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## Avian influenza overview November 2018 – February 2019

European Food Safety Authority,  
European Centre for Disease Prevention and Control and  
European Union Reference Laboratory for Avian Influenza

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### Abstract

No human infections due to highly pathogenic avian influenza (HPAI) A(H5N8) or A(H5N6) viruses - detected in wild birds and poultry outbreaks in Europe - have been reported so far and the risk of zoonotic transmission to the general public in Europe is considered very low. Between 16 November 2018 and 15 February 2019, two HPAI A(H5N8) outbreaks in poultry establishments in Bulgaria, two HPAI A(H5N6) outbreaks in wild birds in Denmark and one low pathogenic avian influenza (LPAI) A(H5N3) in captive birds in the Netherlands were reported in the European Union (EU). Genetic characterisation of the HPAI A(H5N6) viruses reveals that they cluster with the A(H5N6) viruses that have been circulating in Europe since December 2017. The wild bird species involved were birds of prey and were likely infected due to hunting or scavenging infected wild waterfowl. However, HPAI virus was not detected in other wild birds during this period. Outside the EU, two HPAI outbreaks were reported in poultry during the reporting period from western Russia. Sequence information on an HPAI A(H5N6) virus found in a common gull in western Russia in October 2018 suggests that the virus clusters within clade 2.3.4.4c and is closely related to viruses that transmitted zoonotically in China. An increasing number of outbreaks in poultry and wild birds in Asia, Africa and the Middle East was observed during the time period for this report. Currently there is no evidence of a new HPAI virus incursion from Asia into Europe. However, passive surveillance systems may not be sensitive enough if the prevalence or case fatality in wild birds is very low. Nevertheless, it is important to encourage and maintain a certain level of passive surveillance in Europe testing single sick or dead wild birds and birds of prey as they may be sensitive sentinel species for the presence of HPAI virus in the environment. A well-targeted active surveillance might complement passive surveillance to collect information on HPAI infectious status of apparently healthy wild bird populations.

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## 1. Introduction

This scientific report provides an overview of highly pathogenic avian influenza (HPAI) virus outbreaks detected in poultry, captive and wild birds and low pathogenic avian influenza (LPAI) virus outbreaks in poultry and captive birds, as well as human cases due to avian influenza (AI) virus reported in and outside Europe between 16 November 2018 and 15 February 2019. The background, terms of reference (TORs) and their interpretation are described in Appendix A and data and methodologies are reported in Appendix B.

## 2. Conclusions

### Avian influenza outbreaks in European countries and in other countries of interest between 16 November 2018 and 15 February 2019

#### 2.1. Main observations

- No human infections with HPAI or related LPAI viruses of the same genetic composition as those currently detected in domestic and wild birds in Europe have been reported from the EU/EEA MS. However, Russian researchers found antibodies to A(H5) viruses of the clade 2.3.4.4. in people exposed to AI viruses during outbreaks.
- Five human cases caused by AI A(H9N2) virus have been reported from China with the onset of disease since October 2018.
- In Europe, between 16 November 2018 and 15 February 2019 (based on the Animal Disease Notification System (ADNS)):
  - Two HPAI A(H5N8) outbreaks were reported in poultry in Bulgaria.
  - Two HPAI A(H5N6) outbreaks were reported in wild birds in Denmark. Genetic characterisation of the HA genes of these viruses reveals that they cluster with HPAI A(H5N6) viruses that have been circulating in Europe since December 2017. The wild bird species involved, white-tailed eagle (*Haliaeetus albicilla*) and common buzzard (*Buteo buteo*), both birds of prey, are present in the revised list of target species for passive surveillance. Although these birds of prey were likely infected due to hunting or scavenging infected wild waterfowl, HPAI virus was not detected by passive surveillance in wild waterfowl or other wild birds in Denmark in this period.
  - One LPAI A(H5N3) outbreak was reported in captive birds in the Netherlands. Genetic clustering of the partial HA gene indicates that the virus is related to the LPAI A(H5) viruses previously detected in wild and domestic Anseriformes in Europe.
- Two HPAI A(H5N8) outbreaks were reported in poultry during this time period from Russia via the World Organisation for Animal Health (OIE). Early information from GISAID suggested that HPAI A(H5N6) virus found in western Russia in October 2018 in a common gull (*Larus canus*) clusters in the clade 2.3.4.4c which includes viruses that have infected people in China.
- In the time period of this report, compared to the previous reporting period, there was an increasing number of reported outbreaks in poultry and wild birds from Asia, Africa and the Middle East.

#### 2.2. Conclusions

- The risk of zoonotic transmission of AI viruses to the general public in Europe remains very low.
- The few HPAI positive findings reported by three countries in the EU during the period of this report may indicate a lower level of HPAI circulation in Europe or a higher herd immunity in the birds population.
- The mortality due to the HPAI virus A(H5N6) that was reported in wild birds in Denmark underlines the potential for that virus to remain present in free-living wild birds for several months after the peak of an outbreak and emphasises the need for continued vigilance regarding incursion into poultry establishments.

- Increased awareness among stakeholders (e.g. poultry production companies and hunters) and enhanced biosecurity measures could be considered the most rapidly applicable measures in the event that HPAI is found in wild birds.
- More information on the HPAI A(H5N6) virus, isolated from a common gull in Russia in October 2018, which is closely related to A(H5N6) viruses causing human infections in China, is needed to assess the risk of introduction of the virus to poultry in the EU. Such information should include the clinical condition of the gull found infected, whether other wild birds were found affected in that area, if the event occurred in proximity to poultry establishments and the phenotypic properties of the virus in terms of host range, transmissibility and pathogenicity.
- During the period of this report in the EU/EEA, there is no evidence of any new HPAI virus incursion from Asia. However, passive surveillance systems may not be sensitive enough if the prevalence or case fatality in wild birds is very low.

### 3. Suggestions

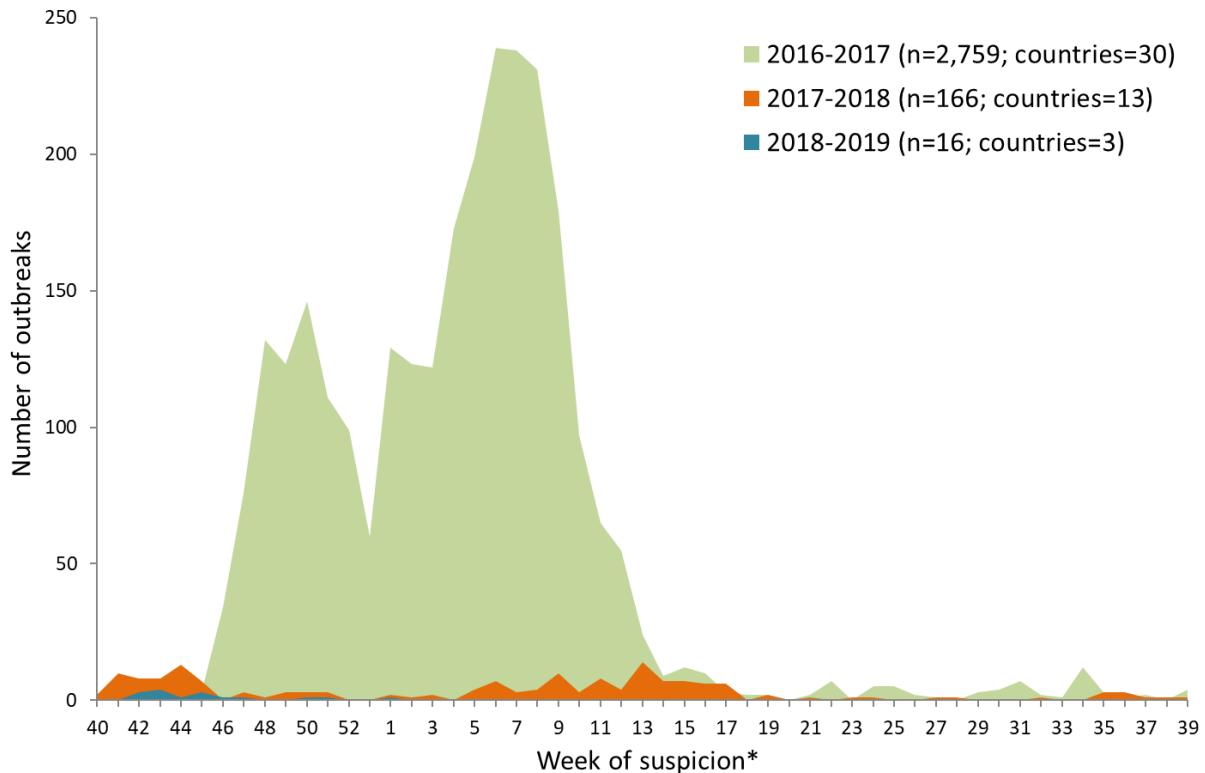
- Continued surveillance for AI virus in wild birds and poultry in Europe and worldwide combined with timely generation of complete viral genome sequences and data sharing among European countries and between animal and human health sectors are crucial to be able to detect and respond promptly to threats that are relevant to animal and public health. It is particularly important that information on the genetic composition and possible origins of recently detected new variants in birds and humans are shared and communicated in a timely manner.
- When the overall mortality rate in wild birds from HPAI is low, it is important to maintain a sufficient level of passive surveillance, also encouraging a search for carcasses of wild birds species that are in the revised list of target species (EFSA et al., 2017a) in order to detect early and initiate warning. This includes testing cases of single sick or dead wild birds, in particular birds of prey (that hunt or scavenge wild waterfowl), because they may be sensitive sentinel species for the presence of HPAI virus in the environment.
- Involvement of citizens in notifying the presence of dead birds through dedicated tools (e.g. smartphone apps) might be exploited as a potential early warning measure, although with low specificity levels.
- In addition to passive surveillance, which remains the most efficient system for the early detection of HPAI viruses, active surveillance could provide more information about the circulation of HPAI strains in wild birds and herd immunity in these populations. This active surveillance needs to be risk based and targeted to appropriate host species, geographical areas, times of year and using suitable methods and reagents (e.g. specific antigens for HI test) to be efficient.
- People exposed to birds which may potentially be infected with AI viruses should take appropriate personal protection measures following national guidelines.
- Because of the extensive genetic diversity existing among HPAI A(H5) viruses of the 2.3.4.4 clade, the adoption of an updated and internationally accepted nomenclature is urgently needed to facilitate epidemiological and evolutionary investigations and to correctly interpret published scientific data.

## 4. Results

### 4.1. Overview of HPAI outbreaks in Europe during the current and previous seasons

Figure 1 shows the HPAI outbreaks detected in birds (poultry, wild and captive birds) in Europe and reported via ADNS for seasons 2016–2017, 2017–2018 and 2018–2019. A season is the period that starts in week 40 and ends in week 39 of the following year.

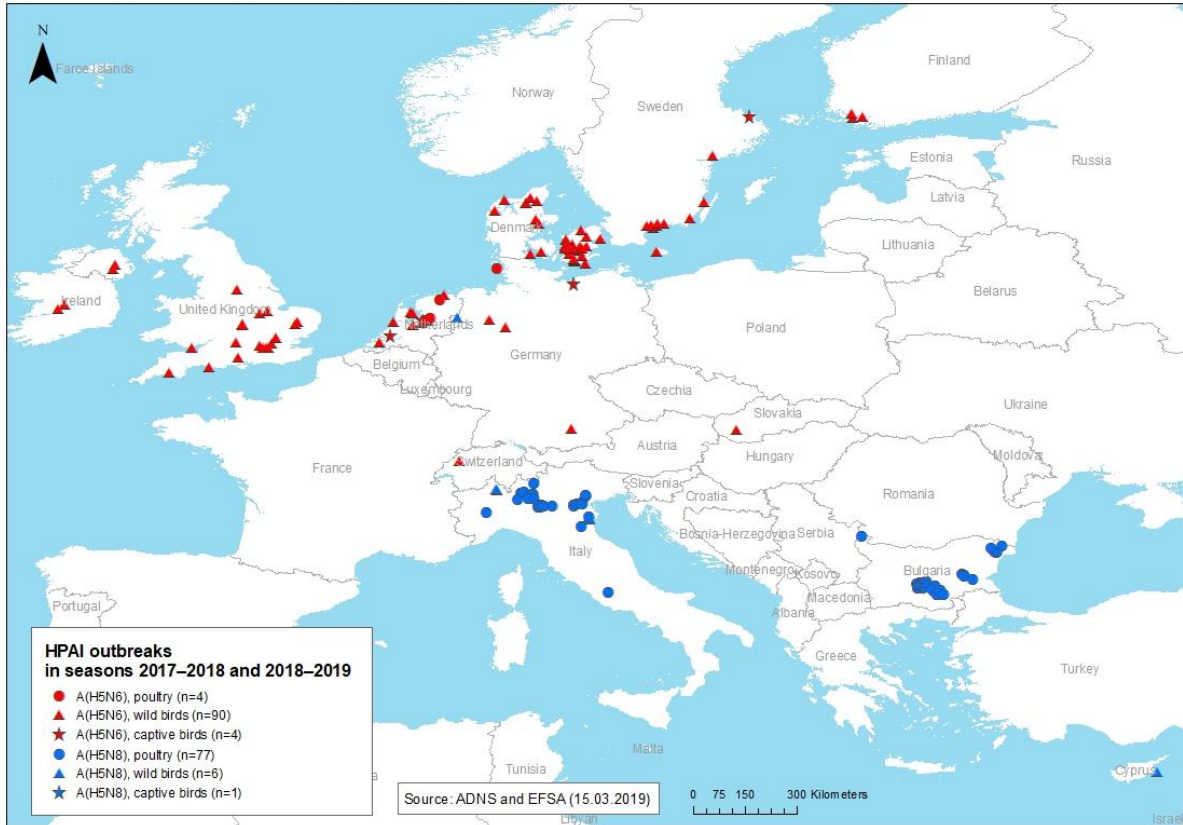
The analysis of the characteristics of the previous and the current AI seasons, i.e. 2017–2018 and 2018–2019 (from 2 October 2017 to 15 February 2019), are reported in Figures 2–6 by geographical distribution, HPAI virus subtype, affected host population and surveillance stream leading to the outbreak detection. Overall, 182 HPAI outbreaks were detected in Europe and reported via ADNS for seasons 2017–2018 and 2018–2019. Of those outbreaks, 98 (54%) were of the A(H5N6) virus subtype and 84 (46%) of the A(H5N8) virus subtype. Of the A(H5N6) outbreaks, 90 (92%) affected wild birds, 4 (4%) poultry and 4 (4%) captive birds; of the A(H5N8) outbreaks, 77 (92%) affected poultry, 6 (7%) wild birds and 1 (1%) captive birds.



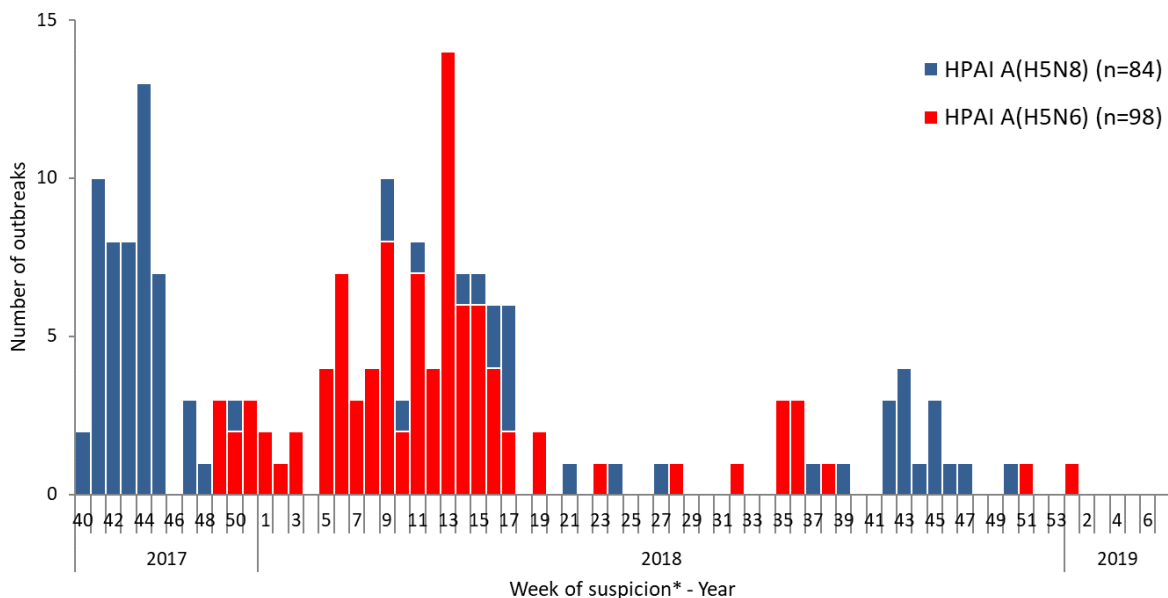
\* When the date of suspicion is not available then the date of confirmation is used to assign the week of suspicion.  
Data source: ADNS, EFSA.

**Figure 1:** Distribution of total number of HPAI outbreaks detected in Europe in seasons 2016–2017 (green), 2017–2018 (orange), 2018–2019 (blue) and reported via ADNS by week of suspicion, 28 September 2015 – 15 February 2019 (n=2,941)



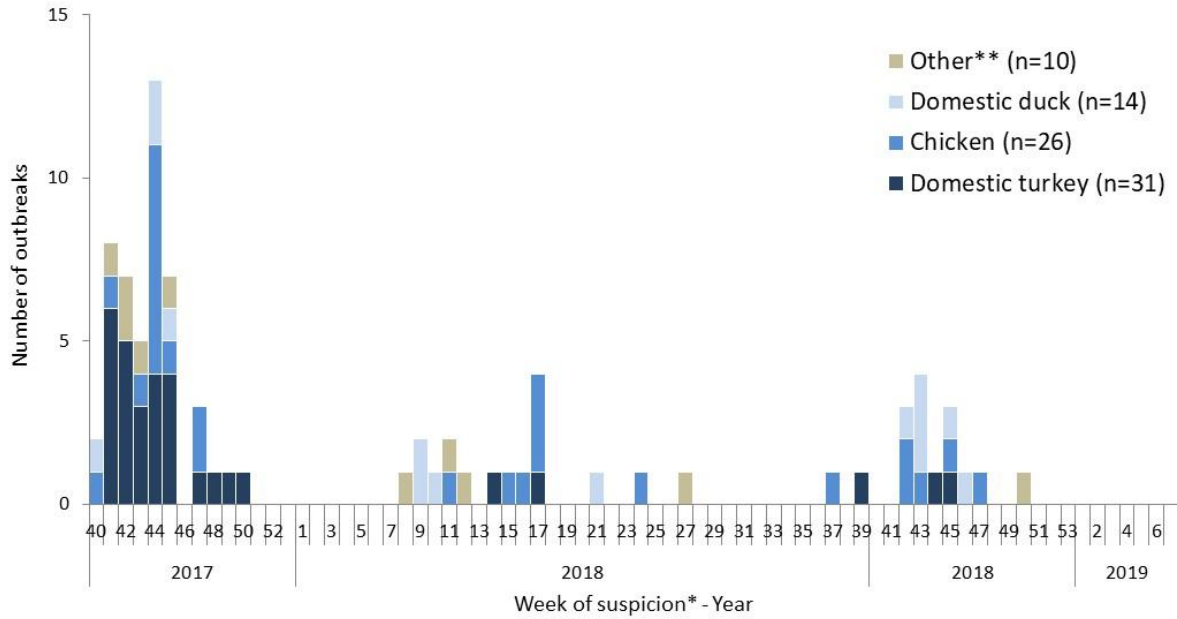


**Figure 2:** Geographical distribution of HPAI outbreaks in Europe based on available geocoordinates by A(H5N6) (red) and A(H5N8) (blue) virus in poultry (circles), wild birds (triangles) and captive birds (stars), in seasons 2017–2018 and 2018–2019 (2 October 2017 – 15 February 2019; n=182)



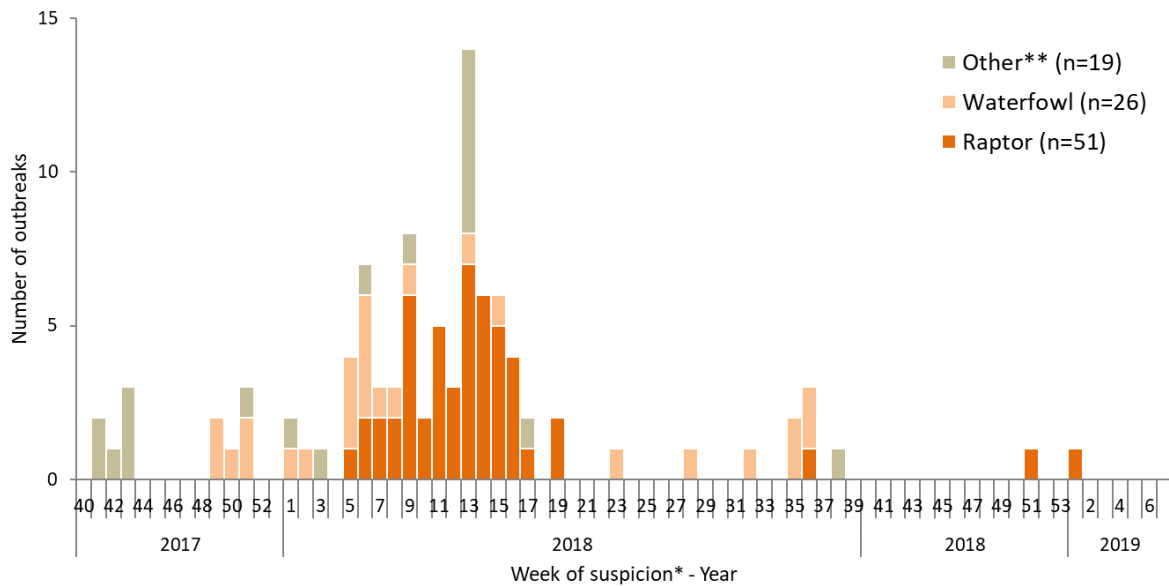
\* When the date of suspicion is not available then the date of confirmation is used to assign the week of suspicion.  
Data source: ADNS, EFSA.

**Figure 3:** Distribution of total number of HPAI A(H5N6) (red) and A(H5N8) (blue) outbreaks in Europe by week of suspicion in seasons 2017–2018 and 2018–2019 (2 October 2017 – 15 February 2019; n=182)



\* When the date of suspicion is not available then the date of confirmation is used to assign the week of suspicion.  
 \*\* 'Other' category contains 'other'<sup>1</sup>, 'mixed' or 'unknown' bird species.  
 Data source: ADNS, EFSA.

**Figure 4:** Distribution of total number of HPAI outbreaks in Europe by week of suspicion in seasons 2017–2018 and 2018–2019 by affected poultry species (2 October 2017 – 15 February 2019; n=81)

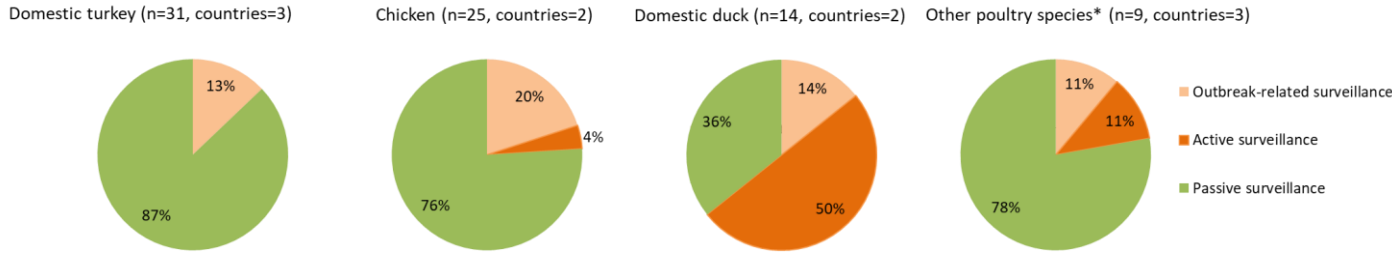


\* When the date of suspicion is not available then the date of confirmation is used to assign the week of suspicion.  
 \*\* 'Other' category contains 'mixed', 'other' or 'unknown' bird species.  
 Data source: ADNS, EFSA.

**Figure 5:** Distribution of total number of HPAI outbreaks in Europe by week of suspicion in seasons 2017–2018 and 2018–2019 by affected wild bird category (2 October 2017 – 15 February 2019; n=96)

<sup>1</sup> black-headed gull (*Chroicocephalus ridibundus*), great cormorant (*Phalacrocorax carbo*), herring gull (*Larus argentatus*), hooded crow (*Corvus cornix*), pheasant (*Phasianus colchicus*), white stork (*Ciconia ciconia*)





\* 'Other poultry species' contains 'other', 'mixed' or 'other' or 'unknown' bird species.  
Data source: ADNS, EFSA.

**Figure 6:** Frequency distribution of HPAI outbreaks in poultry in Europe by bird species and sampling programme leading to the outbreak detection in seasons 2017–2018 and 2018–2019 (2 October 2017 – 15 February 2019; n=79)

## 4.2. HPAI and LPAI outbreaks in Europe, 16 November 2018 – 15 February 2019 (TOR 1 and TOR 2)

### 4.2.1. Description of the avian influenza detections in time and space

#### 4.2.1.1. HPAI and LPAI in poultry, other captive birds and wild birds

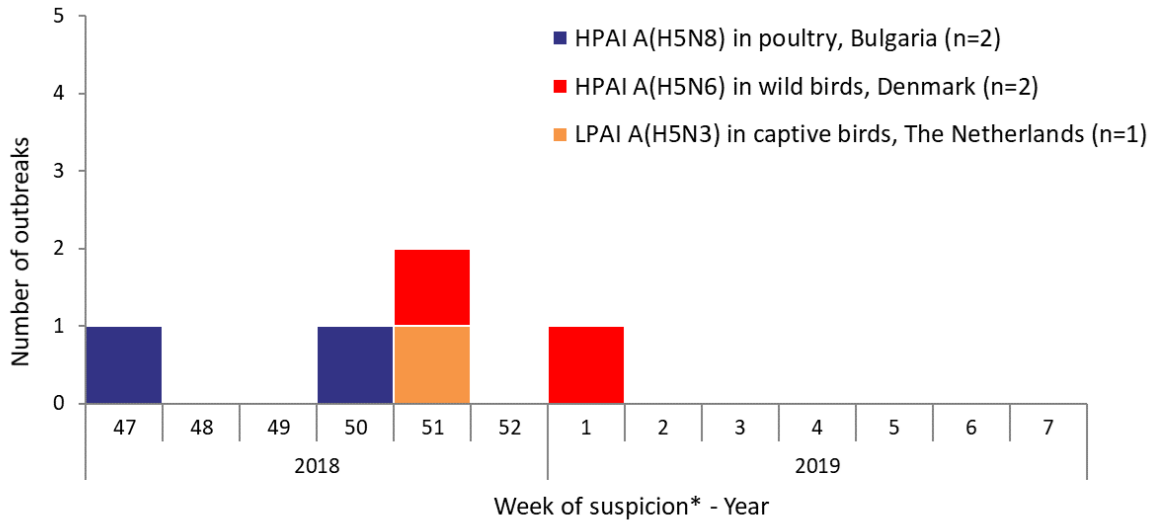
From 16 November 2018 to 15 February 2019, four HPAI outbreaks, two A(H5N6) and two A(H5N8), occurred in European countries and were reported via the ADNS, as presented in Table 1. One LPAI outbreak, an A(H5N3), was also detected during this time period in Europe. The timeline, location and affected subpopulation of the AI outbreaks are reported in Figures 7 and 8. The characterisation of HPAI-affected poultry establishments<sup>2</sup> is reported in Section 4.2.2.1. For wild birds, Table 13 displays the number of outbreaks, whereas the description of cases by outbreak is reported in Section 4.2.2.2. Furthermore, two HPAI A(H5Nx) outbreaks occurred in western Russia; as those outbreaks were not reported via ADNS but via the OIE, they are described in Section 4.4.

**Table 1:** Number of AI outbreaks in Europe by virus subtype and country, 16 November 2018 – 15 February 2019. Data Source: ADNS (15.03.19)

| Country                        | HPAI                  |                    | LPAI                     | All AI |
|--------------------------------|-----------------------|--------------------|--------------------------|--------|
|                                | A(H5N6) in wild birds | A(H5N8) in poultry | A(H5N3) in captive birds |        |
| <b>Bulgaria</b>                | –                     | 2                  | –                        | 2      |
| <b>Denmark</b>                 | 2                     | –                  | –                        | 2      |
| <b>Netherlands</b>             | –                     | –                  | 1 <sup>(a)</sup>         | 1      |
| <b>Total (three countries)</b> | 2                     | 2                  | 1                        | 5      |

(a) Domestic duck and goose species; captive birds are defined as birds kept in captivity for any reason other than the production of commercial products according OIE Terrestrial Animal Health Code as in chapter 10.4 art. 10.4.1 (OIE, online-b).

<sup>2</sup> According to Regulation (EU) 2016/429 'establishment' means any premises, structure, or, in the case of open-air farming, any environment or place, where animals or germinal products are kept, on a temporary or permanent basis, except for: (a) households where pet animals are kept; (b) veterinary practices or clinics. (Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March 2016 on transmissible animal diseases and amending and repealing certain acts in the area of animal health ('Animal Health Law'). OJ L 84, 31.3.2016, p. 1–208).



\* When the date of suspicion is not available then the date of confirmation is used to assign the week of suspicion.  
Data source: ADNS (15.03.19).

**Figure 7:** Distribution of the AI outbreaks in Europe by week of suspicion, virus subtype, affected subpopulation and country, 16 November 2018 – 15 February 2019 (n=5)



**Figure 8:** Geographical distribution of HPAI outbreaks in Europe based on available geocoordinates by virus subtype and affected subpopulation, 16 November 2018 – 15 February 2019 (n=5)

An HPAI A(H5N8) outbreak was confirmed outside the reporting period for this report, on 13 March 2019, in the course of the AI surveillance and control programme, in a duck establishment located in Lovech region, Bulgaria.

Two LPAI outbreaks were detected outside the reporting period for this report in the course of AI surveillance activities in Denmark; an LPAI A(H5) outbreak was detected on 26 February 2019, in a laying hen establishment in the northern part of Denmark; an LPAI A(H7) outbreak was detected on 12 March 2019 in a holding of breeder mallards for the production of gamebirds in the island of Funen in the southern part of Denmark.

#### 4.2.2. Phenotypic characterisation of avian influenza viruses circulating in Europe

##### 4.2.2.1. HPAI in domestic birds

###### *Characterisation of the HPAI-affected poultry establishments*

From 16 November 2018 to 15 February 2019, two HPAI outbreaks A(H5N8) were notified in the poultry sector by Bulgaria (Figure 7). Both outbreaks were detected by passive surveillance as animals reared showed clinical signs of HPAI virus infection. The source of infection has not been identified for either outbreaks. The outcome of the epidemiological investigation for the outbreak affecting mixed poultry species was inconclusive, as no wild birds were found dead in that area, nor was any morbidity or mortality notified in other poultry establishments located in the vicinity of the affected establishment. An overview of the characteristics of the affected establishments and species reared is given in Table 2.

**Table 2:** Characteristics of the A(H5N8) HPAI-affected poultry establishments in Europe, 16 November 2018 – 15 February 2019 (n=2). Data source: ADNS and EFSA

| Country      | Poultry species        | Production category | Surveillance stream | Presence of signs in the outbreaks | Outdoor access | Date of suspicion <sup>(a)</sup> | Number of susceptible animals <sup>(b)</sup> | Number of people exposed |
|--------------|------------------------|---------------------|---------------------|------------------------------------|----------------|----------------------------------|--|--------------------------|
| Bulgaria     | Chicken <sup>(c)</sup> | Egg                 | Passive             | Yes                                | Yes            | 20/11/2018                       | 50   | 2                        |
|              | Mixed <sup>(c,d)</sup> | Mixed               | Passive             | Yes <sup>(e)</sup>                 | Yes            | 14/12/2018                       | 403  | 1                        |
| <b>Total</b> |                        |                     |                     |                                    |                |                                  | 453  | 3                        |

(a) Date of confirmation is provided when the date of suspicion is not available.

(b) Based on the number of susceptible domestic birds reported to EFSA.

(c) Non-commercial establishment.

(d) Pigeons (n=350), laying hens (n=50) and pheasants (n=3).

(e) Clinical signs were observed in laying hens and pheasants; mortality was observed in laying hens (38/50) and pigeons (1/350).

###### *Information extracted from the scientific literature*

No new relevant information was published during the reporting period.

##### 4.2.2.2. HPAI in wild birds

###### *Pathogenicity in the affected species*

From 16 November 2018 to 15 February 2019, two HPAI outbreaks A(H5N6) in wild birds were notified by Denmark (Table 3). This involved a white-tailed eagle and a common buzzard, both found dead in Denmark. Given the susceptibility of these species to severe disease from HPAI virus infections (van den Brand et al., 2015; Krone et al., 2018), it is likely that HPAI virus A(H5N6) infection was the cause of death of these two birds; pathological analysis would be needed to confirm this. The most likely route of infection of these two raptors is hunting or scavenging infected wild waterfowl (van den Brand et al., 2015). Since HPAI virus was not detected by passive surveillance in wild waterfowl or other wild birds in Denmark in this period, it suggests that testing such raptor species could be a sensitive method for detecting the presence of HPAI virus in the environment, when the overall mortality rate in wild birds from HPAI is low.

**Table 3:** Cases of HPAI A(H5N6) infection in free-living wild birds in Europe reported to the World Organisation for Animal Health (OIE) by country, outbreak and species, 16 November 2018 – 15 February 2019 (OIE, online-a)

| OIE report number | Country | Number of outbreaks by country | Number of cases by outbreak | Number of wild bird species involved in the outbreak | Wild bird species involved in the country  | Total wild bird cases by country |
|-------------------|---------|--------------------------------|-----------------------------|--|--|----------------------------------|
| 29272             | Denmark | 2                              | 1, 1                        | 1, 1   | Whitetailed eagle ( <i>Haliaeetus albicilla</i> ), common buzzard ( <i>Buteo buteo</i> ) | 2                                |
| <b>Total</b>      |         | <b>2</b>                       | -                           | -  | <b>2</b>   | <b>2</b>                         |

*Information extracted from the scientific literature*

No new relevant information was published during the reporting period.

#### 4.2.3. 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 H5 viruses has rapidly evolved since the most recent update of the nomenclature of the A/goose/Guangdong/1/1996-lineage H5Nx virus (Smith et al., 2015). While a revised nomenclature of clade 2.3.4.4 viruses is pending, the genetic clustering described by Lee and al., (2016a) is used in this report. The authors recognised four genetic groups (a, b, c, d) within clade 2.3.4.4 that have been identified in China since late 2012. Clades 2.3.4.4a and 2.3.4.4b A(H5N8) viruses spread globally through wild bird migration during 2014–2015 (2.3.4.4.a) and 2016–2017 (2.3.4.4.b), while clades 2.3.4.4c and 2.3.4.4d A(H5) HPAI viruses have mainly circulated in poultry in Asia (Smith et al., 2015; Lee et al., 2016b; Lee et al., 2017; Lee et al., 2018). The latter genetic groups have been sporadically associated with human infections in South-east Asia (Lee et al., 2016b; Lee et al., 2017). One human case in China was infected with A(H5N6) of the 2.3.4.4b clade in 2017 with a different gene composition to viruses circulating in birds in Europe.

*Genetic characterisation of AI viruses circulating in the Europe*

Phylogenetic analysis of the HA gene of the HPAI A(H5N6) viruses identified in wild birds in Denmark between late December 2018 and early January 2019 revealed that they belong to clade 2.3.4.4b and cluster with A(H5N6) viruses that have been circulating in Europe since December 2017. Specifically, the complete HA gene of the virus isolated from the white-tailed eagle, found dead on 22 December 2018, shows the highest similarity with the A(H5N6) strains collected in Denmark, Germany, the Netherlands and Georgia in 2017–2018 (Lee et al., 2018). The phylogeny also confirms that the HA gene sequence of the Danish HPAI A(H5N6) viruses is not related to the zoonotic A(H5N6) virus (clade 2.3.4.4c) currently circulating mainly in poultry in Asia.

The complete genome of one A(H5N6) virus collected in October 2018 from a common gull, subspecies *heinei*, in the Saratov region, western Russian was released by GISAID (online) in February 2019. The HA gene of this virus belongs to zoonotic clade 2.3.4.4c and presents the highest similarity with A(H5N6) viruses responsible for human cases reported in China between August and October 2018 (nucleotide sequence identity of 99%–99.4%). Analyses of the remaining gene segments confirm this clustering. Unlike the Chinese strains associated with human infections, the Russian virus does not contain mutation E627K in the PB2, which is associated with the adaptation of AI viruses to mammalian species (Subbarao et al., 1993). The subspecies *heinei* of the common gull breeds from east of Moscow and between the Kanin Peninsula and the basin of the Lena River. It winters from the Baltic Sea to the Black Sea and in northwest Europe, and more rarely from the Persian Gulf to Pakistan (Olsen and Larsson, 2003).

Furthermore, the complete genomes of the viruses responsible for the A(H5N8) outbreaks reported in poultry in western Russian between June and November 2018 have recently been made available by

GISAID. The phylogenetic tree topology of the A(H5N8) viruses demonstrates that the Russian HA sequences fall within the clade 2.3.4.4b, but are phylogenetically distinguishable from the HA gene of the Bulgarian A(H5N8) viruses described in the EFSA report for August – November 2018 (EFSA et al., 2018d).

Characterisation of the phylogenetic clustering of the partial HA gene of the A(H5N3) LPAI virus detected in captive geese and ducks in late December 2018 in the Netherlands revealed that the virus shows the highest similarity with the sequences of the H5 LPAI viruses previously detected in wild and domestic Anseriformes in Europe (i.e. Italy, France and Ukraine).

#### **4.2.4. Human cases due to A(H5N8) or A(H5N6) viruses detected in Europe**

No human infection with A(H5N6) or A(H5N8) viruses, as detected in wild birds and poultry in Europe, has been reported so far (Adlhoch et al., 2018). However, in a study from Russia, sera from people exposed to infected or perished birds during the AI outbreaks between November 2016 and March 2017 tested reactive for antibodies to A(H5N1) clade 2.3.2.1c and A(H5N8) clade 2.3.4.4. (Ilyicheva et al., 2018). Bulgaria reported to EFSA that a total of three people were exposed to poultry infected with HPAI A(H5N8) during the outbreaks that occurred in the country from 16 November 2018 to 15 February 2019 (Table 2).

### **4.3. Applied prevention and control measures in Europe, 16 November 2018 – 15 February 2019 (TOR 3)**

#### **4.3.1. Bulgaria**

Two more HPAI A(H5N8) cases were confirmed in poultry establishments in Bulgaria before the end of 2018 (Table 1, Figure 7). Control measures already in force were thus prolonged to cover the whole period of reference of this report.

For the detailed description of the control and prevention measures applied, see Annex A.1 in Avian Influenza Overview August – November 2018 (EFSA et al., 2018d).

#### **4.3.2. Denmark**

Following the confirmation of HPAI A(H5N6) in a white-tailed eagle and a common buzzard found dead on 22 December 2018 and 4 January 2019, respectively, a series of measures were applied to raise awareness among poultry associations and hunting associations.

More details on the applied measures can be found in Annex A.

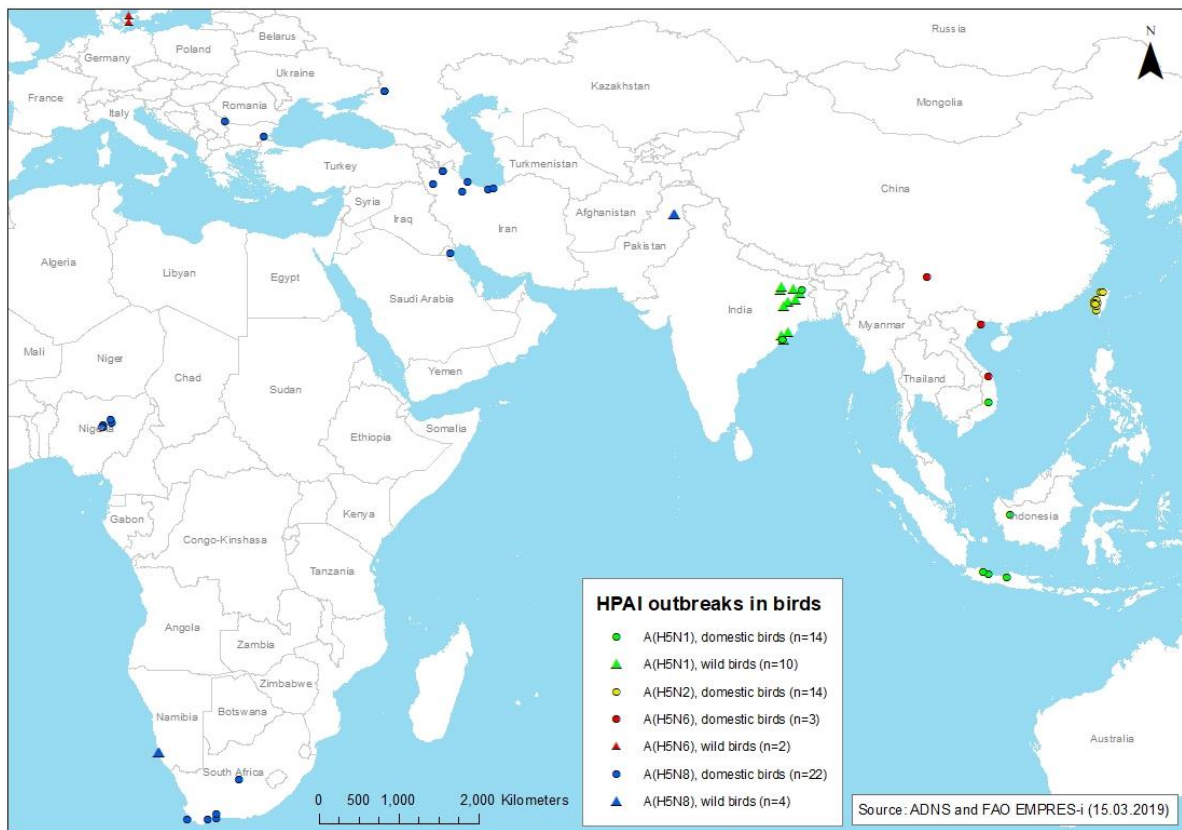
### **4.4. The avian influenza situation in other countries not reporting via ADNS, 16 November 2018 – 15 February 2019 (TOR 4)**

An overview of the HPAI outbreaks reported from other countries not reporting via ADNS but via the OIE or national authorities from 16 November 2018 to 15 February 2019 is presented in Table 4 and Figure 9. For the purposes of this report, only findings of AI viruses occurring in countries that are considered to be of epidemiological interest for the EU/EEA or of public health relevance are described.



**Table 4:** Number of HPAI outbreaks in other countries not reporting via ADNS by virus subtype and country, 16 November 2018 – 15 February 2019 (n=65)

| Region                      | Country       | HPAI A(H5N1)   |            | HPAI A(H5N2)   | HPAI A(H5N6)   | HPAI A(H5N8)   |            | All HPAI  |
|-----------------------------|---------------|----------------|------------|----------------|----------------|----------------|------------|-----------|
|                             |               | Domestic birds | Wild birds | Domestic birds | Domestic birds | Domestic birds | Wild birds | All birds |
| <b>Africa</b>               | Namibia       |                |            |                |                |                | 2          | 2         |
|                             | Nigeria       |                |            |                |                | 5              |            | 5         |
|                             | South Africa  |                |            |                |                | 5              |            | 5         |
| <b>Asia</b>                 | China         |                |            |                | 1              |                |            | 1         |
|                             | India         | 9              | 10         |                |                |                |            | 19        |
|                             | Indonesia     | 4              |            |                |                |                |            | 4         |
|                             | Iran          |                |            |                |                | 7              |            | 7         |
|                             | Kuwait        |                |            |                |                | 1              |            | 1         |
|                             | Pakistan      |                |            |                |                |                | 2          | 2         |
|                             | Taiwan        |                |            | 14             |                |                |            | 14        |
|                             | Vietnam       | 1              |            |                | 2              |                |            | 3         |
|                             | <b>Europe</b> | Russia         |            |                |                |                | 2          |           |
| <b>Total (12 countries)</b> |               | <b>14</b>      | <b>10</b>  | <b>14</b>      | <b>3</b>       | <b>20</b>      | <b>4</b>   | <b>65</b> |



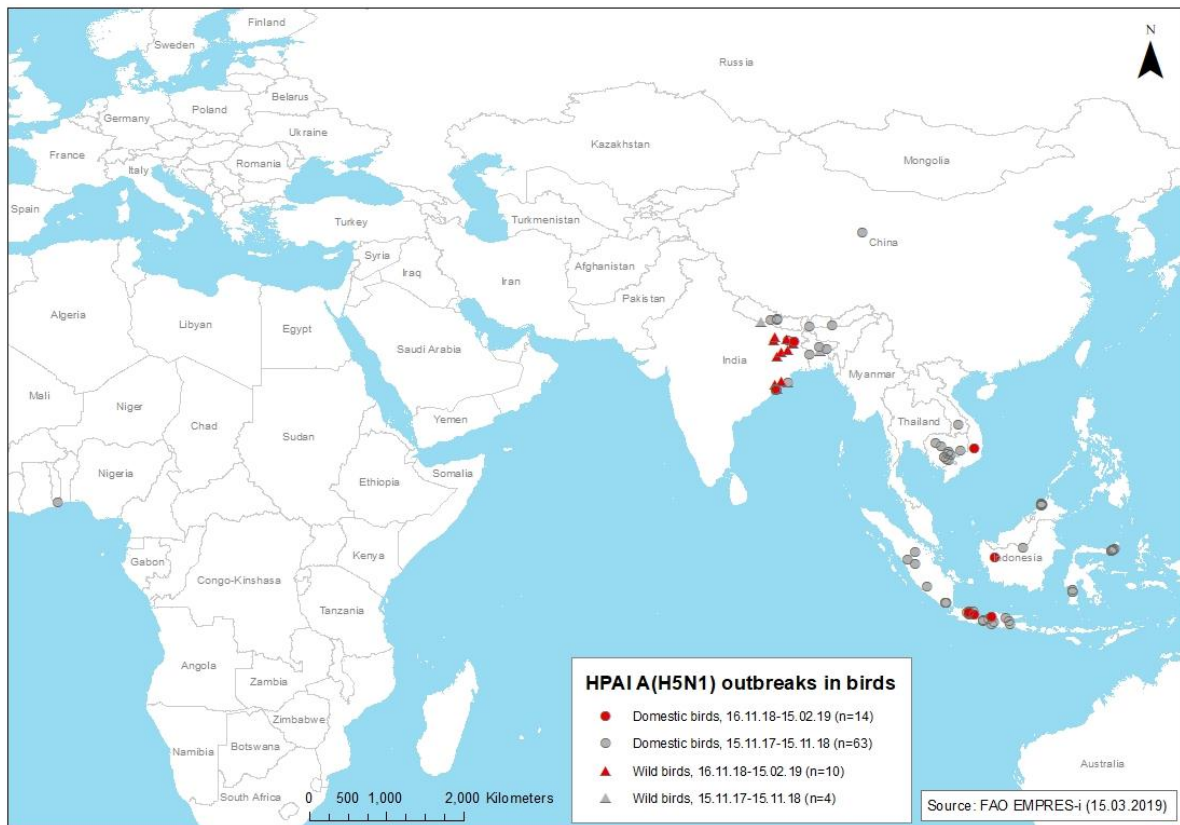
**Figure 9:** Geographical distribution of HPAI outbreaks in Europe, Asia and Africa in domestic birds (circles) and wild birds (triangles) by A(H5N1) (green), A(H5N2) (yellow), A(H5N6) (red), A(H5N8) (blue), based on available geocoordinates, 16 November 2018 – 15 February 2019 (n=69)

#### 4.4.1. HPAI A(H5N1)

##### 4.4.1.1. Domestic and wild birds

###### *Detections*

Outbreaks of the Asian lineage HPAI A(H5N1) in poultry and wild birds have only been reported in Asia. From 16 November 2018 to 15 February 2019, India, Indonesia and Vietnam reported about new outbreaks of HPAI A(H5N1) virus in backyard poultry and on medium-sized commercial establishments. In contrast to the previous reporting periods, India reported the detection of HPAI A(H5N1) in dead house crows (*Corvus splendens*), Indian peafowl (*Pavo cristatus*) and Indian pond herons (*Ardeola grayii*) in the provinces of Bihar and Orissa (OIE, 2019a) (Figure 10). Reports in the media suggest that the outbreak in India is continuing in 2019.



**Figure 10:** Geographical distribution of confirmed HPAI A(H5N1) outbreaks based on available geocoordinates in domestic birds (circles) and wild birds (triangles); grey symbols indicate outbreaks that occurred from 15 November 2017 to 15 November 2018, red symbols indicate outbreaks that occurred from 16 November 2018 to 15 February 2019 (n=91) (FAO, online-b)

###### *Information extracted from the scientific literature*

No new relevant information was published during the reporting period.

##### 4.4.1.2. A(H5N1) in mammals (excluding humans)

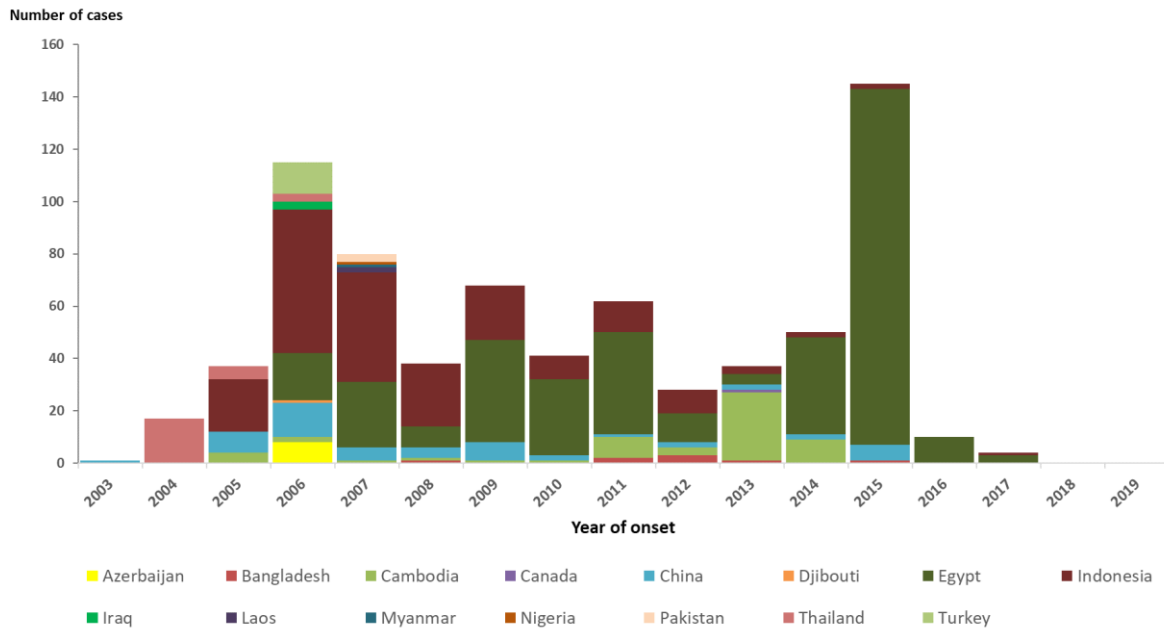
The usefulness of tupaia (northern tree shrew, *Tupaia belangeri*) as an animal model to study human influenza virus infections was checked by (Sanada et al., 2019). Severe pneumonia accompanied by fever and weight loss was observed following infection with A/Vietnam/UT3040/2004 (H5N1) isolate. One animal (out of four) died at 5 days post infection. The viral RNA was detected in nasal, oral and conjunctival swabs. The authors suggest that tupaia can serve as a candidate for alternative animal



model to study AI virus infections due to the relatively close genetic similarity to primates, similar distribution of influenza virus receptors in the respiratory tract, easy handling and low cost of breeding.

#### 4.4.1.3. Human infections due to A(H5N1)

No new human cases due to AI A(H5N1) have been reported worldwide in 2018 and 2019. Since 2003, and as of 15 February 2019, 860 laboratory-confirmed cases of human infection with AI A(H5N1) virus, including 454 deaths, have been reported from 16 countries outside the EU/EEA (WHO, 2019c, b). The latest case was reported in September 2017 by Indonesia (Figure 11).



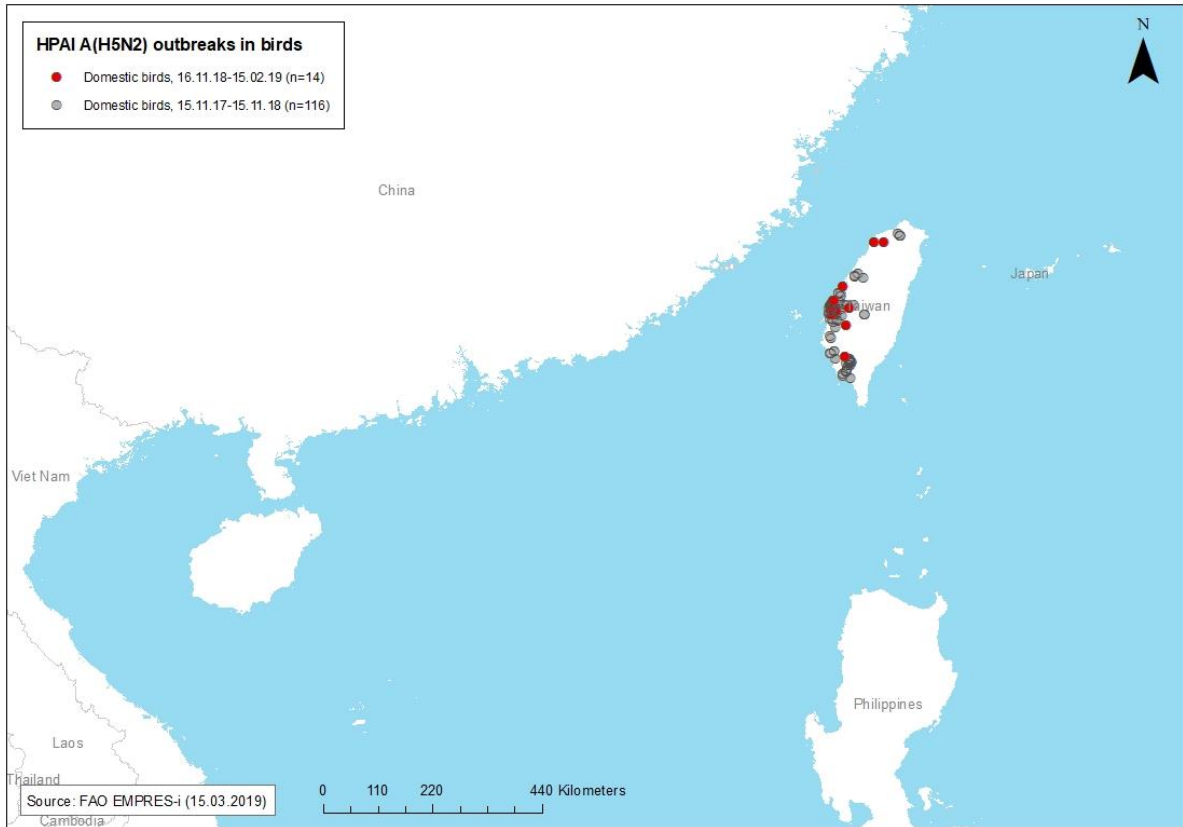
Data source: WHO (WHO, 2019c, b).

**Figure 11:** Distribution of confirmed human cases of A(H5N1) by year and country of reporting, 2003 – 15 February 2019 (n=860)

#### 4.4.2. HPAI A(H5N2)

##### Detections

Asian lineage HPAI A(H5N2), clade 2.3.4.4 has been in circulation in Taiwan since 2012 and caused severe outbreaks on chicken, duck, goose and turkey establishments, but not in wild birds (Lee et al., 2014; Lee et al., 2016c). In the relevant reporting period, Taiwan notified 14 new outbreaks of HPAI A(H5N2) on backyard and mainly medium-sized poultry, duck and goose establishments to the OIE (Figure 12). The Taiwanese lineage of HPAI A(H5N2) differs from the Eurasian HPAI A(H5N2) lineage, belonging to clade 2.3.4.4b, which has been spreading in Russia as well as in Asian countries in 2016 – 2018 (EFSA et al., 2018d).



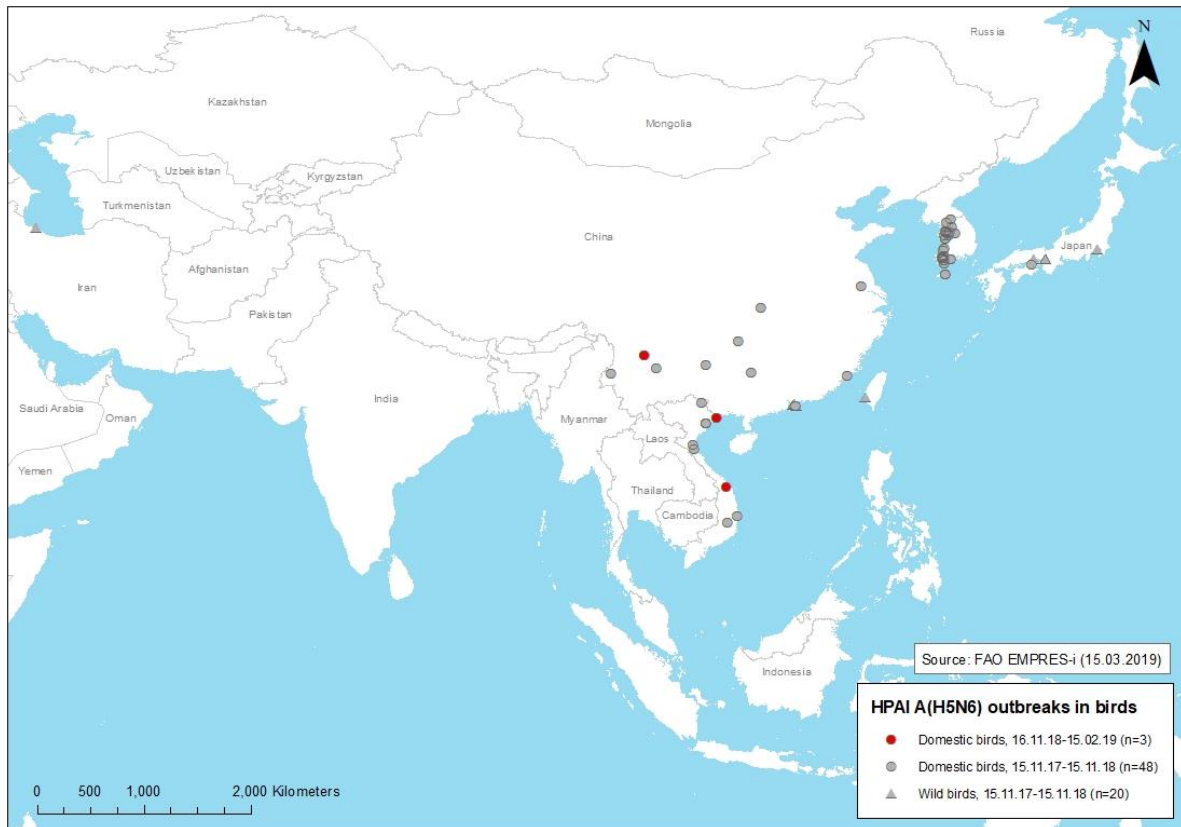
**Figure 12:** Geographical distribution of confirmed HPAI A(H5N2) outbreaks based on available geocoordinates in domestic birds; grey symbols indicate outbreaks that occurred from 15 November 2017 to 15 November 2018, red symbols indicate outbreaks that occurred from 16 November 2018 to 15 February 2019 (n=130) (FAO, online-b)

#### 4.4.3. HPAI A(H5N6)

##### 4.4.3.1. Domestic and wild birds

###### *Detections*

Between 16 November 2018 and 15 February 2019, China and Viet Nam reported further outbreaks of the zoonotic reassortant of HPAI A(H5N6) (2.3.4.4c) on commercial poultry establishments. In the time period relevant for this report, no cases of A(H5N6) in wild birds HPAI virus were detected in Asia (Figure 13).



**Figure 13:** Geographical distribution of confirmed HPAI A(H5N6) outbreaks based on available geocoordinates in domestic birds (circles) and wild birds (triangles); grey symbols indicate outbreaks that occurred from 15 November 2017 to 15 November 2018, red symbols indicate outbreaks that occurred from 16 November 2018 to 15 February 2019 (n=71) (FAO, online-b)

#### *Information extracted from the scientific literature*

Genetic characterisation of HPAI virus A(H5N6) clade 2.3.4.4c from wild birds overwintering on the Izumi plain in Japan in 2016–2017 enabled the identification of two previously unreported genotypes designated C-7 and C-8 in cranes (Ozawa et al., 2019). The PB2, PB1, PA and NS segments of the novel genotypes showed close relatedness to the respective segments of LPAI virus detected in duck faeces and water samples collected from the same sampling site and during the same period, highlighting the high propensity for reassortment between HPAI A(H5N6) virus clade 2.3.4.4 and LPAI virus.

The pathogenicity, infectivity and transmissibility of two South Korean A(H5N6) clade 2.3.4.4 viruses representing distinct genotypes (C-1 and C-4) that differed in their PA and NS genes were tested in two-week-old domestic Pekin ducks. The C-4 genotype showed higher pathogenicity than the C-1, reflected by the higher mortality, more pronounced lesions and higher amount of excreted virus, underlining the importance of an LPAI virus contribution to the genome composition of an HPAI virus reassortant and its impact on the pathobiology of A(H5) clade 2.3.4.4 infections in domestic waterfowl (Kwon et al., 2019).

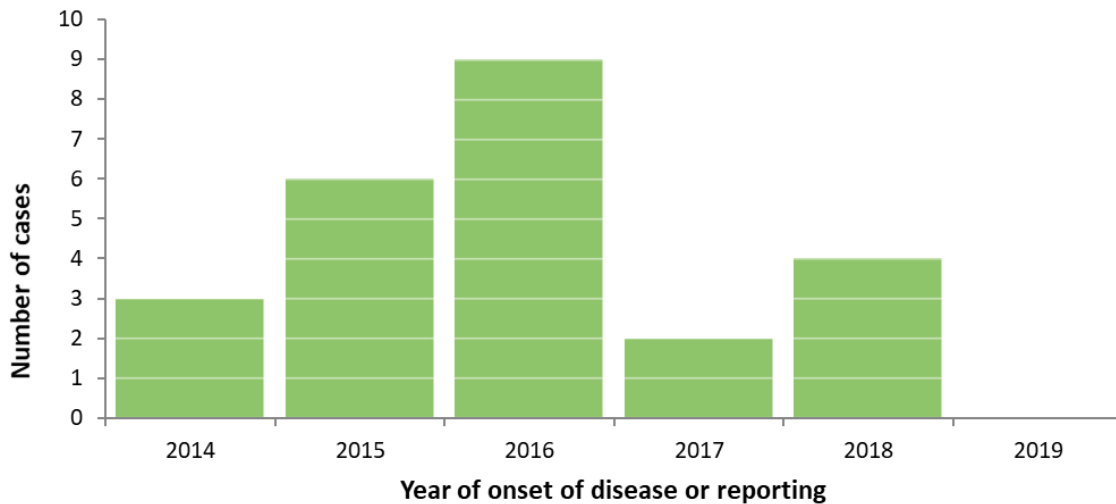
Infection of chickens, Pekin and Muscovy ducks with A(H5N6) clade 2.3.4.4 isolates with different gene constellations confirmed that the virulence in chickens was significantly higher than in ducks. Interestingly, one chicken (out of five) infected with  $10^6$  EID<sub>50</sub> of an A(H5N6) isolate of Muscovy duck-origin survived the 14-day observation period, shed the virus and seroconverted (Uchida et al., 2019).

#### **4.4.3.2. A(H5N6) in mammals (excluding humans)**

No new relevant information was published during the reporting period.

#### 4.4.3.3. Human infections due to A(H5N6)

No new human case due to AI A(H5N6) has been notified since the last EFSA report (EFSA et al., 2018d). Since 2014, and as of 15 February 2019, 24 laboratory-confirmed cases of human infection with AI A(H5N6) viruses of clade 2.3.4.4 circulating in South-east Asia have been reported globally (Figure 14). WHO lists 23 human cases of AI A(H5N6), including 15 with fatal outcomes (WHO, 2019c). One additional case from 2015 was described in a publication (Li et al., 2016). Twelve deaths due to A(H5N6) had been reported between 2014 and 2017 (Jiang et al., 2017). All of the cases were infected and detected in mainland China (WHO, 2018a).



Source: Data used from ECDC line list (described above).

**Figure 14:** Number of human cases due to A(H5N6), clade 2.3.4.4, infection by year of onset, China 2014 – 2019 (n=24)

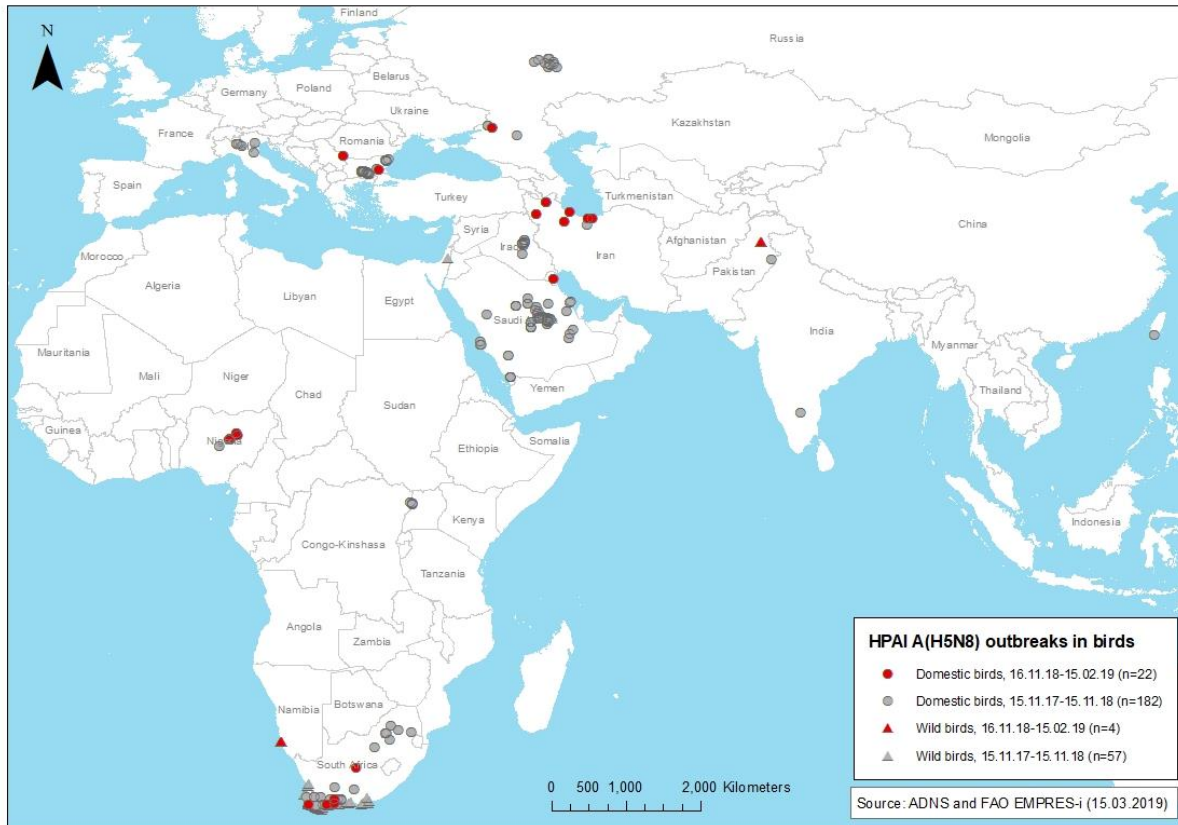
#### 4.4.4. HPAI A(H5N8)

##### 4.4.4.1. Domestic and wild birds

###### Detections

Further outbreaks of HPAI A(H5N8), clade 2.3.4.4b, were reported on ostrich establishments between 16 November 2018 and 15 February 2019 in Northern and Western Cape Provinces, South Africa. Furthermore, in Nigeria, HPAI A(H5N8) was detected on medium-sized poultry establishments for the first time since June 2017. In the reporting period Iran notified several outbreaks of HPAI A(H5N8) in commercial chicken, duck and turkey establishments. The HPAI A(H5N8) positive samples notified by Kuwait were collected from a pet shop at a live bird market in the province of Al Farwaniyah. Furthermore, Russia reported further outbreaks of HPAI A(H5N8) on two large-sized turkey establishments in the Rostovskaya Oblast in January 2019 (OIE, 2019c) (Figure 15).

In January 2019 Namibia reported the first outbreak of HPAI A(H5N8) in the country. The virus was detected in jackass penguins (*Spheniscus demersus*) showing clinical signs on Halifax Island near Lüderitz in the Karas region in the southern parts of the country. According to the report, no further wild bird species on the island were affected. Furthermore, Pakistan notified to OIE several detections of HPAI A(H5N8) in mallards (*Anas platyrhynchos*), common guineafowl (*Numida meleagris*), Coscoroba swan (*Coscoroba coscoroba*) and house crows (*Corvus splendens*) in Islamabad in February 2019 (OIE, 2019b) (Figure 15).



**Figure 15:** Geographical distribution of confirmed HPAI A(H5N8) outbreaks based on available geocoordinates in domestic birds (circles) and wild birds (triangles); grey symbols indicate outbreaks that occurred from 15 November 2017 to 15 November 2018, red symbols indicate outbreaks that occurred from 16 November 2018 to 15 February 2019 (n=265) (FAO, online-b)

#### *Information extracted from the scientific literature*

As a response to large die-offs of wild pigeons and doves during the HPAI A(H5N8) epidemic in South Africa in 2017, an experiment was carried out in which 11-week-old pigeons were infected with an A(H5N8) clade 2.3.4.4 B virus isolated from a speckled pigeon (Abolnik et al., 2018). Three different doses were used: low ( $10^3$ EID<sub>50</sub>), medium ( $10^{4.5}$ EID<sub>50</sub>), and high ( $10^6$ EID<sub>50</sub>). Contact pigeons and SPF chickens were co-housed with inoculated pigeons. No mortality or clinical signs were observed in any of the birds during the 14-day observation period. Low amounts of the virus ( $< 10^3$ EID<sub>50</sub>/ml) were shed from the oropharynx and cloaca of pigeons inoculated with medium and high doses and were successfully transmitted to contact pigeons (but not to chickens). The authors concluded that the mass mortality of pigeons and doves observed in the field was most likely caused by potential concurrent infections with other highly virulent agents (e.g. avian avulavirus -1), and that pigeons are unlikely to play a role in the maintenance and transmission of HPAIV H5 clade 2.3.4.4 to other avian hosts.

#### **4.4.4.2. A(H5N8) in mammals (excluding humans)**

No new relevant information was published during the reporting period.

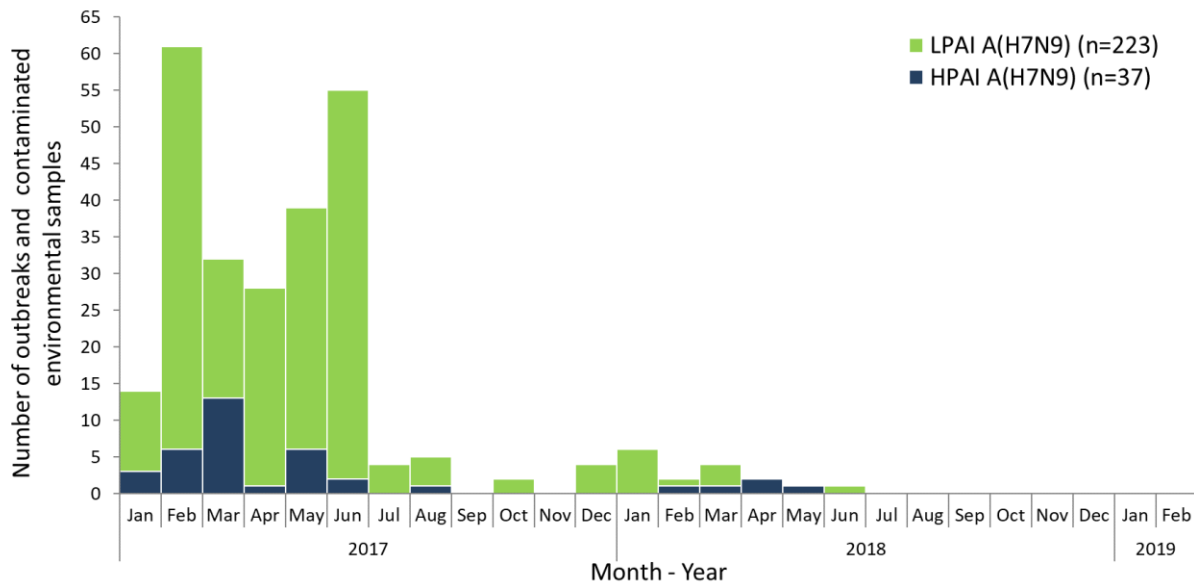
#### **4.4.5. HPAI-LPAI A(H7N9)**

##### **4.4.5.1. Domestic and wild birds**

#### *Detection*

No LPAI or HPAI A(H7N9) cases were notified in poultry or in wild birds within the time period being relevant for this report. The last case had been reported from Anhui province on the 29 June 2018 (see

Figure 16). By providing monthly publications, the Chinese Ministry of Agriculture and Rural Affairs (MoA, online) guarantees regular updates on the outcomes of surveillance activities and vaccination campaigns conducted since September 2017 (Zeng et al., 2018). These results are also available on the EMPRES-i website of the Food and Agriculture Organization (FAO, online-b). However, since the last official information in June 2018, no further reports were provided by the Chinese Ministry of Agriculture and Rural Affairs (MoA, online). Furthermore, LPAI A(H7N9) virus was detected in January 2019 in an environmental sample from wild birds at a live bird market in South Korea. The information received detailed no evidence whether this virus is closely related to the A(H7N9) circulating in China (FAO, online-a).



Data source: FAO EMPRES-i (16.02.2019)

**Figure 16:** Distribution of confirmed LPAI and HPAI A(H7N9) outbreaks in birds and contaminated environmental samples in China by month, 1 January 2017 – 15 February 2019 (n=260)

#### *Information extracted from the scientific literature*

The complete genome sequence of a multiple reassortant A(H7N3) HPAI virus detected in duck meat illegally carried on board an aircraft from China to Japan in March 2018 revealed that the HA gene of the isolate showed a close relationship with a Chinese A(H7N9) HPAI virus (Shibata et al., 2019).

AI A(H7N6) identified in poultry in China might have emerged from reassortant events between A(H7N9) and A(H5N6) viruses. A study demonstrates binding affinity for human-like  $\alpha 2, 6$ -linked sialic acid receptors and virulence in mice without prior adaptation (Zhao et al., 2019). The analysed viruses were transmissible in guinea pigs directly and via respiratory droplets.

#### **4.4.5.2. Human infections due to A(H7N9)**

No human cases due to AI A(H7N9) have ever been reported from Europe and no human cases have been reported globally since the last EFSA report published in December 2018 (WHO, 2018b, online-a). The latest case was reported from China in February 2018. Since February 2013, a total of 1,567 human cases have been reported from outside of Europe, including at least 615 deaths (39%) (WHO, online-a). Thirty-two human cases have been due to infection with HPAI virus A(H7N9) according to the Chinese National Influenza Center (Chinese National Influenza Center, online).

#### *Information extracted from the scientific literature*

Patients infected with LPAI or HPAI A(H7N9) showed similar clinical disease severity. However, a higher case–fatality and prevalence of resistance to neuraminidase inhibitors were identified in patients infected with HPAI (Yang et al., 2019b).



A retrospective cohort study of A(H7N9) cases identified age, number of days between onset and confirmation or oseltamivir treatment, body temperature and white blood cell count to be associated with fatal outcome (Yang et al., 2019a).

A recent study analysed packaging signals that serve as segment identifiers and enable segment-specific packaging in respect to the reassortment of A(H5N8) and A(H7N9) viruses with seasonal A(H3N2) influenza viruses (White et al., 2019). HA segments carrying A(H5) or A(H7) packaging signals were shown to be significantly disfavoured for incorporation into a seasonal A(H3N2) virus and showed a reduced likelihood of reassortment feasibility of seasonal and AI viruses due to the divergence of the packaging signals of the HA segment.

Amino acid changes in A(H7N9) viruses were studied over time and a series of such changes was identified that might be associated with cross-species transmission from avian to human in both human- and avian-isolated A(H7N9) viruses. Six of the identified amino acid sites in HA1 are receptor binding sites and PB2-A588V was shown to promote mammal adaptation (Pu et al., 2018).

The effect of meteorological factors including total rainfall, average wind speed, average temperature, average relative humidity, and sunshine duration on the risk of human A(H7N9) infection in Zhejiang was studied. Rainfall and wind speed were found to be associated with the risk of human A(H7N9) infection (Lau et al., 2018).

#### 4.4.6. LPAI A(H9N2)

##### 4.4.6.1. Domestic and wild birds

###### *Detection*

As mentioned in previous reports (EFSA et al., 2018b; EFSA et al., 2018c), A(H9N2) is the most commonly detected non-notifiable subtype of influenza viruses in poultry in Asia, the Middle East and North Africa (Bonfante et al., 2018; Chrzastek et al., 2018; Xu et al., 2018; Zhu et al., 2018). The endemic status of these regions continued between 16 November 2018 and 15 February 2019.

###### *Information extracted from the scientific literature*

The close genetic similarity of an A(H9N2) isolate detected in a broiler flock in Iran at the end of 2017 and A(H9N2) strains in Pakistan and other neighbouring Middle-Eastern countries provided additional evidence of a continued circulation of the G1-lineage A(H9N2) in the region (Fallah Mehrabadi et al., 2019; Zhang et al., 2019) found that internal gene sequences of four A(H9N2) viruses from domestic birds in 2015–2016 in China (Guangdong) are similar to human A(H7N9) viruses.

##### 4.4.6.2. Human infections due to A(H9N2)

Six additional human cases have been reported or identified from peer-reviewed literature since the last EFSA report (Ali et al., 2019; WHO, 2019a; Macau Special Administrative Region Government, online; Taiwan Centres for Disease Control, online). The most recent case was reported from China on 15 February 2019 with disease onset on 27 January 2019 (Macau Special Administrative Region Government, online). Since 1998, and as of 15 February 2019, 54 laboratory-confirmed cases of human infection with AI A(H9N2) virus, including one death, have been reported globally. Cases were reported from China (46), Egypt (4), Bangladesh (3), and Pakistan (1) (Figure 17). The latest case had been reported from China on 15 February 2019 with disease onset 27 January 2019 (Macau Special Administrative Region Government, online)

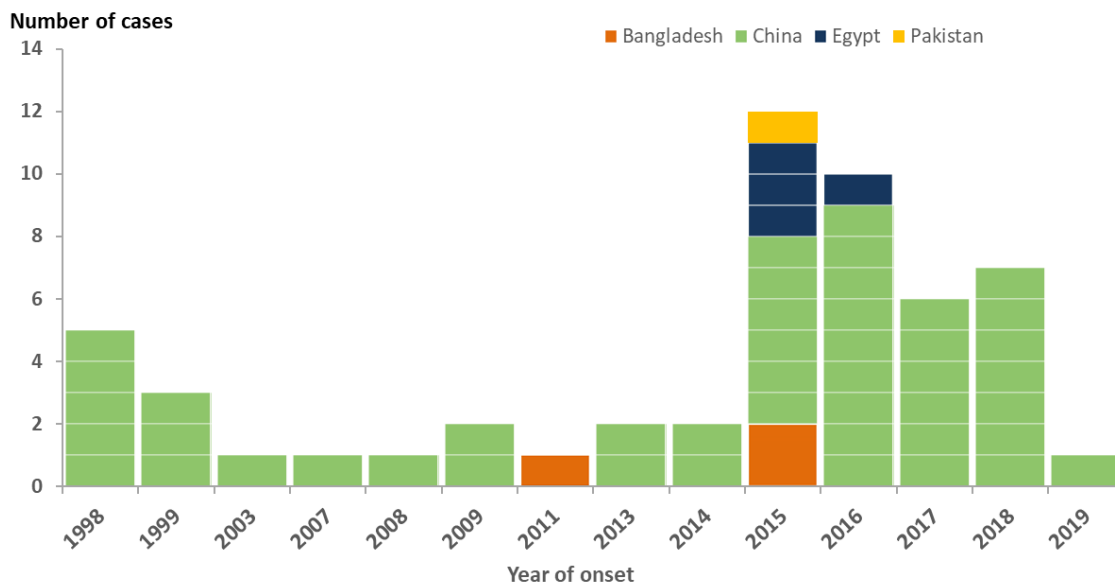
###### *Information extracted from the scientific literature*

Some recent studies analysed mutations related to mammalian adaptation of AI A(H9N2) viruses and identified several mutations relevant for mammalian adaptation (Kamiki et al., 2018; Mosaad et al., 2018; Obadan et al., 2018; Zhang et al., 2018).

Receptor binding tests indicated that most of the A(H9N2) isolates analysed from poultry-related environmental surveillance in China bound to the human-type receptors (Zou et al., 2019).



Research data on reassortant viruses of A(H5N1) and A(H9N2) viruses showed a fairly high genetic compatibility and suggest higher pathogenicity in mammals for the reassortant than the parental viruses, which highlights a risk for public health should such viruses emerge in the field (Arai et al., 2019).



Data source: ECDC line list (WHO, 2018e, b; Ali et al., 2019; WHO, 2019a; Macau Special Administrative Region Government, online; Taiwan Centres for Disease Control, online).

**Figure 17:** Distribution of confirmed human cases of A(H9N2) by reporting country, 1998 – 15 February 2019 (n=54)

#### 4.5. Scientific analysis of avian influenza spread from non-EU/EEA countries to poultry in the EU/EEA

Possible pathways by which AI viruses can be brought into the EU have been described in previous EFSA reports (EFSA AHAW Panel et al., 2017; EFSA et al., 2018a; EFSA et al., 2018d).

In contrast to the last report (EFSA et al., 2018d), Section 4.4 shows that from 16 November 2018 to 15 February 2019, the time period of this report, there was an increasing number of reported outbreaks in poultry and wild birds in Asia, Africa and the Middle East. The outbreaks of HPAI A(H5N1) clade 2.3.2.1c continued in Asia (India, Indonesia and Vietnam), but no further outbreaks were reported in the relevant time period from Africa or the Middle East. However, cases of HPAI A(H5N1) in wild birds were reported from India for the first time since March 2018. Only two outbreaks of the novel zoonotic reassortant HPAI A(H5N6) belonging to clade 2.3.4.4c were notified by China and Vietnam to the OIE during the relevant time period for this report. In contrast, A(H5N8) clade 2.3.4.4b outbreaks were reported from Russia, Africa, Asia and the Middle East. Besides the detection of HPAI A(H5N8) on ostrich establishments in South Africa, outbreaks were also reported from poultry establishments in Nigeria for the first time since June 2017. Furthermore, Namibia was affected for the first time by an outbreak of HPAI A(H5N8). The disease was detected in sick jackass penguins (*Spheniscus demersus*) on an island of the Namibian Atlantic coast. During the relevant period for this report, only HPAI A(H5N8) viruses have been detected in wild waterfowl in Pakistan. However, there is considerable uncertainty regarding the real geographical distribution of these viruses, particularly in wild birds. Furthermore, spring migration from the wintering to the breeding regions will start soon, depending on the climate conditions. Aggregation before and during migration, as well as mixing of wild birds from different geographic origins during migration and spring time, will increase the risk of the infection spreading via this pathway.

## 4.6. Surveillance and diagnosis of human infections and public health measures for prevention and control

### 4.6.1.1. Surveillance in the EU

As outlined in the EFSA report for November 2017 – February 2018 (EFSA et al., 2018c), human infections with zoonotic and other novel influenza strains are notifiable under EU legislation<sup>3</sup> and the International Health Regulations (IHR) through the Early Warning and Response System and the IHR notification system, respectively (WHO, 2016). WHO recently published a 'Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases', which also covers AI viruses (WHO, 2018c).

### 4.6.1.2. Diagnosis

Routine laboratory diagnostics were described in the EFSA report covering November 2017 – February 2018 (EFSA et al., 2018c). All influenza A virus isolates or clinical samples that cannot be subtyped are to be submitted to the appropriate national reference laboratory (National Influenza Centres; NICs), and to a WHO Collaborating Centre for Reference and Research on Influenza for characterisation (WHO, 2017). Influenza virus sharing is coordinated by the WHO Global Influenza Surveillance and Response System (GISRS) (WHO, online-b). An updated protocol for the molecular diagnosis of influenza viruses has recently been published (WHO, 2018d).

### 4.6.1.3. Options for public health control measures (in relation to the EU)

Options for public health control measures remain the same as those outlined in the EFSA report for November 2017 – February 2018, and should follow national guidelines and recommendations (EFSA et al., 2018c). The public health measures taken in 22 EU/EEA Member States and Israel during the A(H5N8) outbreaks in 2016–2017 have been summarised (Adlhoch et al., 2018). The use of personal protective measures for people exposed to birds that are infected with AI viruses will minimise the risk of transmission to humans.

### 4.6.1.4. Vaccines

WHO published a status update on the available and recommended vaccines or candidate vaccine viruses (CVVs) for pandemic preparedness in February 2019 following the vaccine composition meeting (WHO, 2019c). A new A/chicken/Jiangsu/1/2018 (H7N4)-like CVV for A(H7) virus related to the human case due to A(H7N4) (EFSA et al., 2018b) and a A/Guangdong/18SF020/2018-like A(H5N6) CVV have been proposed.

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

The risk of zoonotic influenza transmission to the general public in EU/EEA countries remains very low. Outbreaks due to AI viruses or detections of infected wild birds continued at a very low level. Although no transmission of viruses detected in wild birds or poultry to humans has been observed in Europe, zoonotic transmission of viruses related to AI A(H5) clade 2.3.4.4 circulating in wild birds and poultry in Europe cannot be fully excluded, as these viruses reassort readily and new viruses may emerge or be introduced e.g. via migratory birds. AI virus transmission to humans is a rare event overall and the risk is considered very low for viruses with an avian-adapted genetic makeup. The use of personal protective measures for people exposed to AI viruses will minimise any residual risk.

The risk of travel-related importation of human AI cases, particularly from Asia, is very low. Currently, a very low number of human cases are reported from China and other countries in South-east Asia. Surveillance of AI viruses in wild birds and poultry in the EU/EEA is important for detecting further virus spread among birds and reducing the possible risk of exposure of humans to infected birds. Controlling illegally imported poultry products is also important to prevent the importation of AI viruses relevant for both public and veterinary health.

<sup>3</sup> Commission Implementing Decision (EU) 2018/945 of 22 June 2018 on the communicable diseases and related special health issues to be covered by epidemiological surveillance as well as relevant case definitions. OJ L 170/1, 6.7.2018, p. 74

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## Abbreviations

|         |  |
|---------|--|
| ADNS    | Animal Disease Notification System                   |
| AI      | Avian influenza                                      |
| CVV     | Candidate vaccine virus                              |
| ECDC    | European Centre for Disease Prevention and Control   |
| EFSA    | European Food Safety Authority                       |
| EEA     | European Economic Area                               |
| EU      | European Union                                       |
| EURL    | European Union Reference Laboratory                  |
| FAO     | Food and Agriculture Organization                    |
| HPAI    | Highly pathogenic avian influenza                    |
| IHR     | International Health Regulations                     |
| LPAI    | Low pathogenic avian influenza                       |
| MS      | Member State   |
| OIE     | World Organisation for Animal Health                 |
| SCOPAFF | Standing Committee on Plants, animals, food and feed |
| SPF     | Specific pathogen free                               |
| TOR     | Terms of reference                                   |
| WHO     | World Health Organization                            |

## 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.

Since late October 2016 up to early February 2017, highly pathogenic avian influenza (HPAI) of the subtype A(H5N8) has been detected in wild migratory birds or captive birds on the territory of 21 Member States, namely Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, the Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom. In 17 Member States the virus has spilled over to poultry holdings leading also to lateral spread between holdings in a few Member States, in particular in those with a high density of duck and geese holdings where the poultry cannot sufficiently be protected against contacts with wild birds. A second HP AI subtype A(H5N5) has been detected in wild birds and recently also in poultry holdings in Germany.

The number of infected migratory wild birds found dead and the geographical extent of these findings are posing an immense threat for virus introduction into poultry or captive birds holdings as demonstrated by the high number of outbreaks (~700 as of 08/02/2017).

In the event of an outbreak of avian influenza, there is a risk that the disease agent might spread to other holdings where poultry or other captive birds are kept. As a result it may spread from one Member State to other Member States or to third countries through trade in live birds or their products.

There is knowledge, legislation<sup>4</sup>, technical and financial tools in the EU to effectively deal with outbreaks of avian influenza in poultry and captive birds. However, the very wide virus spread by wild birds and the increased risk of direct or indirect virus introduction into poultry or captive bird holdings has led to the largest HPAI epidemic in the EU so far. This situation calls for a reflection and evaluation how preparedness, risk assessment, early detection and control measures could be improved.

The Commission and Member States are therefore in need of an epidemiological analysis based on the data collected from the disease affected Member States. The use of the EFSA Data Collection Framework is encouraged given it promotes the harmonisation of data collection. Any data that is available from neighbouring third countries should be used as well, if relevant.

Therefore, in the context of Article 31 of Regulation (EC) No. 178/2002<sup>5</sup>, EFSA should provide the technical and scientific assistance to the Commission based on the following Terms of Reference:

<sup>4</sup> Council Directive 2005/94/EC of 20 December 2005 on Community measures for the control of avian influenza and repealing Directive 92/40/EEC. OJ L 10, 14.1.2006, p. 16.

<sup>5</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.

1. Analyse the epidemiological data on highly pathogenic avian influenza (HPAI) and low pathogenic avian influenza (LPAI), where co-circulating or linked within the same epidemic, from HPAI disease affected Member States.
2. Analyse the temporal and spatial pattern of HPAI and LPAI as appropriate in poultry, captive birds and wild birds, as well the risk factors involved in the occurrence, spread and persistence of the HPAI virus in and at the interface of these avian populations.
3. Based on the findings from the points above, describe the effect of prevention and control measures.
4. Provide for regular quarterly reports updating on the avian influenza situation within the Union and worldwide, in particular with a view to describe the evolution of virus spread from certain regions towards the EU. In case of significant changes in the epidemiology of avian influenza, these reports could be needed more frequently. These reports should in particular closely follow the developments of zoonotic avian influenza viruses (such as HPAI A(H5N6) and LPAI A(H7N9)) in collaboration with the European Centre for Disease Prevention and Control (ECDC).

## A.2. Interpretation of the terms of reference

In reply to TOR 1 and TOR 2, this scientific report gives an overview of the HPAI and LPAI outbreaks in poultry, captive and wild birds detected in Europe between 16 November 2018 and 15 February 2019 and reported by Member States and neighbouring countries via ADNS. Member States where HPAI outbreaks occurred in poultry submitted additional epidemiological data to EFSA, which have been used to analyse the characteristics of poultry establishments affected between 16 November 2018 and 15 February 2019.

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

A description of the applied prevention and control measures (TOR 3) is given based on case reports provided by representatives from Bulgaria and Denmark and attached as Annex A to previous EFSA report for Bulgaria (EFSA et al., 2018d) and to this report for Denmark. The main topics covered are increasing awareness, release and repeal of housing order, strengthening biosecurity, preventive culling, implementation of a regional standstill, ban of hunting and derogations from restriction zone implementation after a risk assessment.

Monitoring of the AI situation in other countries (TOR 4) was based on data submitted via OIE or reported to the FAO. The description focuses only on findings of AI viruses occurring in countries that are considered to be of epidemiological interest for the EU/EEA or of public health relevance, specifically on HPAI A(H5N1), HPAI A(H5N2) HPAI A(H5N6), HPAI A(H5N8), HPAI/LPAI A(H7N9) and LPAI A(H9N2). Background and epidemiology, detections, phenotypic and genetic characterisations are described based on information from confirmed human, poultry and wild bird cases that occurred between 16 November 2018 and 15 February 2019 and on information gathered by performing a literature search from papers published in PubMed from 16 November 2018 and 15 February 2019. Possible actions for preparedness in the EU are discussed.

The report mainly describes information that became available since the publication of the EFSA report for August – November 2018 (EFSA et al., 2018d) and that might affect the interpretation of risks related to AI introduction and/or spread in Europe.

## Appendix B –Data and methodologies

### B.1. Data on animals

#### B.1.1. Overview of avian influenza outbreaks in Europe (TOR 1 and TOR 2)

Data on the AI outbreaks that occurred in Europe from 16 November 2018 to 15 February 2019 submitted by Member States (MSs) to the ADNS (European Commission, online-b) were taken into account for this report. In addition, Bulgaria and Denmark were asked to provide more detailed epidemiological data (see Table A.1, Appendix A in EFSA (EFSA et al., 2018c)) directly to EFSA on the HPAI outbreaks that occurred in poultry, captive and wild birds during the same period.

The information, which EU MSs affected by HPAI and LPAI presented to the Standing Committee on Plants, Animals, Food and Feed (SCOPAFF) meetings, and the evidences on HPAI and LPAI outbreaks provided in the info notes by the affected MSs to the European Commission, were consulted to extract relevant information which is reported in Sections 4.2, 4.3 and 4.4. The PDFs of the SCOPAFF presentations are available on the European Commission website (European Commission, online-a).

The Bulgarian, the Danish and the Dutch National Reference Laboratories for Avian Influenza and Newcastle Disease were asked to provide the genetic sequences obtained from the AI viruses detected in the respective countries during the reporting period mentioned above. The public GISAID's EpiFlu™ Database was accessed to download newly released avian influenza sequences.

##### B.1.1.1. Literature review on phenotypic characterisation of HPAI viruses circulating in the EU

Information on the phenotypic characterisation of AI viruses circulating in the EU was extracted from the scientific literature by performing a literature review.

*Review question* Update on the phenotypic characterisation of HPAI viruses circulating in the EU in domestic and wild birds within the reporting period.

*Search* The PubMed database was searched by using subject index terms and free-text terms combined with the appropriate Boolean operators. Scientific articles added to the database from 16 November 2018 to 15 February 2019 were searched; the search was run on 18 February 2019.

*Relevance criteria* Scientific articles added to the database from 16 November 2018 to 15 February 2019 and reporting information on the presence or absence of clinical signs or pathological changes or mortality due to HPAI infection with viruses circulating within the last two years in the EU in domestic or wild birds.

*Eligibility criteria* Host species all domestic birds or wild birds present in the EU; the virus subtype should be reported; - for experimental studies only, the age of the infected animals should be reported (at least as juvenile/adult).

*Results* The search retrieved 116 papers. The articles were subsequently screened against the relevance and eligibility criteria. None of the screened paper was in the end taken into consideration in the description of the phenotypic characterisation of HPAI viruses circulating in the EU in domestic and wild birds in the reporting period.

The search protocol and the results can be consulted at <https://doi.org/10.5281/zenodo.2592141>.

#### B.1.2. AI prevention and control measures in Europe (TOR 3)

Bulgaria and Denmark expressed an interest in supporting the analysis of the HPAI outbreaks occurred from 16 November 2018 to 15 February 2019, and submitted case reports on the prevention and control measures that have been applied as consequences of the outbreaks. The case reports provided to EFSA can be consulted in Annex A of previous EFSA report for Bulgaria (EFSA et al., 2018d), and of this report for Denmark.

#### B.1.3. Overview of AI outbreaks on other countries not reporting via ADNS (TOR 4)

Data from FAO EMPRES-i (FAO, online-b) on HPAI A(H5N1), HPAI A(H5N2), A(H5N6), A(H5N8), HPAI and LPAI A(H7N9) in domestic, captive and wild birds, and environmental samples, were used to map the geographical distribution of AI cases in domestic and wild birds in Africa, Asia, the Middle East and Europe on the basis of the observation dates. With the purpose of avoiding over-complication of the maps, captive birds and environmental samples have been mapped as domestic birds. Despite the fact that some of these kept animals may be of wild species, in most of the cases captive birds, or, for environmental samples, the birds from which samples have been taken (mainly at live market places) will not move around and not spread the infection by migrating and for this reason have been considered as domestic birds in the maps provided in this report. Only when there was a strong discrepancy among the locality, the administrative regions and geocoordinates, and the outbreaks were not officially reported to the OIE, the confirmed outbreaks were not taken into account in the analysis.

### **B.1.3.1. Literature review on phenotypic and genetic characterisation of HPAI viruses circulating on other continents**

Information on phenotypic and genotypic characterisation of HPAI viruses circulating on other continents and regions (Africa, Asia, the Middle East) in domestic or wild birds or mammals (excluding humans) were extracted from the scientific literature by performing a literature review.

*Review questions* Update on the phenotypic and genetic characterisation of HPAI viruses circulating on other continents and in other regions (Africa, Asia, the Middle East) in domestic or wild birds or mammals (excluding humans).

*Search* The PubMed database was searched by using subject index terms and free-text terms combined with the appropriate Boolean operators. Scientific articles added to the database between 16 November 2018 and 15 February 2019 were searched; the search was run on 18 February 2019.

*Relevance criteria* Scientific articles added to the database between 16 November 2018 and 15 February 2019 that report information on the presence or absence of clinical signs, pathological changes or mortality or genotypic characterisation (only new information) due to HPAI infection with viruses circulating within the last two years in Asia, Africa or the Middle East in domestic or wild birds or mammals other than humans.

*Eligibility criteria* Host species all domestic birds or wild birds present in the EU or mammals other than humans; the virus subtype should be reported; for experimental studies only the age of the infected animals should be reported (at least as juvenile/adult).

*Results* The search retrieved 108 papers. The articles were subsequently screened against the relevance and eligibility criteria. Nine papers were in the end taken into consideration in the description of phenotypic and genotypic characterisation of HPAI viruses circulating on other continents and in other regions (Africa, Asia, the Middle East) in domestic or wild birds or mammals (excluding humans) in the reporting period.

The search protocol and the results can be consulted at <https://doi.org/10.5281/zenodo.2592141>.

## **B.2. Data on humans**

The numbers of human cases due to infection with AI viruses have been collected by ECDC. Multiple sources are scanned regularly as part of epidemic intelligence activities at ECDC to collect information about 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 of time 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.

Literature searches were performed until 15 February 2019 in the PubMed database with the key words: 'humans' and 'A(H5N1)'; 'A(H5N6)'; 'A(H5N8)'; 'A(H7N4)'; 'A(H7N9)'; 'A(H9N2)'; and narrowed to the most recent available publications as well as using specific search parameters such as 'seroprevalence'; 'risk factors'; 'transmission'; 'humans'; 'mammals'. The literature search was not systematic or comprehensive.

## Annex A – Applied prevention and control measures on avian influenza in Denmark

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### Scope

This document provides a brief overview of specific prevention and control measures applied in Denmark from 16 November 2018 to 15 February 2019 in relation to the detection of HPAI in wild birds. This document is made to support the EFSA working group in generating an overview on the application of the measures to prevent HPAI spread from wild birds into poultry holdings at EU level.

### Timing of the applied prevention and control measures

Tables A.1 provides timelines for the main events that triggered actions in relation to the selected prevention and control measures in Denmark. More information on the actions taken is provided in the sections below the table.

**Table A.1:** Overview of main actions

| Date              | Event that triggered action   | Type of action taken   | Target audience (if applicable)  |
|-------------------|---|--|--|
| <b>14/01/2019</b> | Confirmation of HPAI A(H5N6) in a wild white-tailed eagle ( <i>Haliaeetus albicilla</i> ) | 16/01/2019 <ul style="list-style-type: none"> <li>- Meeting in the AI expert group.</li> <li>- Press release about the finding with information about biosecurity.</li> <li>- Poultry associations (industry and hobby) and hunter associations were contacted directly via electronic media.</li> <li>- Poultry owners were recommended to protect poultry against contact with wild birds with roofs, horizontal fabrics or nets and implement biosecurity measures e.g. change of footwear.</li> <li>- Hunters were informed about biosecurity in connection with hunting.</li> </ul> | Poultry industry and general public - especially owners of hobby poultry/backyard flocks.<br><br>Hunter associations and hunters |
| <b>15/01/2019</b> | Confirmation of HPAI A(H5N6) in a wild common buzzard ( <i>Buteo buteo</i> )              | Both findings were included in the action taken on the 16 January  |  |

### Action taken

On 22 December 2018, a white-tailed eagle was found dead near the city Næstved in the municipality of Næstved in the Southern part of Zealand near 'Smålandsfarvandet' (a sea-area where HPAI positive wild birds previously have been found latest in September 2018). On 14 January 2019 the National Veterinary Institute confirmed HPAI A(H5N6) virus in the samples from the eagle.

On 4 January 2019, a common buzzard was found dead in Rørvig, municipality of Odsherred. On 15 January 2019, the National Veterinary Institute confirmed HPAI (H5N6) virus in the sample from the common buzzard.

A meeting in the AI expert group was held on 16 January 2019 and subsequently a press release was issued with focus on protection of poultry against wild birds in the infected area. The Danish Veterinary and Food Administration recommended to protect poultry against contact with wild birds with roofs, horizontal fabrics or nets and implement biosecurity measures as change of footwear and other hygienic measures when entering and leaving the poultry. Detailed information about biosecurity measures were circulated via electronic media to poultry associations (industry and hobby). In addition, hunters' associations were informed about the importance of biosecurity in connection with hunting and how to report findings of dead wild birds using the app 'Fugleinfluenza Tip'.