*Mephitis mephitis*) | Canada; USA | 2021-2022;<br>2022-2023 | (CTV News, online; USDA, online; WOAH, online-b) |
| | | *Otaridae* | South American sea lion (*Otaria flavescens*) | Peru;Chile | 2022-2023 | (Gamarra-Toledo et al., 2023; WOAH, online-b)ref |
| | | *Phocidae* | Grey seals (*Halichoerus grypus*) | USA; Canada; UK | 2021-2022<br>2022-2023 | (AMMI, 2022; Agriland, online; WOAH, online-b) |
| | | | Harbour seals (*Phoca vitulina*) | USA; Canada; UK | 2021-2022<br>2022-2023 | (Agriland, online; WOAH, online-b) |
| | | *Ursidae* | American black bear (*Ursus americanus*) | Canada<br>USA | 2021-2022<br>2022-2023 | (Healthy Wildlife, online; KTOO, online; WOAH, online-b) |
| | | | Brown bear (*Ursus arctos*) | USA | 2022-2023 | (Kiniradio, online; USDA, online) |
| | Artiodactyla | *Suidae* | Domestic pigs (*Sus scrofa*), serological detection[a] | Italy | 2021-2022 | EURL |
| | Didelphimorphia | *Dedelphidae* | Virginia opossum (*Didelphis virginiana*) | USA | 2021-2022<br>2022-2023 | (USDA, online; WOAH, online-b) |
| | Cetacea | *Phocoenidae* | Porpoise (*Phocoena phocoena*) | Sweden | 2021-2022 | (SVA, online-a) |
| | | *Delphinidae* | Bottlenose dolphin (*Tursiops truncatus*) | USA | 2021-2022 | (UFHealth, online; WOAH, online-b) |
| | | | White-sided dolphin (*Lagenorhynchus acutus*) | Canada | 2022-2023 | (Avian Flu Diary, online-a) |
| | | | Common dolphin (*Delphinus delphi*) | Peru | 2022-2023 | (Leguia et al., 2023) |

(a) Serological detection in a HPAI outbreak in a backyard poultry

(b) Captive bird into a zoo

## 2.3 Genetic characterisation of avian influenza viruses

### 2.3.1 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 (WHO, 2020) 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).

### 2.3.2 Global overview of HPAI viruses of the A(H5) subtype of clade 2.3.4.4b

Since their first identification in late 2020 in Northern Europe, A(H5N1) viruses of clade 2.3.4.4b have spread globally, reaching even countries where the HPAI (H5) viruses of the Gs/GD lineage had never been found, and undergoing multiple reassortment events. In January 2021, an A(H5N1) related to the 2020–2021 European viruses was reported in West Africa (Lo et al., 2022) and subsequently in South and North African countries (Makalo et al., 2022; El-Shesheny et al., 2023). Since then, this virus has been persistently circulating in this geographic areas, and in West Africa it reassorted with the A(H9N2) subtype of the zoonotic G1 lineage (Ouoba et al., 2022). From late 2021, clade 2.3.4.4b A(H5N1) viruses, some of them closely related to the ones previously identified in Europe, have been detected in South and East Asia (Cui et al., 2022). In December 2021, A(H5N1) viruses of clade 2.3.4.4b, strongly related to the A(H5N1) identified in Northern Europe during the 2020-2021 epidemiological year, were introduced from the Atlantic flyway in North America (Bevins et al., 2022; Caliendo et al., 2022). This was followed, at the beginning of 2022, by a second introduction from the Pacific flyway of an A(H5N1) virus related to the ones circulating in Japan (Alkie et al., 2022). Since then the virus has spread all over North America further evolving through reassortment events with LPAI viruses of the American lineages (Alkie et al., 2022). In October 2022, the A(H5N1) was identified for the first time in Mexico and soon after in Central and South America, where the virus affected twelve countries causing episodes of mass mortality events in wild birds and in sea lions (BBC, online; KFGO, online). The characterized viruses from South America are related to the A(H5N1) circulating in North America (ProMed, online) and have been described as reassortant between the Eurasian and American lineages (WOAH, 2022). Based on the limited genetic information available to date on the viruses collected from mammals (one dolphin and one sea lion), no mutation associated to mammalian host adaptation has been observed (Leguia et al., 2023).

### 2.3.3 Genetic characteristics of HPAI viruses of the A(H5N1) subtype circulating in Europe

*Genetic diversity of A(H5N1) viruses in avian species*

Since October 2020, 6 subtypes (A(H5N1), A(H5N2), A(H5N3), A(H5N4), A(H5N5), A(H5N8)) and more than 60 different genotypes have been identified in Europe. While the 2020-2021 epidemiological year was dominated by the H5N8-A/Duck/Chelyabinsk/1207-1/2020-like genotype, the 2021–2022 epidemiological year was mainly driven by three H5N1 genotypes, H5N1-A/Eurasian_Wigeon/Netherlands/1/2020-like, H5N1-A/duck/Saratov/29-02/2021-like and H5N1-A/Herring_gull/France/22P015977/2022-like. Differently from the previous epidemics in Europe and based on the available genetic data, no new virus incursions seem to have occurred in Europe during the 2022-2023 epidemiological year. Since October 2022, 16 distinct genotypes have been identified among the characterized viruses. Four of them have been circulating from the 2021-2022 epidemiological year, while the remaining 12 genotypes have newly emerged very likely from reassortment events with AIVs circulating in Eurasian wild bird populations. The majority of the characterized viruses belong to genotype H5N1-A/duck/Saratov/29-02/2021-like, which has been the most prevalent since the beginning of 2022. However, starting from December 2022, a rapid increase in the number of detections of the H5N1 A/Herring_gull/France/22P015977/2022-like genotype has been recorded.

Genotype H5N1 A/Herring_gull/France/22P015977/2022-like had emerged through reassortment events with the gull-adapted H13 subtype. It was identified for the first time in May 2022 in France and since then it has been extensively circulating mainly in sea birds in Northern Europe (France, The Netherland and Belgium) throughout the summer months, with the European herring gull representing the most affected species based on the analysed sequences. In October 2022, this genotype was also identified in Ireland and Spain. From December 2022, we have assisted to a rapid escalation in the number of detections of the H5N1 A/Herring_gull/France/22P015977/2022-like genotype, associated to the increase in the number of cases in black-headed gulls, mainly in Belgium, France and for the first time also in northern Italy.

Besides sea birds, this genotype has sporadically infected also wild anseriformes, raptors, domestic birds (chicken, turkey and duck), at least 2 in Belgium, 2 in Ireland and 1 in France, and mammals, including a red fox in Belgium and domestic minks reared for fur in Spain (Aguero et al., 2023).

*Mutations identified in A(H5N1) viruses from avian species*

Molecular analyses of the A(H5N1) viruses circulating in birds in Europe during the 2022–2023 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 the literature (Suttie et al., 2019) to i) enhance polymerase activity and replication in mammals or mammalian cells, ii) increase virulence, iii) increase/confer resistance toward antiviral drugs, iv) in vitro increase binding to human-type receptors alpha2,6-SA, and v) decrease antiviral response in ferrets were observed with a frequency varying for the distinct mutations. The real effect of these mutations on the biological characteristics of the viruses is still unknown and further studies are needed to improve existing knowledge. Among the detected mutations, it is worth mentioning the detection of the mutation PB2-E627K, an adaptive marker associated with an increased virulence and replication in mammals, in two A(H5N1) viruses, one collected from a domestic bird in Belgium in December 2022 and one in a wild bird in Sweden in January 2023. Moreover, about 3% of the European viruses belonging to the H5N1 A/Herring_gull/France/22P015977/2022-like genotype show mutations in the NA protein which cause disruption of the second sialic acid binding site (2SBS), a feature typical of human-adapted influenza A viruses (de Vries and de Haan, 2023). Among the mutations in the HA protein which have been previously demonstrated to increase the binding to human–type receptor, some of them (ie. S137A, S158N, T160A, S128P and R496K) have been identified in the majority of the A(H5N1) viruses circulating in Europe since October 2022, while others (ie. T192I, S159N, Q196R, V214I) have been sporadically observed. All the mutations associated to antiviral resistance were identified only sporadically in the circulating viruses.

*Genetic diversity of A(H5N1) viruses in mammals*

Since October 2020, complete genome sequences of 57 HPAI A(H5) viruses of clade 2.3.4.4b collected from 12 distinct mammalian species (badger, cat, coati, ferret, fox, lynx, mink, otter, polecat, porpoise and seal) in 13 European countries were generated. The characterized viruses belong to 8 different A(H5N1) and A(H5N8) genotypes previously identified in birds, with most of the viruses (75%) belonging to the two most widespread genotypes in birds in Europe (H5N1 A/Eurasian_Wigeon/Netherlands/1/2020-like, H5N1 A/duck/Saratov/29-02/2021-like).

*Mutations identified in A(H5N1) viruses from mammals*

About half of the characterized viruses contain at least one of the adaptive markers associated with an increased virulence and replication in mammals in the PB2 protein (E627K, D701N or T271A) (Suttie et al., 2019). These mutations have never (T271A) or rarely (E627K, D701N) been identified in the HPAI A(H5) viruses of clade 2.3.4.4b collected in birds in Europe since October 2020 (<0.5% of viral sequences from birds). This observation suggests that these mutations with potential public health implications have likely emerged upon transmission to mammals.

Moreover, the viruses collected in October 2022 from a HPAI A(H5N1) outbreak in intensively farmed minks in northwest Spain (Aguero et al., 2023) shows mutations in the NA protein which cause disruption of the second sialic acid binding site (2SBS). This feature is typical of human-adapted influenza A viruses, which may favour the emergence of mutations in the receptor binding site of the HA protein (de Vries and de Haan, 2023). These same mutations were detected also in seven A(H5N1) viruses from birds.

## 2.4 Avian influenza virus infections in humans

### 2.4.1 Most recent human infections with avian influenza A(H5N1) and A(H5N6) virus

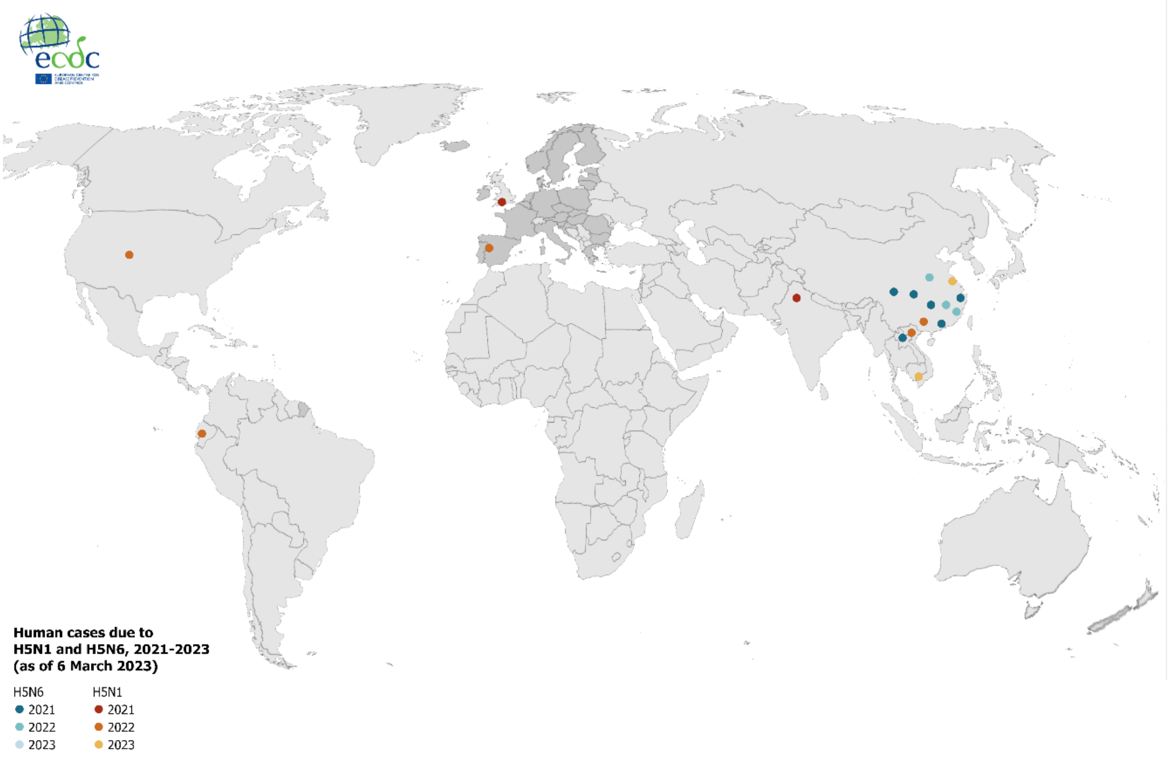
Since 3 December 2022 and as of 8 March 2023 six new human cases with avian influenza A(H5N1) infection were reported from four countries Cambodia (2), China (2), Ecuador and Vietnam (previously reported as A(H5) case), including two deaths (Table 4):

Ecuador for the first time reported a human infection with avian influenza A(H5N1) (clade 2.3.4.4b), marking the first human infection with A(H5N1) in South America (WHO, online-b). The virus was detected in a 9-year old girl with severe symptoms following exposure to sick and dead backyard poultry.

Vietnam reported for the first time since 2014, one human infection in a 5-year-old girl, who developed severe symptoms (WHO, 2023). This case was previously reported as A(H5) with missing neuraminidase, later confirmed as A(H5N1) virus infection with unspecified clade.

Two more cases, both with A(H5N1) clade 2.3.4.4b virus infection were reported in China for the first time since 2015. Both women, 38-year and 53-year-old, developed severe symptoms following exposure to poultry, the 38-year old woman died (WHO, 2023; BNO, online; CHP, online)

In February 2023, Cambodia reported two cases in a family cluster involving an 11-year-old girl (index case) and her 49-year-old father infected with A(H5N1) following exposure to infected sick and dead backyard poultry (ECDC, 2023a, b; CDC, online-d) The girl developed cough, sore throat and fever on 16 February 2023, was hospitalised due to severe disease development and died on 21 February. The father of the girl developed symptoms such as fever and cough and was isolated for several days in a referral hospital, following A(H5N1) confirmation. All identified contacts tested negative for A(H5N1). Viral sequencing of both specimens confirmed A(H5N1) virus clade 2.3.2.1c viruses, similar to the viruses circulating in birds in Southeast Asia since 2014. The symptoms of both cases occurred on the same day and both had the same exposure (sick poultry). Human-to-human transmission has been ruled out by the local authorities.



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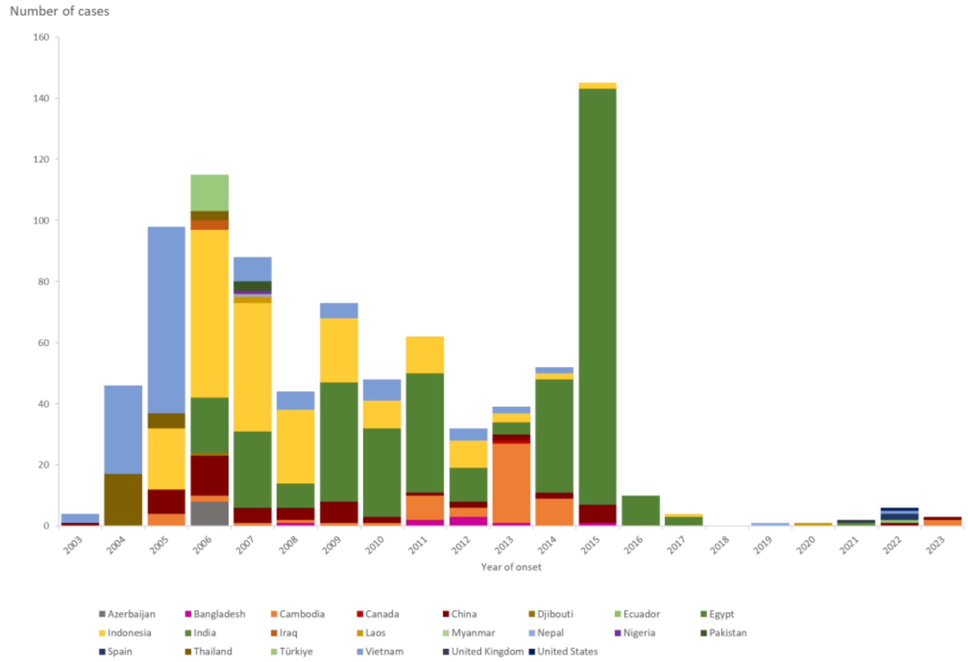
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on: 7 March 2023

**Figure 9:** Geographic distribution of human H5N1 and H5N6 cases, 2021-2023 (source: ECDC line list)

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

IAs of 3 March 2023, there have been 873 cases, including 458 deaths of human infection with avian influenza A(H5N1) reported from 22 countries (Azerbaijan, Bangladesh, Cambodia, Canada, China, Djibouti, Ecuador, Egypt, Indonesia, India, Iraq, Laos, Myanmar, Nepal, Nigeria, Pakistan, Spain, Thailand, Türkiye, Vietnam, United Kingdom and United States).



2022: China (1), Spain (2), United States of America (1), Vietnam (1)
2023: Cambodia (2), China (1), Ecuador (1)

**Figure 10:** Distribution of confirmed human cases of avian influenza A(H5N1) virus infection by year of onset and country, 2003–2023 (updated on 2 March 2023, n=873)

## 2.4.3 Human A(H5N6) cases, summary

As of 3 March 2023, China (83) and Laos (1) reported a total of 84 human infections with avian influenza A(H5N6) including 29 (35%) with fatal outcome. Since 2021, A(H5N6) viruses cluster also in clade 2.3.4.4b although sequence information is only available for a minority of viruses.

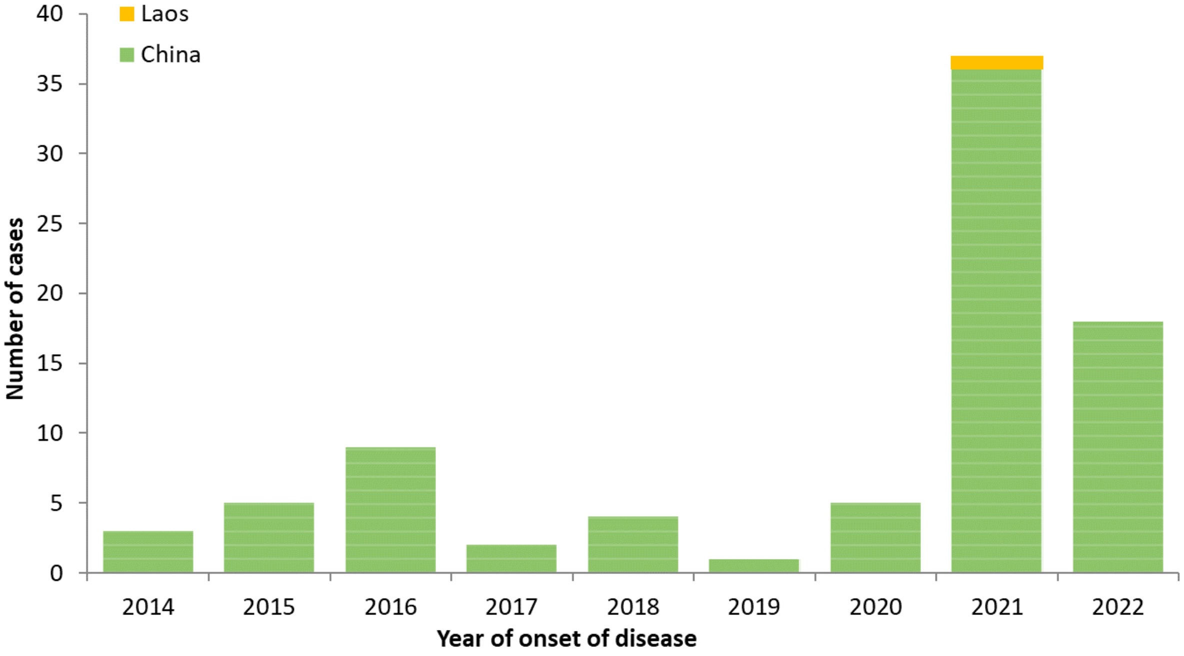


**Figure 11:** Distribution of confirmed human cases of avian influenza A(H5N6) virus infection by year of onset and country, 2014–2023 (updated on 2 March 2023, n=84)

### 2.4.4 Details about human infections with avian influenza A(H5Nx) virus clade 2.3.4.4b related to viruses circulating in Europe, 2021–2023

In October 2022, Spanish authorities reported two workers involved in culling and cleaning activities to have tested positive for A(H5N1). However, due to low virus load no full genome could be generated and no seroconversion was present in the workers. This indicates rather a contamination of the mucosa with avian influenza viruses due to exposure to highly contaminated environment despite wearing personal protective equipment (PPE) and not a systemic infection (Aznar et al., 2023) (ECDC, 2022a, b; Sanidad, 2022; WHO, online-a). Other farm workers involved in the culling activities during the outbreak at the same farm tested negative. Close contacts were followed up and all tested negative, providing evidence that there was no human-to-human transmission. Spanish authorities consider these findings the result of an environmental contamination and not an active replication of the virus in the human hosts. This is also reflected in the low virus load in the tested specimens resulting in high Ct values in the initial PCR tests at the detection limit of the assay, the inability to generate full length genomes, the lack of virus cultivation and inconclusive or negative serological findings (Table 3).

In a mink farm an outbreak of H5N1 was identified following increased mortality in the animals (Aguero et al., 2023). All workers on this farm were wearing PPE and tested negative for influenza.

Earlier human infections with A(H5N1) or A(H5N8) viruses of clade 2.3.4.4b were reported since 2021, in the US, the United Kingdom, Russia and Nigeria, all related to outbreaks in poultry or wild birds (Pyankova et al., 2021; WHO, 2021b; CDC, online-b). So far, information from some of these human A(H5) cases suggested PCR amplification of low-level virus RNA following exposure to contaminated environment and infected birds during culling activities and no active viral replication in infected human cells or tissues with lack of seroconversion (Table 3).

Sequence data from A(H5N1) viruses detected in China in birds and shared through GISAID have shown that the HA genes of the viruses belong to clade 2.3.4.4b and cluster with viruses collected in Europe, Africa and other Asian countries since 2020, however, the other gene segments indicate a high genetic variability among the circulating viruses in China and differ in at least one gene segment from European viruses.

H5Nx detections in human reported as asymptomatic or with mild symptoms are mostly related to male workers involved in culling activities and wearing personal protective equipment (PPE) (Table 3). Recent human cases reported with severe or fatal outcome have all been women exposed without personal protective equipment to sick or dead backyards poultry (Table 4). This indicates the increased risk associated with backyard settings and with unprotected exposure to infected birds likely due to lack of knowledge or awareness of the risk of avian influenza for human health.

**Table 3:** Human cases due to clade 2.3.4.4b viruses – asymptomatic cases

| Date reported | Country (subtype) | Case(s) | Exposure | Symptom | Confirmation |
|---|---|---|---|---|---|
| Sept/Oct 2022 (27 Sept/13 Oct) | Spain (H5N1) | 19-year male<br>27-year male | Culling (PPE) | Asymptomatic | PCR, partial sequencing, no culture, no serological reactivity against H5 |
| Apr 2022 (20 April) | USA (H5N1) | 18+ male | Culling (PPE) | Fatigue | PCR, partial sequence data, no virus isolation possible |
| Jan 2022 (24 Dec 2021) | UK (H5N1) | 80+ male | Raised birds, “lived with” | Asymptomatic | PCR, reproduced on two successive swabs following days high Ct values |
| Apr 2021 | Nigeria (H5 related to H5N1 outbreak) | 3 (7) | Culling | Asymptomatic | 7 type A positive, 3 H5 positive PCR, no full sequencing or culture |
| Feb 2021 | Russia (H5N8) | 7 | Culling (PPE) | Asymptomatic | 7 PCR, 1 isolated, 4 pos focus reduction neutralisation assay (FRNA) serum titres, 1 4-fold in sample 14d after (1:20), decreased titre 44d after; 5 samples positive for IgG biolayer interferometry |

Source: (Pyankova et al., 2021; WHO, 2021a, c; Oliver et al., 2022; WHO, 2022b; Aznar et al., 2023; CDC, online-c; ECDC, online; WHO, online-c)

**Table 4:** Human cases due to clade 2.3.4.4b viruses - symptomatic cases

| Date reported (symptom onset) | Country (subtype) | Case(s) | Exposure | Symptoms | Confirmation |
|---|---|---|---|---|---|
| 14 Oct 2022 (22 Sept) | China (H5N1) | 38-year woman | Backyard poultry | Hospitalised with severe pneumonia, died 18 Oct | Low concentration of virus, only partial sequences of eight segments all avian influenza virus origin. Sequence of HA belonged to Clade 2.3.4.4b, and clustered with Asian viruses, not European viruses.<br>The receptor binding site not determined. PB2: 591Q and 627E low reads). |
| 22 Oct 2022 (5 Oct) | Vietnam (H5N1) | 4-year girl | Backyard poultry sick/dead | cough, fever and jaundice, hospitalised, renal and liver failure, ICU admission | Only weak PCR, no NA-typing, no sequence data |
| 9 Jan 2023 (25 Dec 2022) | Ecuador (H5N1) | 9-year girl | Backyard poultry sick/dead | Conjunctival pruritus, coryza, nausea, vomiting, constipation, meningitis, admitted to hospital and ICU with pneumonia and septic shock, mechanical ventilation | PCR with high Ct values, no NA-typing, partial sequence data available |
| 1 Mar 2023 (31 Jan) | China (H5N1) | 53-year woman | Exposure to poultry | Symptomatic, no details available | Sequence data available |

Source: (WHO, 2022b; ECDC, 2023a; OPS, 2023; WHO, 2023; BNO, online; WHO, online-b)

### 2.4.5 Genetic characteristics of HPAI viruses of the A(H5NX) subtype from human

Based on the data available from the GISAID EpiFlu database, since 2020 human infections have been caused by four different A(H5) clades of the A/goose/Guangdong/1/1996-lineage, namely 2.3.2.1c (Laos, 2020 and Cambodia, 2023), 2.3.2.1a (India, 2021), 2.3.4.4h (China, 2020-2021), 2.3.4.4b (China, Europe, North and South America).

Mutation Q226L was identified in two A(H5N6) viruses of clade 2.3.4.4b collected in China in 2021 (Zhu W Fau - Li et al.)to the switch in the receptor specificity from avian-type to human-type receptor (Stevens et al., 2006; Chutinimitkul et al.; Russell et al., 2012). This mutation was previously detected in two A(H5N1) viruses of clade 1 collected from human infections in Cambodia in 2013 (Rith et al., 2014) and, based on the available sequence data, it is not present in the clade 2.3.4.4b A(H5Nx) viruses currently circulating in the avian population in Europe. Moreover, six clade 2.3.4.4b A(H5N6) viruses collected from human infections in China in 2021 possessed one of the adaptive markers in the PB2 protein (Q591K, E627K or D701N) associated with an increased virulence and replication in mammals (Zhu W Fau - Li et al., 2022)

### 2.4.6 Additional information and international risk assessments

A study on currently circulating A(H5N1) viruses in North America showed that these viruses are able to replicate efficiently in human respiratory tract cell types and that in ferret infection and transmission studies, animals got infected but showed only very mild symptoms mostly limited to upper respiratory tract and viruses did not transmit to other ferrets kept in a direct-contact setting (Pulit-Penaloza et al., 2022).

The previously issued risk assessment using the Influenza Risk Assessment Tool (IRAT) of the United States Centers for Disease Control and Prevention (US CDC) placed the risk of clade 2.3.4.4b viruses in the lower moderate category (CDC, 2021). The risk of the A(H5N1) clade 2.3.4.4b viruses currently circulating in the United States bird and poultry populations, and which are closely related to European viruses, were assessed by the US CDC to be of low risk for human health in the general population and higher for people occupationally or recreationally exposed to birds (CDC, online-a, c) . The WHO assessed the risk related to the recent (H5N1) human cases as low for the general public and low to moderate for occupationally exposed people  (WHO, 2022a, online-a). WHO previously assessed the risk for A(H5N6) that "the zoonotic threat remains elevated due to spread of the viruses in birds, based on evidence available so far, the overall pandemic risk is considered not significantly changed in comparison to previous years" (WHO, 2021d). The UKHSA assesses that 'at present there are 'no indicators of increasing risk to human health with a low confidence' (GovUK, online). A joint EFSA, ECDC, EURL publication from 2021 already described the threat to humans with the objective to raise awareness among clinicians in the EU around zoonotic avian influenza virus infection and consider testing (Adlhoch et al., 2021).

## 2.5 ECDC risk assessment for the general public in the EU/EEA

Sporadic human cases of different avian influenza A(H5Nx) subtypes have been previously reported globally and current epidemiological and virological evidence suggests that A(H5N1) viruses remain avian-like. Mutations associated with mammalian adaptation such as in the PB2 that confer an increased replication have been observed, however, no mutations in the Hemagglutinin (HA) gene have been detected in A(H5N1) viruses from birds or mammals that would support a switch of the viruses from avian-like alpha2.3 to human-like alpha 2.6sialic acid receptors (Shinya and Kawaoka, 2006; de Graaf and Fouchier, 2014).

Despite the high number of exposure events due to the large outbreaks in poultry and wild birds over the last three years, no symptomatic human infection due to avian influenza A(H5Nx) have been reported from EU/EEA countries. Only sporadic human infections have been reported globally, and transmission to humans remains a rare event. No sustained transmission between humans has been observed.

Currently developed and proposed Candidate Vaccine Viruses (CVVs) for pandemic preparedness by WHO have been assessed to be antigenically similar to currently circulating viruses in Europe and a more US-virus related new CVV has been proposed (WHO, 2022a, 2023).

ECDC published a Threat Assessment Brief in February 2021 that assessed the risk as very low for the general population and low for occupationally exposed people (ECDC, 2021b) and revised the risk to low for the general population and low to moderate for occupationally exposed people in December 2021 due to the increase in transmission events to mammal species including sporadic human cases with no or mild symptoms. The assessment remains valid.

Overall, the risk of infection with avian influenza viruses of the currently circulating clade 2.3.4.4b in Europe for the general public in EU/EEA countries is considered to be low. The risk to occupationally or otherwise exposed groups to avian influenza infected birds or mammals such as cullers or veterinarians has been assessed as low to moderate.

The high diversity and ongoing reassortment events globally also after the introduction into the Americas add a high uncertainty to the assessment, and sporadic transmission events to humans causing also severe infections cannot be excluded.

Avian influenza virus transmission to humans is a rare event, viruses remain avian-like adapted. Mutations in the HA gene have been identified from *in vitro* studies associated with increased binding to human-type receptor. However, the viruses do not show the key mutations in the receptor binding domain that cause the switch from avian to human type receptors and do not possess all the mutations that have been shown in gain of function studies to be determinant for H5 droplet respiratory transmission in ferrets (Herfst et al., 2012; Imai et al., 2012). However, detections of Q226L mutation in the HA gene in two human cases with A(H5N6) in 2021 in China are important indicators that need to be considered relevant, but these mutations seem to be isolated and have not been described in any recent human A(H5N1) cases and any other human avian influenza case since 2021 (Zhu W Fau - Li et al., 2022). WHO also assessed these findings as isolated and 'molecular markers were not identified in viruses collected from environmental surfaces or poultry indicating that these amino acid substitutions occurred sporadically during human infection' (WHO, 2021d).

However, the expansion of mammal species identified infected with A(H5N1) viruses as well as the detection of viruses carrying markers for mammalian adaptation in other genes such as the PB2 that correlated with increased replication and virulence in mammals, is of concern. The additional reports of transmission events to and potentially between mammals, e.g. mink, sea lion, seals, foxes and other carnivores as well as seroepidemiological evidence of transmission to wild boar and domestic pigs, associated with evolutionary processes including mammalian adaptation are of concern and need to be closely followed up.

With the wide geographical distribution of avian influenza viruses and high number of detections also in wild birds and mammals, sporadic human cases infected with HPAI viruses cannot be ruled out whenever people are exposed to infected sick or dead birds. The likelihood of travel-related importation of human avian influenza cases from countries where the viruses are detected in poultry or wild birds is considered to be *very low*.

The uncertainty of this risk assessment is high due to the high variability and diversification of the avian influenza viruses of clade 2.3.4.4 with many reassorted subtypes and genetic lineages co-circulating in Europe and globally. Reassortment events will continue and zoonotic transmission of avian influenza viruses cannot be fully excluded in general when avian influenza viruses are present in birds.

## 2.6 Options for public health response

Direct contact with infected birds or a contaminated environment is the most likely source of infection. The use of personal protective equipment for people exposed to dead birds or their droppings is recommended to minimise the risk of infection. Detailed information on occupational safety and health in the work place has been provided in the last report (EFSA et al., 2022).

The recent severe cases in Asia and South America in individuals exposed to infected sick and dead backyard poultry underline the risk associated with unprotected contact with infected birds.

People should avoid touching sick or dead birds or their droppings and should wear personal protective equipment (PPE) when in direct contact. In general, sick and dead wild mammals should not be touched without proper precautionary measures such as PPE. Workers should be protected following an updated workplace risk assessment and preventive measures should be set accordingly[10]. Active or passive follow-up measures should be in place for people exposed to potentially infected birds (and mammals) for 10-14 days. Testing should be initiated immediately for symptomatic people and contact people of confirmed cases.

ECDC jointly with EFSA, EU-OSHA and the EURL published a separate document that provides guidance for the testing of humans for zoonotic influenza viruses. The document describes different exposed groups at risk and raises awareness about the possibility of atypical presentations in humans similar to what has been recently observed in other mammals with severe infection of the brain, i.e. encephalitis or meningoencephalitis (ECDC, 2022d).

A guidance document on integrated surveillance of respiratory viruses has been published in 2022 that is also relevant for zoonotic incl avian influenza virus infections in humans (ECDC, 2022c). Primary and secondary health care sentinel systems as well as molecular surveillance have been strengthened during the COVID-19 pandemic to integrate respiratory viruses as well as e.g. monitor the emergence of SARS-CoV-2 variants and will be useful for any other emerging respiratory viruses. Surveillance and options for public health measures have been outlined in previous reports (EFSA et al., 2021b) and remain valid.

Human infections with avian influenza viruses are notifiable under EU legislation within 24 hours through the Early Warning and Response System (EWRS) according to EU Decision 1082/2013/EU[9]. Reporting is also required through the International Health Regulations (IHR) notification system (WHO, 2017).

A guidance on infection prevention and control measures in health care in regard to respiratory viruses has been updated and includes also high threat pathogens (ECDC, 2021a).

The use of antiviral pre- and postexposure should be considered for exposed people and in particular for possible cases of avian influenza infection according to national guidelines.

Candidate vaccine viruses (CVV) developed, under development or proposed are listed at WHO (WHO, 2021b). A new CVV for H5 viruses more antigenically like a new clade 2.3.4.4b CVV that is antigenically like A/American wigeon/South Carolina/22-000345-001/2021 has been proposed during the Vaccine Composition Meeting for the Northern Hemisphere in February 2023 more similar to recently circulating avian influenza H5 viruses in the US (WHO, 2023).

# 3 Conclusions

Birds in Europe:

- During the current reporting period, from 3 December to 1 March, an unexpected increased detection of HPAI A(H5N1) virus was reported in gull species, particularly in black headed gulls linked to mortality events in France, Belgium, the Netherlands, Italy.
- Genetic analysis based on the available data support the hypothesis that HPAI viruses persisted in Europe in residential wild bird populations during and after the summer months as no new virus introductions were identified; the increased genetic diversity observed since autumn 2022 has very likely emerged from reassortment events with avian influenza viruses circulating in Eurasian wild bird populations.
- The viruses which have been badly affecting the black-headed gulls in The Netherlands, Belgium, France and Italy since December 2022 are closely related and belong to the genotype H5N1 A/Herring_gull/France/22P015977/2022-like. This genotype had emerged during the summer in Europe through reassortment events with the gull-adapted H13 subtype and have mainly been detected in gulls. The behavior of this genotype in poultry species will have to be studied in the coming months
- The A(H5N1) viruses currently circulating in Europe retain a preferential binding for avian-like receptors; however, several mutations associated to increased zoonotic potential have been detected. AllTheir effects on the biological characteristics of the viruses are not fully unknown.
- As for poultry, whilst most outbreaks have been identified as primary introductions (likely from infected wild birds), secondary spread in both poultry and captive birds has taken place. Regardless of the source of infection, primary introduction or secondary spread, high levels of biosecurity measures and prompt reporting of suspicions need to be kept in order to minimize the risk of infection and further transmission.
- From October 2020 to date, the trend in the numbers of outbreaks in poultry correlates mainly with the trend in the number of detections in waterfowl. Increased detections in seabirds, during the summer months of 2022 were in contrast with the lower number of detections in poultry. However, detections in those summer months involved mostly herring gulls on coastal locations, whilst detections during the current reporting period extended inland and involved mostly black headed gulls.
- The sustained circulation of HPAI virus in black headed gull and other gull species, during the last winter weeks and the coming spring/summer months, might increase the risk of infection for poultry as breeding colonies spread mostly inlands possibly overlapping with poultry production areas.

Birds outside Europe:

- In the current reporting period from 3 December 2022 to 1 March 2023 the HPAI (H5N1) virus continued to spread in South America, from Mexico to Chile to the furthest south that the virus has reached (latitude: 42 degrees South), near to the southern tip of South America.

- Based on the observed temporal and geographical distribution of HPAI (H5N1) in wild birds during the reporting period, virus spread in South America corresponds to the Pacific Americas Flyway along the west coast of South America, the Mississippi Flyway along the Caribbean and the north-central part of South America, and the Atlantic Americas Flyway along the east coast of South America.

- Given the rapid southwards spread of HPAI A(H5N1) virus, and the known movements of wild birds between South America and the Antarctic, e.g. sheathbills

(Mead CJ and Richford AS, 2003), there is risk of virus spread to seabirds (100 million breeding birds) and pinnipeds (seven pinniped species, including 15 million crabeater seals) of the Antarctic[9]

- The results of the genetic analysis conducted on HPAI viruses isolated from South America indicate multiple virus introductions events from North to South America, followed by local spread.

- The spread of HPAI virus in South America has also reached domestic birds, with the majority of the reported outbreaks involving captive (backyard) birds. Backyard keeping of poultry is done with low levels of biosecurity and may represent a public health risk, as exemplified by infection of a girl in Ecuador. In addition, depending on the production and commercial structure of poultry in those countries, backyard may also represent a source of infection for commercial farms. New outbreaks in domestic birds are being reported, which indicates that the epidemiological situation in this region is still evolving.

Mammals:

- During this reporting period the reports of HPAI (H5N1) virus in individual mammals, mainly carnivores, that were likely infected through feeding on infected wild birds continued.
- In addition to the mass mortality events in mammals due to HPAI (H5N1) observed in free-living harbour seals in the USA in summer 2022 and in American mink in Spain in autumn 2022, in this reporting period there was a mass mortality of South American sea lions associated to HPAI A(H5N1) virus in Peru in January and February 2023. In all three events, there may have been mammal-to-mammal transmission of HPAI A(H5N1) virus. A(H5) infections in mammalian species appear to favour the emergence of molecular markers of virus adaptation to mammals (ie. PB2 E627K, D701N or T271A).

Human cases:

- Sporadic human infections with avian influenza viruses of different H5 clades are reported from different countries globally
- Human infections are related to unprotected exposure to sick and dead poultry particularly in backyard settings also causing severe disease and fatal outcome

# 4 Options for response

In birds:

- It is important to accurately report infected wild birds—including identification of species—and the associated mortality and, where appropriate, to remove wild bird carcasses from affected sites to limit virus spread. The benefits of wild bird carcass removal—reduction of virus load—need to be weighed up against the possible disturbance of wildlife.
- Considering the high negative impact of HPAI A(H5) epidemics in the last years, short-term preparedness and medium- and long-term prevention strategies should be identified and implemented, primarily in densely populated poultry areas and poultry production systems that are highly susceptible to avian influenza exposure. These were described in detail in Avian influenza overview September – December 2021 (EFSA, 2021) and in 2022 EFSA Avian influenza Quarterly Reports.

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[9] https://en.wikipedia.org/wiki/Southern_Ocean#cite_note-FOOTNOTE''EB''1878-1

In mammals:

- Extended and enhanced surveillance of both wild mammals (particularly carnivores) and farmed mammals (particularly American mink and domestic pigs) in risk areas where HPAI is present in wild birds and poultry is recommended.
- Improve virological and serological surveillance in scavenger mammals to prompt identify viruses with zoonotic potential and evaluate the real magnitude of the spread of HPAI viruses in these species.
- In domestic mammals, to prevent exposure to possible infected wild birds by increasing biosecurity at farm.
- Timely producing and sharing viral sequences, which should be analysed in real-time to assess the pandemic risk.
- Better, more accurate and timely reporting of HPAI virus detections in mammals in a way that reliable numbers of infected animals could be used as quantitative information for risk assessment.
- Thoroughly investigate the dynamic of the infection in case of mass mortality events associated with HPAI virus detected in mammalian species. Testing a high number of animals and assuring a prompt generation and sharing of viral sequences data are of utmost importance to shed light on the virus origin, evolution and possible transmission between individuals.

In humans:

- Appropriate use of personal protective equipment when in contact with potentially infected birds and animals.
- Follow-up exposed people (also to infected mammals), test and identify transmission events early.
- Suspicion and detection of human infection with avian influenza should be identified and reported as early as possible.
- Antiviral pre-and post-exposure prophylaxis should be considered following national guidelines.
- Timely producing and sharing of virus sequence information is crucial for assessment and development of candidate vaccine viruses.

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## Annex A - Data on birds

The Annex contains tables and figures on wild birds species and movements and HPAI virus detections in birds.

The annex is available on the EFSA Knowledge Junction community on Zenodo at: https://doi.org/10.5281/zenodo.7707605