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Avian influenza overview November 2017 – February 2018

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

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Abstract

Between 16 November 2017 and 15 February 2018, one highly pathogenic avian influenza (HPAI) A(H5N6) and five HPAI A(H5N8) outbreaks in poultry holdings, two HPAI A(H5N6) outbreaks in captive birds and 22 HPAI A(H5N6) wild bird events were reported within Europe. There is a lower incursion of HPAI A(H5N6) in poultry compared to HPAI A(H5N8). There is no evidence to date that HPAI A(H5N6) viruses circulating in Europe are associated with clades infecting humans. Clinical signs in ducks infected with HPAI A(H5N8) seemed to be decreasing, based on reports from Bulgaria. However, HPAI A(H5N8) is still present in Europe and is widespread in neighbouring areas. The majority of mortality events of wild birds from HPAIV A(H5) in this three-month period involved single birds. This indicates that the investigation of events involving single dead birds of target species is important for comprehensive passive surveillance for HPAI A(H5). Moreover, 20 low pathogenic avian influenza (LPAI) outbreaks were reported in three Member States. The risk of zoonotic transmission to the general public in Europe is considered to be very low. The first human case due to avian influenza A(H7N4) was notified in China underlining the threat that newly emerging avian influenza viruses pose for transmission to humans. Close monitoring is required of the situation in Africa and the Middle East with regards to HPAI A(H5N1) and A(H5N8). Uncontrolled spread of virus and subsequent further genetic evolution in regions geographically connected to Europe may increase uncertainty and risk for further dissemination of virus. The risk of HPAI introduction from Third countries via migratory wild birds to Europe is still considered much lower for wild birds crossing the southern borders compared to birds crossing the north-eastern borders, whereas the introduction via trade is still very to extremely unlikely.

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

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Competing interests: In line with EFSA's policy on declarations of interest, the following working group (WG) experts: Adam Brouwer, Paolo Mulatti, Krzysztof Smietanka and Christoph Staubach, have declared that they have current involvement in risk assessment activities at national level related to avian influenza, which constitutes a conflict of interest (CoI) with the mandate of the EFSA WG in hand. The CoIs have been waived and the waivers were adopted in accordance with Article 16(5) of the Decision of the Executive Director on Declarations of Interest of 31 July 2017 EFSA/LRA/DEC/02/2014, available at http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/independencerules2014.pdf. Pursuant to Article 16(7) of the above mentioned Decision, the concerned experts were allowed to take part in the discussions and in the drafting phase of the EFSA Scientific report on Avian influenza monitoring (Art. 31) - overview November 2017 – February 2018, and have not been allowed to be, or act as, a chairman, a vice-chairman or rapporteur of the WG.

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1. Introduction

The present document gives an overview of the HPAI and LPAI outbreaks in poultry and captive birds as well as HPAI events in wild birds detected in and outside Europe between 16 November 2017 and 15 February 2018. The background, Terms of Reference (ToR) and their interpretation are reported in Appendix A, data and methodologies are reported in Appendix B.

2. Conclusions

HPAI and LPAI outbreaks in Europe between 16 November 2017 and 15 February 2018 (TOR 1 and TOR 2)

Main observations:

- No human infections with HPAI or related LPAI viruses currently circulating in Europe have been reported.
- In the EU, between 16 November 2017 and 15 February (based on Animal Disease Notification System (ADNS)):
 - six HPAI outbreaks were reported in poultry: four A(H5N8) in Italy, one A(H5N8) in Bulgaria, one A(H5N6) in the Netherlands;
 - two HPAI A(H5N6) outbreaks were reported in captive birds in the Netherlands;
 - 22 HPAI A(H5N6) events were reported in wild birds: one in Denmark, one in Germany, one in Ireland, five in the Netherlands, one in Sweden, one in Switzerland and 12 in United Kingdom;
 - 20 A(H5) LPAI outbreaks were reported in poultry in three Member States (MSs) (16 in France, one in Germany and three in Italy).
- Mortality of wild birds from HPAIV A(H5N6) was reported in Denmark, Germany, Ireland, Italy, the Netherlands, Sweden and United Kingdom. The majority of events involved single dead birds and 7 of 10 events involving more than one bird were found in United Kingdom. Nearly all of the species involved were those listed in the revised list of target species for passive surveillance.

Conclusions:

- The risk of zoonotic transmission to the general public in the EU/EEA countries is considered to be very low.
- Despite the wide spread presence of HPAIV A(H5N6) in wild bird populations throughout the EU, the level of observed mortality was limited. The Community Veterinary Emergency Team (CVET) mission's conclusions from the outbreaks in Bulgaria were that clinical detection of signs from infection with this HPAI A(H5N8) virus seemed to be decreasing in domestic ducks, although the age-dependency of the observed mortality was not analysed.

Applied prevention and control measures (TOR3)

Main observations:

- Particular focus has been given to the application of biosecurity measures at the farm level to prevent lateral spread of avian influenza virus (AIV).
- Italy has developed a list of biosecurity measures to be checked on farm to guarantee that adequate requirements are fulfilled before re-stocking birds (Ministerial Provision of 19 February 2018¹).

¹ Ministerial Provision No 4122 of 19 February 2018 - influenza aviaria ad alta patogenicità. Applicazione misure di riduzione del rischio e di biosicurezza.

AI situation in other continents between 16 November 2017 and 15 February 2018 (TOR4)

Conclusions:

- The probability of AIV introductions from Third countries via wild birds is decreasing with increasing temperatures during spring, whereas introduction into EU poultry holdings is still possible due to presence of the virus in the environment.
- Close monitoring is required of HPAI of the subtypes A(H5N1) and A(H5N8) in Africa and Middle East, given the propensity for further genetic diversity as a result of uncontrolled spread in poultry and increased opportunity for further genetic reassortment adding uncertainty on the geographical distribution of these viruses.
- There is continuing evidence of the occurrence of intersubtype and interclade reassortants between A(H5N1), A(H5N6), A(H9N2) and A(H7N9) in both poultry and wild birds in multiple areas of the world; this situation should be closely monitored and ongoing timely genetic characterisation of the circulating viruses is recommended.
- The risk of HPAI introduction from Third countries via migratory wild birds to Europe is still considered much lower for wild birds crossing the southern borders compared to birds crossing the north-eastern borders based on species found positive in current surveillance, whereas the introduction via trade is still very unlikely to extremely unlikely.
- The recent human case of A(H7N4) in China underlines the continuing threat of new emerging avian influenza viruses to human health.

3. Suggestions

- Continued surveillance for AIV in wild birds and poultry combined with timely data sharing among MSs as well as between animal and human health sectors is crucial to detect and respond early to threats relevant to animal and public health.
- Based on the apparent decline in clinical signs from HPAI A(H5N8) virus infection in ducks, raising awareness on the mild or absent clinical signs from HPAI A(H5N8) virus infection could improve passive surveillance for duck farmers. In addition to passive surveillance, intensifying serological screening of duck farms should be considered, in particular when mild clinical signs are observed.
- Many MSs only test sick/dead wild birds of target species for HPAI if several birds are found sick/dead at the same location on the same day. However, since most events involve only one or a few sick/dead bird(s), there is an increased need to include events involving single sick/dead birds of target species for comprehensive passive surveillance for HPAI A(H5).
- Timely generation of complete viral genome sequences, coupled with intensified surveillance for avian influenza virus in wild birds on wetlands of ecologic importance, is important to improve our understanding of the virus dissemination routes and support early detection of viruses highly pathogenic to poultry or believed to be of immediate concern to human health.
- Robust consistent approaches for the genetic analyses of viruses and interpretation of data to inform decision making for control would be beneficial amongst EU providers. Additionally there is a need for a more consistent approach evaluating the zoonotic risk based on molecular data.
- People exposed to birds potentially infected with Avian Influenza (AI) should consider appropriate personal protection measures.

4. Results

4.1. Overview of HPAI and LPAI outbreaks in Europe between November 2017 and February 2018 (TOR 1 and TOR 2)

4.1.1. Description of the AI-detections in time and space

4.1.1.1. HPAI A(H5N8) and A(H5N6) in poultry, other captive birds, and wild birds

From 16 November 2017 to 15 February 2018, a total of 29 outbreaks of A(H5) HPAI occurred in EU, as presented in Table 1. The timeline and location of A(H5) HPAI outbreaks are reported in Figure 1-4. For wild birds Table 1 displays the number of events, the description of cases by event is reported in section 4.1.3. The characterisation of HPAI affected poultry holding is reported in Section 4.1.5.

Table 1: Number of A(H5) HPAI outbreaks by country from 16 November 2017 to 15 February 2018 in Europe

Country	HPAI A(H5N8) Poultry	HPAI A(H5N6)			All HPAI
		Poultry	Captive Birds ^(a)	Wild Birds	
Bulgaria	1				1
Denmark				1	1
Germany				1	1
Ireland				1	1
Italy	4				4
The Netherlands		1	2*	5	8
Sweden				1	1
Switzerland				1	1
United Kingdom				12	12
Total (9 Countries)	5	1	2	22	30

(a) According to the Council Directive 2005/94/EC, 'other captive bird' means any bird other than poultry that is kept in captivity for any reason other than production of meat or eggs for consumption, the production of other products, for restocking supplies of game birds or for the purposes of any breeding programme for the production of these categories of birds, including those that are kept for shows, races, exhibitions, competitions, breeding or selling

* One outbreak occurred in galliformes and anseriformes species (49 cases out of 58 susceptible birds present), and another one in galliformes species (2 cases out of 32 susceptible birds present)

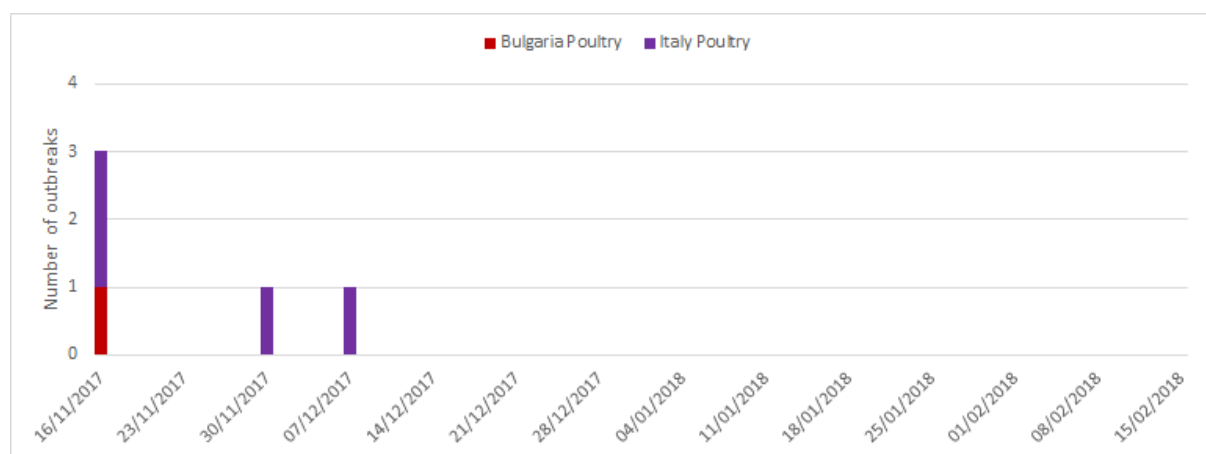


Figure 1: Number of A(H5N8) HPAI outbreaks from 16 November 2017 to 15 February 2018 in Europe

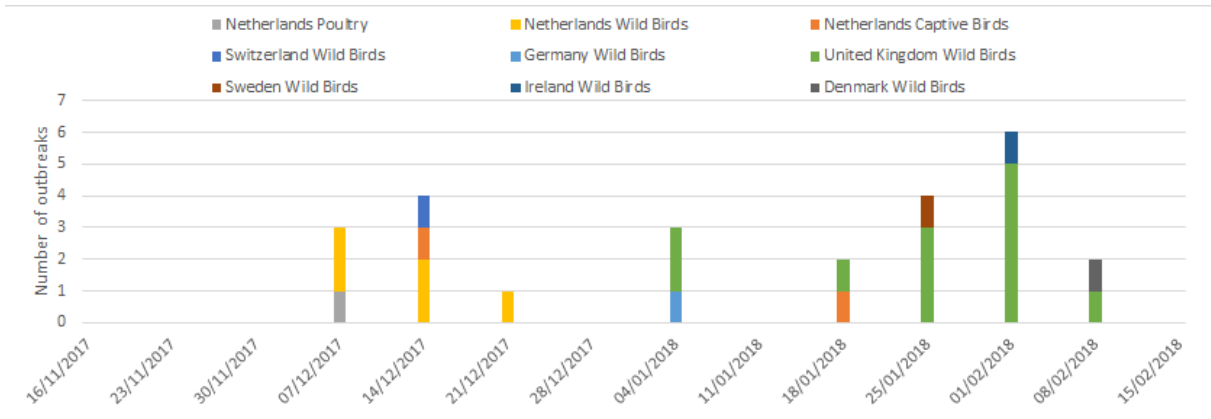


Figure 2: Number of A(H5N6) HPAI outbreaks from 16 November 2017 to 15 February 2018 in Europe

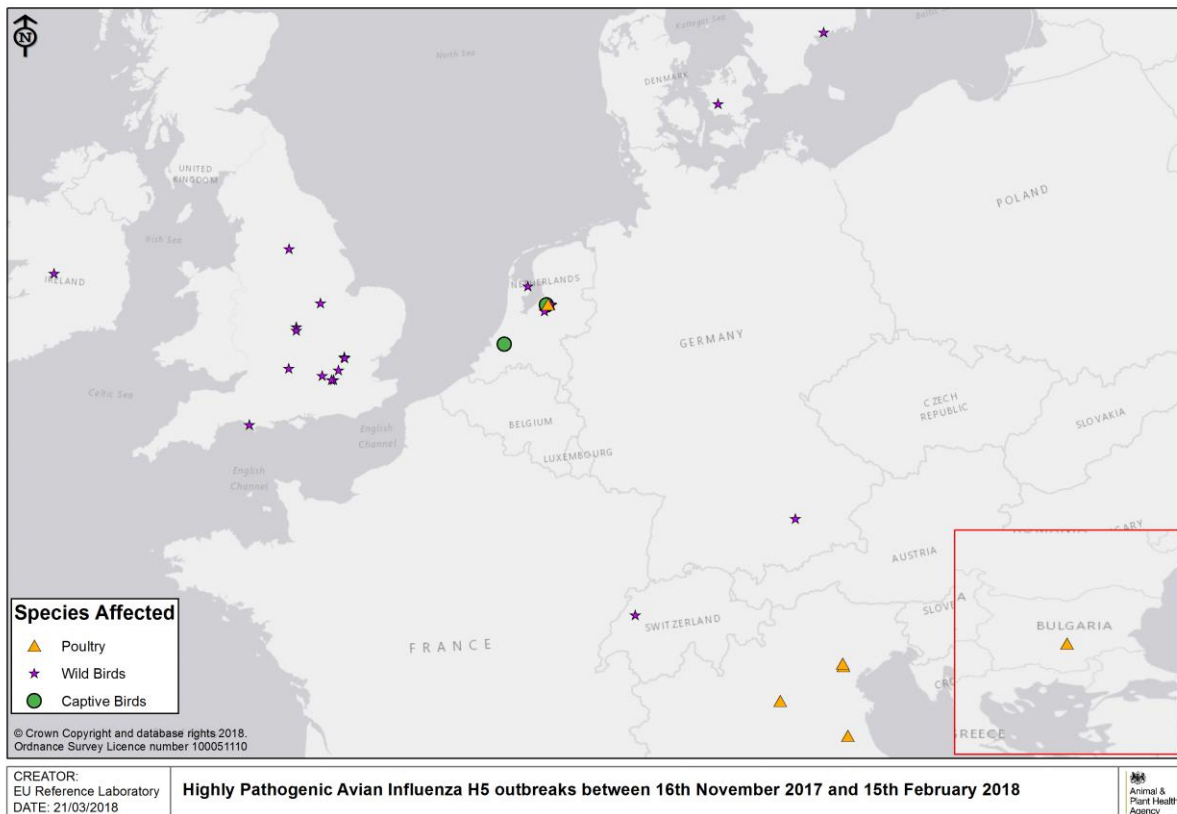


Figure 3: Location of A(H5Nx) HPAI outbreaks from 16 November 2017 to 15 February 2018 in Europe by affected population

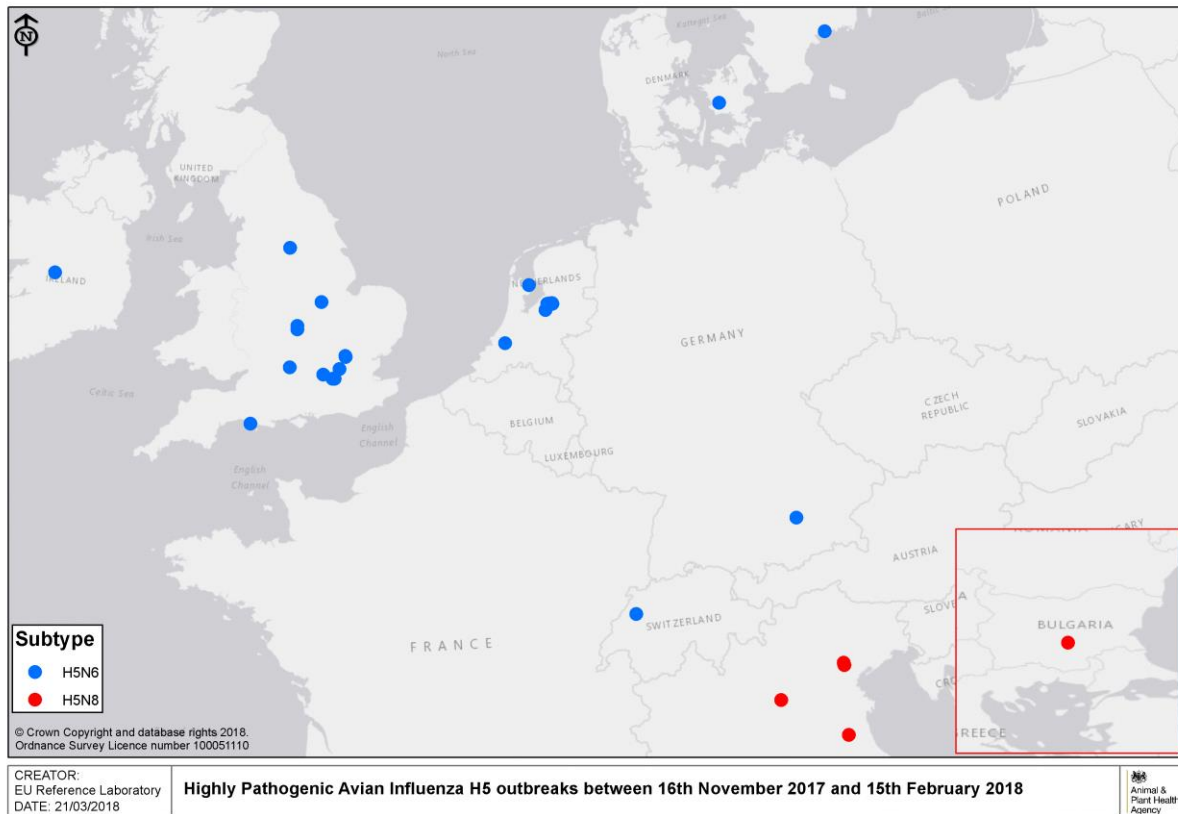


Figure 4: Location of A(H5Nx) HPAI outbreaks from 16 November 2017 to 15 February in Europe by virus subtype

4.1.1.2. LPAI in poultry holdings

From 16 November 2017 to 15 February 2018, a total number of 20 outbreaks of LPAI occurred in the EU, as presented in Table 2. The timeline and location of LPAI outbreaks are reported in Figures 5 and 6.

Table 2: Number of LPAI outbreaks by country and virus subtype from 16 November 2017 to 15 February 2018

Country	Poultry				Total
	A(H5N1)	A(H5N2)	A(H5N3)	A(H5Nx)	
France		2	9	5	16
Germany		1			1
Italy	1			2	3
Total (3 MSs)	1	3	9	7	20

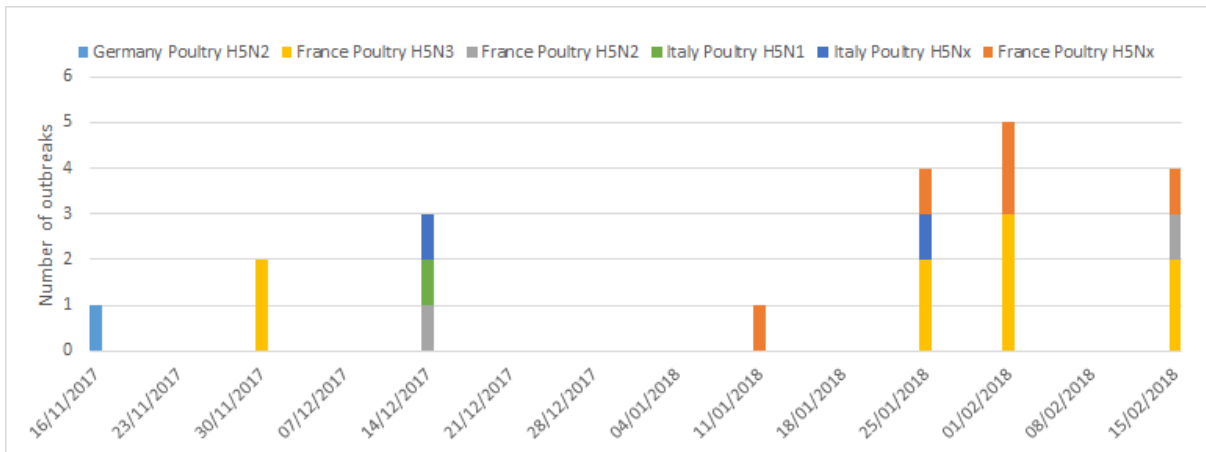


Figure 5: Number of LPAI outbreaks from 16 November 2017 to 15 February 2018 in Europe

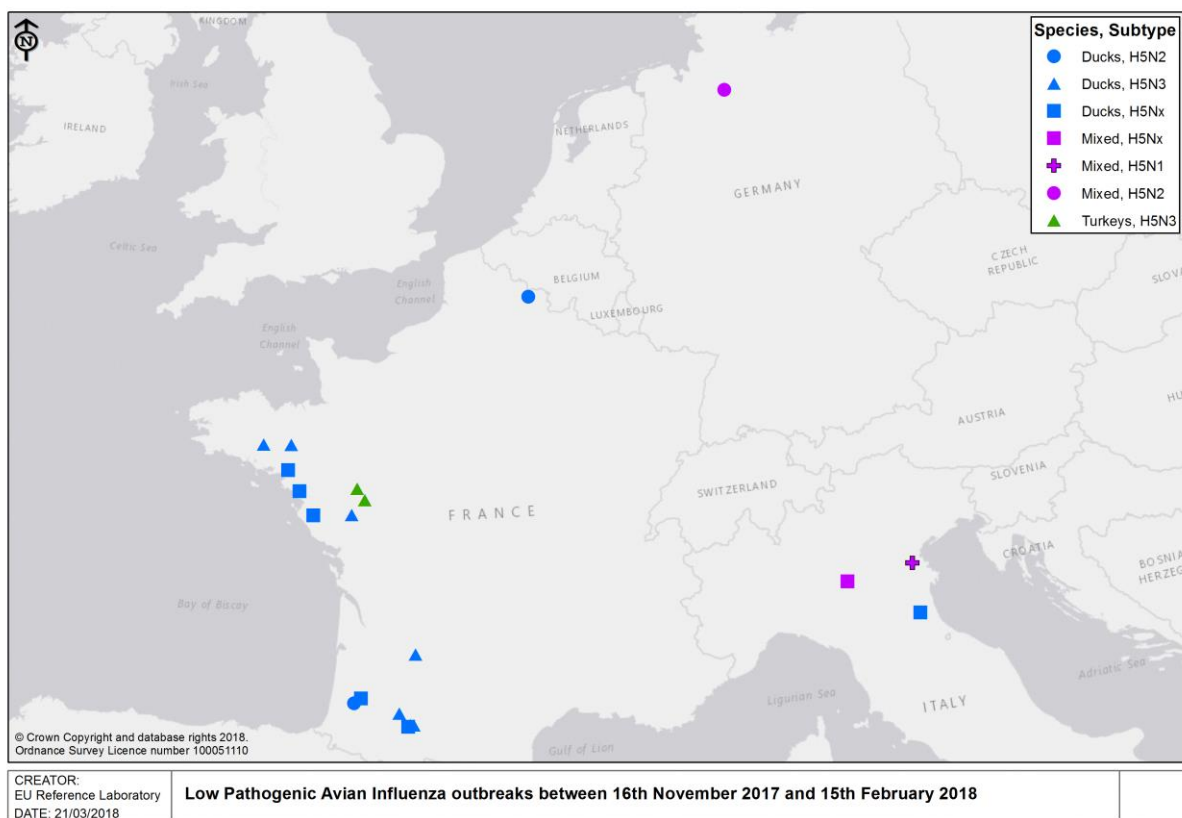


Figure 6: Location of LPAI outbreaks from 16 November 2017 to 15 February 2018 in Europe

4.1.2. Genetic characterisation of the circulating viruses

The HA gene sequences from October 2016 to November 2017 are genetically very similar to each other, but distinguishable phylogenetically from the viruses detected in the Russian Federation in June 2016, and also from the A(H5N8) HPAI viruses present in the EU in 2014/15 (see phylogenetic tree elaborated by EURL in supporting information <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2018.5240/suppinfo/>). The most recent HPAI A(H5N8) viruses that circulated in both Italy and Bulgaria were genetically very similar to the HA gene of the viruses that were analysed earlier in the epizootic in 2016/2017. Co-circulation of LPAI and HPAI viruses in wild birds has led to multiple reassortment events throughout the period from 2016 to the present, involving all gene segments with the exception of MP and NS for the A(H5N8) viruses. In

particular, the NA gene segment derived from currently circulating LPAI viruses in wild birds has reassorted to result in A(H5N5), A(H5N6) and A(H5N8) subtypes infecting poultry. Since November 2017, novel HPAI A(H5N6) viruses have been detected in predominantly wild birds in Europe. Although analyses suggest that owing to multiple reassortment events, epizootic A(H5) strains show significant variability across the genome (due to acquisition of gene segments from influenza A viruses circulating in wild birds) the HA gene by comparison is relatively conserved. From currently available data, the HA still shows relatively little diversity, with currently circulating viruses closely associated with two separate introduction events in late 2016. No subsequent statistically supportable evidence of geographic restriction of particular subclades or variants within the EU are available, except where there is evidence of lateral transmission amongst poultry. Thus, the HA gene is similar to the A(H5N8) HPAI viruses. As with the previously detected A(H5N6) virus in Greece in 2017, the N6 gene is similar to other N6's circulating in wild waterfowl. The internal genes mostly belong to sub-clades similar to genes from the A(H5N8) HPAI viruses with the exception of the PA and PB2 genes which have undergone further reassortment. There is heterogeneity among the currently emerging strains, with some viruses being more closely related for some genes with A(H5N6) viruses circulating in other parts of Eurasia (Figure 7). Sharing of the genome data behind the Beerens et al. paper recently published (Beerens et al., 2018) would allow further analysis on the origin of the A(H5N6) circulating virus. However there is no evidence to date of any reassortment which has resulted in the inclusion of A(H5N6) genes from clades that have been associated with human infections. To date, there has not been detection of mammalian adaptation - associated mutations with these viruses still being assessed as having predominantly avian affinity. The linked tree file shows a Maximum likelihood phylogenetic tree of the HA gene with the latest A(H5N6) emerging strains shown in red (phylogenetic tree in supporting information). The A(H5N6) strain isolated from chickens in Greece in 2017 is shown in blue (phylogenetic tree in supporting information). The latest strains do not cluster with the A(H5N6) clade associated with human infections, predominantly circulating in poultry in China and with sporadic detections in both wild birds and poultry in South-East Asia.

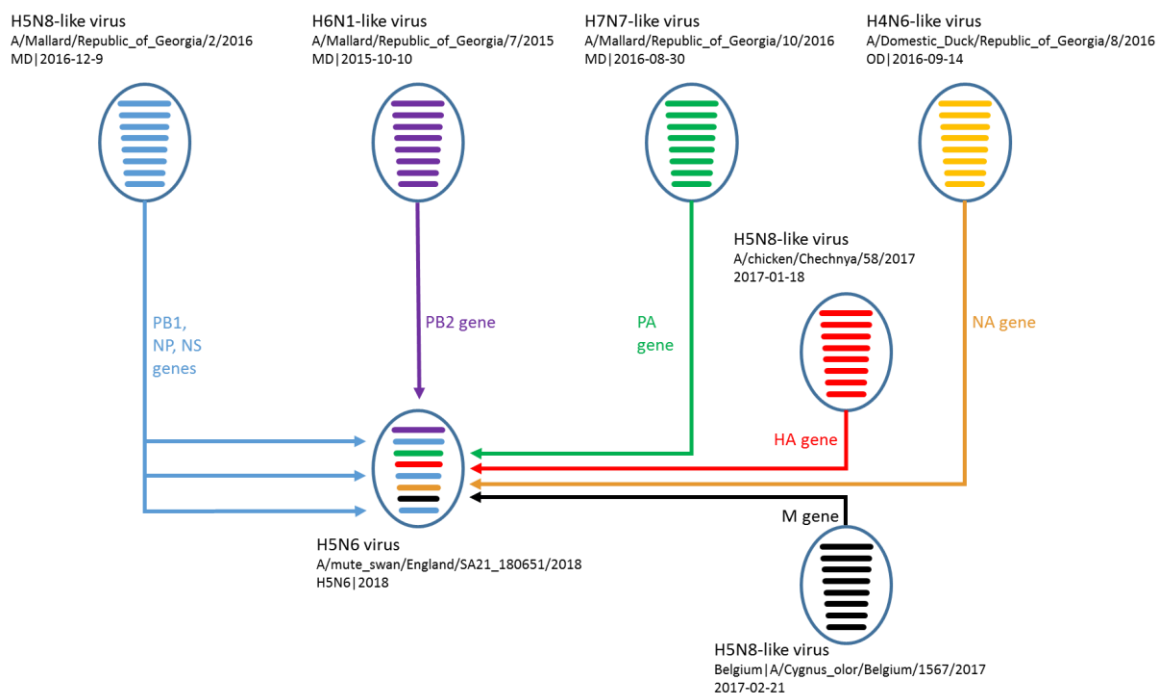


Figure 7: Genotype illustration of the reassortment process leading to the 2017/2018 HPAI A(H5N6), Europe

4.1.3. Phenotypic characterisation of AI viruses circulating in the EU

4.1.3.1. HPAI in domestic birds

Information extracted from PAFF Committee presentations

Between 16 November 2017 and 15 February 2018, there were slide presentations by Bulgaria (30 November 2017), France (17 January 2018), Germany (30 November 2017), Italy (30 November 2017, 18 January 2018), and the Netherlands (18 January 2018), as well as by CVET missions to Bulgaria (17 January 2018) and Italy (30 November 2017) at meetings of the Standing Committee on Plants, Animals, Food and Feed (EC, online-a). The pdfs of these slide presentations are available at https://ec.europa.eu/food/animals/health/regulatory_committee/presentations_en.

In the reports on Bulgaria (30 November 2017 and 17 January 2018), HPAI A(H5N8) was diagnosed on 5 poultry holdings (3 duck holdings, 2 backyard holdings with multiple poultry species) between 18 October 2017 and 22 November 2017. In one of the duck holdings, consisting of parent ducks, HPAI was suspected based on egg drop and diarrhea, while mortality seemed normal. In another duck holding, HPAI was detected through a serological monitoring; according to the owner no clinical signs were seen, although mortality was greater than 10%. The conclusion from these outbreaks of HPAI A(H5N8) was that detection of clinical signs from infection with this virus seemed to be decreasing, especially in ducks, although the age-dependency of the observed mortality was not analysed. Raising awareness on the mild or absent clinical signs from HPAI A(H5N8) virus infection could improve passive surveillance, particularly for duck farmers and non-commercial holders. In addition to passive surveillance, intensifying serological screening duck farms should be considered.

The first two reports on Italy (30 November 2017) contained no information on phenotypic characterisation of HPAI viruses. In the third report on Italy (18 January 2018), two outbreaks of HPAI A(H5N8) were detected, one in a holding with multiple poultry species, and the other in a turkey holding. In both, HPAI was suspected based on increased mortality.

In the report of the Netherlands (28 January 2018), an outbreak of HPAI A(H5N8) was detected in a duck holding on 8 December 2017. It was suspected based on (unstated) clinical signs of AI, decreased food intake, and 2% mortality in one day.

Information extracted from the scientific literature

Liu et al. (2018b) reported on experimental infections of ducks and chickens with three isolates of HPAI A(H5N6) virus detected in China in 2015 to 2016 in chickens. Four-week-old mallards were inoculated intranasally with 10^4 to 10^7 EID₅₀ virus. The median duck lethal dose was calculated as $>10^7$ EID₅₀, indicating that less than half of the ducks inoculated with that dose died. Four-week-old chickens (breed not specified) inoculated with 10^3 EID₅₀ virus were systemically infected and died within 4 dpi. These results indicate that these viruses, while highly virulent for chickens, cause asymptomatic infection in mallards, which may aid their maintenance and dissemination in free-living mallard populations.

Xiang et al. (2017) reported on experimental infections of chickens, geese, and pigeons with a HPAI A(H5N6) isolate from a domestic goose in China in 2016. Six-week-old white leghorn chickens, 3-week-old geese, and six-week-old pigeons (three individuals per species) were inoculated intranasally with 10^6 EID₅₀ virus. All three species became systemically infected. The chickens showed obvious clinical signs of disease and all died within 4 dpi. The geese showed clinical signs of disease including depression and 1 goose died at 5 dpi. The pigeons became systemically infected, but showed neither clinical signs nor mortality. Based on cohousing with sentinel birds of the same species, the virus was transmitted among chickens and geese, but not among pigeons.

4.1.3.2. LPAI in domestic birds

The presentations of France (17 January 2018), Germany (30 November 2017), and Italy (18 January 2018) contained information on the phenotypic characterisation of LPAI viruses.

In the report of France (17 January 2018), four outbreaks of LPAIV were detected between 25 September and 28 December 2017, two in turkey breeding holdings (A(H5N3)) and two in duck holdings (A(H5N3) and A(H5N2)). In the turkey breeding holdings, AIV was suspected based on

production decline, which was 20% in three days on one of the holdings. In the duck holdings, AIV was detected by active surveillance (PCR on cloacal and tracheal swabs of 20 birds per flock); no clinical signs were reported.

In the report of Germany (30 November 2017), LPAI A(H5N2) virus was detected on 22 November 2017 in a holding with both ducks and geese. The virus was detected by active surveillance; no clinical signs were reported.

In the report of Italy (18 January 2018), outbreaks of LPAIV A(H5) were detected between 28 November and 15 December 2017 in two holdings with multiple poultry species. In one, detection was based on active surveillance and no clinical signs were reported. In the other, HPAI was suspected based on increased mortality; however, LPAIV A(H5) was detected and mortality was attributed to another, unstated, cause.

4.1.3.3. HPAI in wild birds

Pathogenicity in the affected species

Information extracted from the World Organisation for Animal Health (OIE) reports

The HPAIV subtype that was identified in carcasses of wild birds submitted for AIV testing was A(H5N6) (91 cases) (Table 3). The reports to OIE provide the numbers of virus-positive dead birds per species, but not the average population size of the affected wild bird species from which wild bird carcasses were obtained, let alone the number of animals at risk in these populations. Therefore it is not possible to make an objective estimate of the mortality rate in order to assess the pathogenicity of infection with these subtypes of HPAIV in wild bird populations. Some information may be gained by data on the number of carcasses of the different wild bird species that tested positive for HPAIV during surveillance activities. However, these figures need to be interpreted with caution, because they need to take into account multiple factors, including ease of detection of carcasses of different wild bird species, selection of carcasses biased towards certain species, abundance of species, and species range.

Taking all HPAIV A(H5N6) together, five or more dead birds were found virus-positive in the following species: Mute Swan, Tufted Duck, Mallard, Great black-backed gull, Greylag Goose (Table 3). The species for which the highest number of virus-positive carcasses was found was the Mute Swan, with more than twice more than any other species. Although this number may be biased by the visibility of Mute Swan carcasses, it probably also reflects the high pathogenicity of HPAIV A(H5) for this species. The next three species for which the highest number of virus-positive carcasses was found were Tufted Duck, Mallard, Great black-backed gull. The susceptibility of these species for HPAIV A(H5N6) is similar to their susceptibility to HPAIV A(H5N1) in the epidemic of 2005-2006 (Olsen et al., 2006). An apparent difference in the pathogenicity of HPAIV A(H5) between November 2017 and February 2018 compared to HPAIV A(H5N1) in 2005-2006, is the apparently higher pathogenicity for dabbling ducks (Mallard, Eurasian Wigeon), gulls (Great black-backed Gull, Herring Gull, Mew Gull), and geese (Greylag Goose, Canada Goose), although other factors, such as differences in exposure, cannot be ruled out.

Two variables are noteworthy in the mortality of wild birds from HPAIV A(H5) in this three-month period. First, the majority of events involved single dead birds. Except for one Common Moorhen, nearly all of the species involved were those listed in the revised list of target species for passive surveillance (Table 3). This indicates that the investigation of events involving single dead birds of target species is important for comprehensive passive surveillance for HPAI A(H5).

Second, the minority of events involving multiple dead birds of a species were from the United Kingdom (7 of 12) and the Netherlands (3 of 5); most events reported from continental Europe all involved single cases (Table 3). Possible explanations include a higher genetic resistance, a higher HPAIV-H5-specific immunity, or a lower prevalence of virus infection in wild bird populations in continental Europe than in the United Kingdom. Support for HPAIV-H5-specific immunity in wild birds in continental Europe comes from the study of Poen et al. (2018), who found 4.2% incidence of HPAI A(H5) clade 2.3.4.4.-specific antibodies in the 2016/17 winter in wild birds in the Netherlands. A higher incidence of specific antibodies may confer a higher herd immunity to HPAIV A(H5) infection, and therefore higher resistance to mortality from HPAIV A(H5) infection. Comparable data for other countries, including the United Kingdom, are not available. These authors suggested that further

optimisation and validation of the serological assays, and application across multiple MSs, are required to provide rough estimates of the seropositivity in subsequent years.

Table 3: Cases of HPAI A(H5N6) infection in free-living wild birds, ordered by country and species, occurred from 16 November 2017 to 15 February 2018 and reported to OIE (OIE, online)

OIE report no.	Country	No. of events	Species	No. of events in which the species was involved	No. of cases/event	Total no. of cases
26065	Denmark	1	White-tailed eagle	1	1	1
25844	Germany	1	Unidentified	1	1	1
25927	Ireland	1	White-tailed eagle	1	1	1
25986	Sweden	1	White-tailed eagle	1	1	1
25551	Switzerland	1	Mute swan	1	1	1
25786	The Netherlands	5	Black-headed gull	1	1	1
			Great black-backed gull	1	1	1
			Mute swan	4	1, 1, 4, 6	12
25963	United Kingdom	12	Canada goose	1	1	1
			Common moorhen	1	1	1
			Common pochard	1	1	1
			Great black-backed gull	1	6	6
			Great crested grebe	1	1	1
			Greylag goose	1	7	7
			Herring gull	1	1	1
			Mallard	3	1, 2, 8	11
			Mew gull	1	1	1
			Mute swan	6	1, 1, 1, 2, 5, 15	25
			Tufted duck	4	1, 1, 5, 5	12
			Unidentified	2	2, 3	5
Total	(7)	22	(13)	-	-	91

Information extracted from the scientific literature

Tsunekuni et al. (2018) reported on the HPAI A(H5N6) outbreak in Japan in 2016/17. There was mortality in mute swans and black swans in the first half of outbreak, and in black-headed gulls, great crested grebes, and Eurasian pochards in the second half of outbreak. Pathological examination of mute swans and black swans showed severe necrosis and inflammation in multiple organs, similar to that seen in these species from other HPAI A(H5) viruses. Other species cohabiting with affected wild birds, including mallards, did not show mortality, suggesting that these unaffected species may have been subclinically infected and may have contributed to the spread of the virus to other locations. Globig et al. (2018) reported on the HPAI A(H5N8) virus outbreak in Germany from November 2016 to September 2017. In the list of wild bird species found ill or dead and testing positive for HPAI A(H5N8) virus, they reported several species not reported as HPAI-positive in the ADNS list updated to November 2017. These were common scoter (*Melanitta nigra*), red-necked grebe (*Podiceps grisegena*), red-breasted goose (*Branta ruficollis*), little gull (*Hydrocoloeus minutus*), and redshank (*Tringa totanus*). All these birds were free-living, except the red-breasted goose, which was feral.

Meier et al. (2017) also reported on the HPAI A(H5N8) virus outbreak in winter 2016/17, but in Switzerland. In the list of wild bird species found ill or dead and testing positive for HPAI A(H5N8) virus, they reported one species not present as HPAI-positive in the ADNS list updated to November 2017, the common moorhen (*Gallinula chloropus*). Based on the detection of HPAI A(H5N8) virus in

juvenile mute swans and mallards found dead as late as August 2017, they concluded that the virus is maintained to some extent in healthy waterbirds and circulates in the local population, necessitating constant vigilance.

Poen et al. (2018) also reported on the HPAI A(H5N8) virus outbreak in winter 2016/17, in the Netherlands. They collected faecal swabs or environmental swabs from various species of free-living birds, and detected HPAI A(H5N8) virus in 14 of 118 Eurasian wigeons (*Anas penelope*), 17 of 1,824 mallards, and 1 of 1 common buzzard (*Buteo buteo*) sampled between November 2016 and March 2017. Together with the paucity of mallards found dead and infected during the same outbreak, this provides evidence from the field that mallards might be more resistant to disease due to HPAI A(H5N8) virus compared to other wild bird species, and might therefore act as a reservoir species. The presence of antibodies to HPAI A(H5) virus was compared between winters 2014/15, 2015/16, and 2016/17 in Eurasian wigeons, lesser white-fronted geese, mute swans, common coots, black-headed gulls, mallards, and Egyptian geese. Over all species, the incidence of HPAI A(H5) clade 2.3.4.4.-specific antibodies was 0% before 2014, increased to 4.6% during the first outbreak of HPAI A(H5N8) virus in 2014/15, decreased to 3.5% in the 2015/16 winter, when HPAI A(H5N8) was not detected in the Netherlands, and rose to 4.2% in the 2016/17 winter, when there was a large HPAI A(H5N8) virus outbreak in the Netherlands.

4.1.4. Human cases due to A(H5N8) or A(H5N6) viruses detected in Europe

No transmission of avian influenza virus A(H5N8) to humans has been observed in Europe or worldwide. As stated in 3.1.2., molecular data do not indicate a pattern for increased transmission to humans yet. No airborne transmission between ferrets has been observed (Pulit-Penalosa et al., 2015; Kaplan et al., 2016; Herfst et al., 2018). The haemagglutinin phenotype was assessed to be poorly adapted for infection of mammals (Lee et al., 2018). However, mutations or reassortment events could contribute to enhanced pathogenicity, virulence and potentially transmissibility: in a study analysing genomic signatures, three positions that exhibited human-like signatures (polymerase acidic protein (PA)-404S, polymerase basic protein 2(PB2)-613I and PB2-702R) were increasingly detected in recent viruses. Also substitutions S137A and S227R in the receptor-binding site and A160T in the glycosylation site of the HA protein might indicate viral adaptation processes towards increased ability to bind human-type receptors (Xu et al., 2017). Wang et al have previously shown that 283M and 526R in PB2 can contribute to enhanced virulence in mammals (Wang et al., 2017b). Another study has shown that an exchange of internal genes with genes deriving from A(H5N1) viruses enhance pathogenicity and virulence (Park et al., 2018). Such reassorted viruses with different gene compositions have already been discovered (Beerens et al., 2018; Ma et al., 2018; Poen et al., 2018). Not even reassortment events with other viruses, but substitution of amino acids (PB2 (E627K), PA (F35S), HA (R227H), and NA (I462V)) can also alter the virulence in a mammalian model mouse (Yu et al., 2018). The capacity of 2.3.4.4 viruses to frequently reassort has been observed in 2017 (Pohlmann et al., 2018). Tate (Tate, 2018) warned about severe consequences for global health if A(H5N8) viruses would acquire mutations or reassort with viruses leading to increased capability to transmit to or between humans.

The newly emerging reassorted A(H5N6) viruses detected in Europe and a few Asian countries have not been described to have transmitted to humans. As described in chapter 2.1.2., no markers for mammalian adaptation or increased transmissibility to humans have been identified in these viruses.

4.1.5. Characterisation of the HPAI-affected poultry holdings

From 16 November 2017 to 15 February 2018, six HPAI outbreaks, five A(H5N8) and one A(H5N6), have been reported in the poultry sector in EU. Four HPAI A(H5N8) outbreak occurred in Italy and one in Bulgaria. The outbreak of HPAI A(H5N6) occurred in the Netherlands. All of the outbreaks considered occurred in 2017 and one was a secondary outbreak. Poultry types and species of the affected holdings are presented in Figure 8.

In the reference period, around 100,000² domestic birds were affected by HPAI A(H5N8) and A(H5N6) outbreaks in EU. Susceptible birds per holding and holding size are reported in Figure 9.

² Based on the number of susceptible animals reported to EFSA

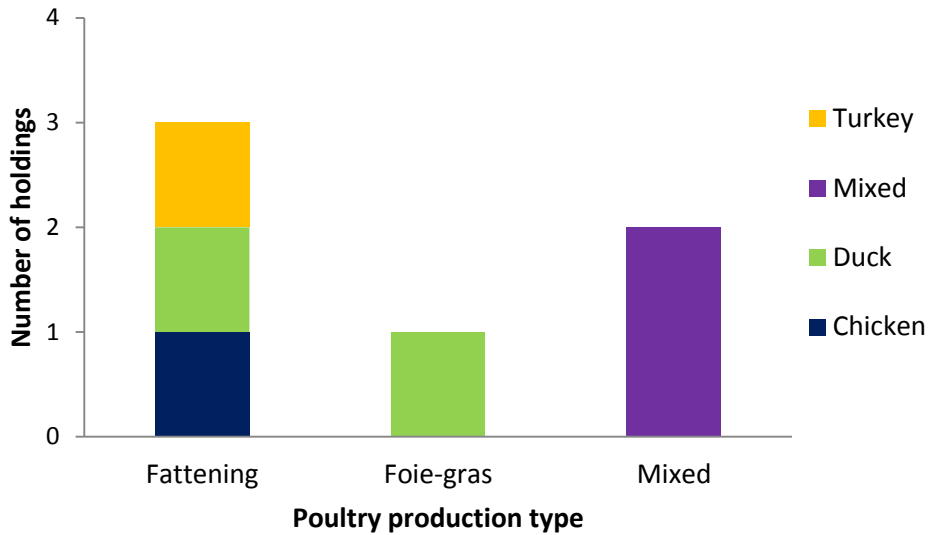


Figure 8: Number of HPAI affected holdings by poultry species and poultry production type occurred in EU from 16 November 2017 to 15 February 2018 (n=6)

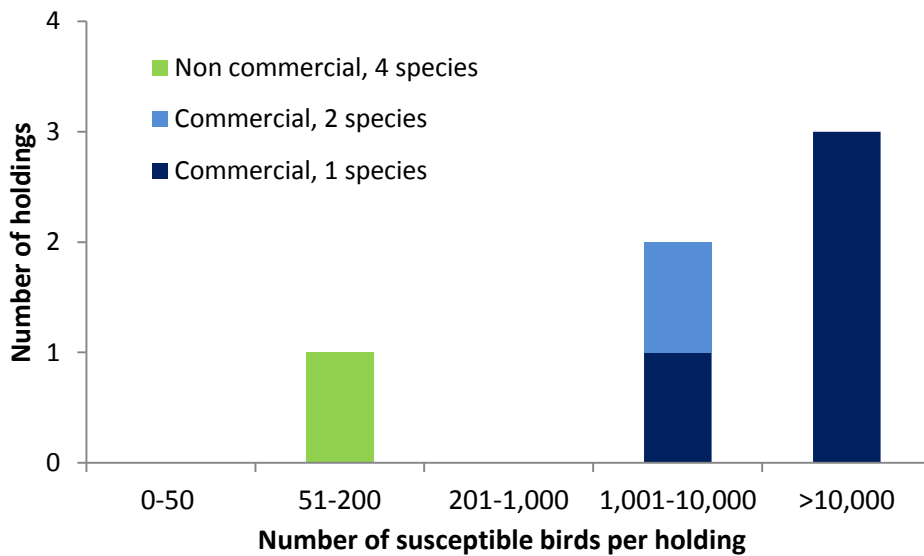


Figure 9: Number of HPAI affected commercial and non-commercial holding by class of number of susceptible birds per holding and by number of species bred per holding in EU from 16 November 2017 to 15 February 2018 (n=6)

The sampling strategy leading to outbreak detection at holding level is reported in Figure 10. Only the secondary outbreak was detected by means of outbreak related surveillance.

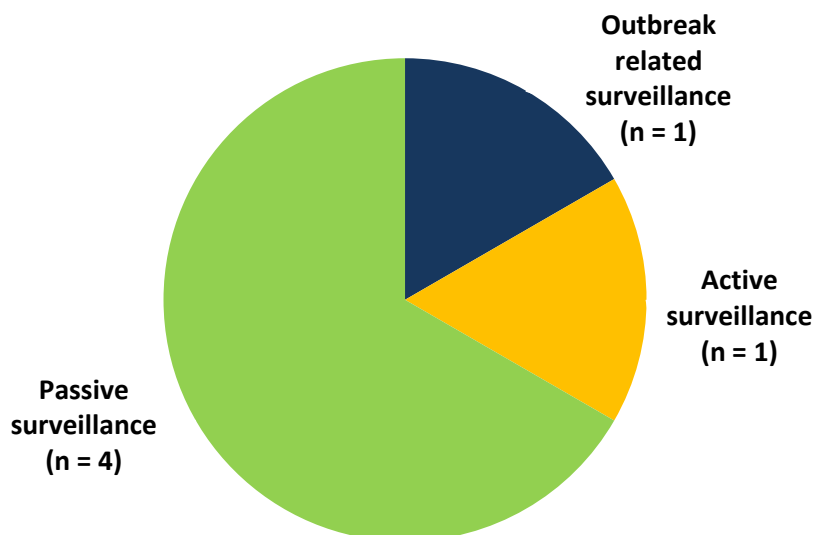


Figure 10: Number of HPAI outbreaks by sampling strategy leading to outbreak detection in EU from 16 November 2017 to 15 February 2018

As pointed out in the preceding report (EFSA et al., 2017a), the dataset does not contain information on non-affected/ reference poultry holdings. Without this information, firm conclusions are impossible to draw about the risk of HPAI incursion into particular categories of poultry holdings, e.g. as far as potential risk factors, such as flock size, outdoor access, biosecurity measures in place, etc.. A possible, simple and efficient way to obtain the needed information would be to collect those data from the poultry flocks located within the 3 km protection zone in an outbreak situation (i.e. a matched case-control design – matching on time and location), as the official veterinarians have to visit those neighbouring flocks anyway according to the EU legislation. In addition, neighbouring flocks are the most relevant comparisons to evaluate the effect of biosecurity measures, since the virus is known to have been present in that neighbourhood at the time, when the affected flock became infected. As an example, information extracted from PAFF Committee presentations (EC, online-a) for the Netherlands (18 January 2018) report that 2 fattening duck holdings, 1 broiler, and 1 laying hen holdings in 3 km zone were checked and found negative for AIV. The provision of information on the holding characteristics for those neighbouring holdings (same parameters as reported for affected holdings) would allow the European Food Safety Authority (EFSA) to carry out risk factor analysis. It would be a limited burden to the MSs since veterinary inspectors must visit the neighbouring holdings to check for AIV presence.

4.1.5.1. HPAI A(H5N6)-affected poultry holdings in the Netherlands

From 16 November 2017 to 15 February 2018, one HPAI A(H5N6) outbreak was identified in a poultry holding in the Netherlands. Characteristics of the affected holding and species are reported in Table 4.

The outbreak was identified as a primary outbreak through passive surveillance activities: 2% mortality in one day, clinical signs and drop in feed intake were observed in the holding.

The animals had no outdoor access in the 21 days before the outbreak and the most likely source of virus introduction is unknown.

A second HPAI A(H5N6) outbreak in a fattening duck holding was reported on 14 March 2018 (outside reporting period of this report) in the province of Overijssel in the framework of the surveillance and control programme.

4.1.5.2. HPAI A(H5N8)-affected poultry holdings in Italy

From 16 November 2017 to 15 February 2018, a total number of four HPAI A(H5N8) outbreaks were identified in poultry holdings of Italy. Characteristics of the affected holding and species are reported in Table 4.

Three out of four outbreaks detected in Italy in the period were primary outbreaks. A secondary outbreak occurred in a commercial holding related to the cluster occurring in Brescia province that has been reported in the former report (EFSA et al., 2017a). The secondary outbreak was identified through outbreak related surveillance activities. No clinical signs were reported. In the other three HPAI A(H5N8) primary outbreaks, infection was detected via passive surveillance. Increased mortality was reported in all three holdings regardless of the poultry species reared.

The two commercial fattening holdings had no outdoor access in the 21 days before the outbreak. The commercial mixed species and mixed productions holding had part of the day outdoor access. The non-commercial mixed species and productions holding had part of the day or whole day outdoor access, depending on the species.

For all the primary outbreaks indirect contact with wild birds has been reported as the most likely source of infection, whereas for the secondary outbreak the most likely source of virus introduction was indirect contact with poultry faeces/products from another infected premise by personnel, equipment, vehicles, feed/bedding.

A HPAI A(H5N8) outbreak in a commercial holding with laying hens was reported on 2 March 2018 (outside reporting period of this report) in Bergamo province (Lombardy region) in the framework of the surveillance and control programme. On 8 March a second HPAI A(H5N8) outbreak was confirmed in a laying hens holding located in Brescia province (Lombardy region) which is epidemiologically linked to the previous outbreak. On 12 March a third HPAI A(H5N8) outbreak was confirmed in a fattening turkey holding in Bergamo province (Lombardy region) situated in the protection zone established in relation to the first outbreak in this province.

4.1.5.3. HPAI A(H5N8)-affected poultry holdings in Bulgaria

One outbreak of HPAI A(H5N8) has been identified in Bulgaria from 16 November 2017 to 15 February 2018. Four more outbreaks have previously been notified in poultry holdings in October 2017. They were excluded from the past report and they have been considered in the present report, therefore data from Bulgaria are presenting a total number of 5 outbreaks. Characteristics of the affected holding and species are reported in Table 4.

All five outbreaks were primary outbreaks. Infections in the three commercial holdings were highlighted during active surveillance activities, and no clinical signs or mortality or drop in feed/water intake were reported. The two non-commercial holdings were identified as affected through passive surveillance: the animals presented mortality, clinical signs, drop in egg production and drop in feed/water consumption in both premises.

Regarding outdoor access in the 21 days before the outbreak, the commercial fattening duck holding had no outdoor access. The two commercial ducks holdings (for the production of foie gras) reported outdoor access in the 21 days before the outbreak for part of the day and the whole day, respectively. The two non-commercial mixed poultry holdings had outdoor access the whole day in the 21 days before the outbreak.

The most likely source of virus introduction in the fattening ducks commercial holding has been reported as indirect contact with wild birds: feed transport equipment/pallets were kept unprotected outside the farm, in a wild bird high density area. Possibly, the infection has been carried through the contamination of pellets with wild bird faeces. In the remaining four outbreaks the most likely source of virus introduction is unknown. Nevertheless, in the two commercial duck holdings (for foie-gras production) breaches of the biosecurity strategy and possible contamination through faeces of wild birds and contaminated means of transport used in the farm were suggested as likely sources of the infection, and no biosecurity measures were in place in the two non-commercial holdings.

An HPAI A(H5N8) outbreak in a commercial holding with laying hens was reported on 2 March 2018 (outside reporting period of this report) in General Toshevo city (Dobrich region) in the framework of the surveillance and control programme.

Table 4: Outbreaks of HPAI occurred in the poultry sector in EU from 16 November 2017 to 15 February 2018

Country	Holding production category	Species	Production type	Date of suspicion	Number of susceptible animals
NL	Commercial	Duck	Fattening	07/12/2017	15,985
IT	Commercial	Chicken	Fattening	22/11/2017	56,491
		Turkey	Fattening	10/12/2017	17,000
		Chicken, duck	Mixed*	30/11/2017	7,421
	Non-commercial	Chicken, duck, goose, peacocks	Mixed	22/11/2017	142
BG	Commercial	Duck	Fattening	13/10/2017	10,883
			Foie-gras	31/10/2017	10,830
				15/11/2017	3,000
	Non-commercial	Chicken, duck, turkey, pheasant, guinea fowl, pigeon	Mixed**	30/10/2017	450
			Mixed***	18/10/2017	148

* Breeding and fattening ducks and chickens were present in the holding;

** Laying hens and fattening turkeys, pheasants, ducks, pigeons and guinea fowls were present in the holding;

*** Laying hens and fattening turkeys were present in the holding;

4.1.6. Follow-up of the Italian AI situation

Italy had been the only MS being largely affected by circulation of HPAI A(H5N8) viruses in summer 2017, with a second epidemic wave that started in July. Differently from the first wave, which occurred between January and May 2017, in the second semester also secondary cases were recorded. In particular, in October and November 2017 lateral spread of HPAI A(H5N8) affected the industrial poultry sector, leading to a large cluster that affected 23 farms located in the same province in the most densely populated poultry area (EFSA et al., 2017a).

However, between 16 November 2017 and 15 February 2018, only 4 HPAI A(H5N8) cases were reported in Italy. All of the cases were located in the northern regions of Lombardy (n = 1), Veneto (n = 2), and Emilia Romagna (n = 1). The outbreak recorded in Lombardy had been considered as a secondary outbreak related to the large Brescia cluster; although epidemiological connections were not clearly indicated, the location of the farm and the results of phylogenetic analyses clearly indicated that the infection was related to lateral spread occurring in the area.

The two outbreaks reported in the Veneto region were detected in a non-commercial farm and in a premise rearing multiple species (confirmation dates: 23 November and 1 December respectively). Phylogenetic analyses indicated that the viruses identified in the two cases in Veneto belonged to the group of viruses circulating in the region, and which were not reported since mid-October 2017. In particular, high similarity was detected with viruses circulating in poultry and wild birds since July 2017.

The last HPAI A(H5N8) case in Italy was detected in a fattening turkey farm in Emilia Romagna on 11 December 2017. The isolated virus resulted related to the group of viruses circulating in the western part of the Italian affected areas (i.e. Lombardy, Piedmont, and some findings in Emilia-Romagna regions); nevertheless no connections were detected with the large cluster occurred in Lombardy. Furthermore phylogenetic analyses detected a higher similarity with viruses circulating in the area in wild birds.

4.2. Applied prevention and control measures (TOR3)

4.2.1. In the Netherlands

As of December 2017, the Netherlands faced multiple introductions of a HPAI A(H5N6) virus, which resulted as reassortant of HPAI A(H5N8) viruses circulating in Europe and Eurasian LPAI viruses (Beerens et al., 2018). Prevention and control measures applied in the reference period are therefore related to the new introductions. Measures were applied starting on 8 December, after the detection of HPAI A(H5N6) in a duck farm. Measures included:

- Housing order for commercial poultry, hobby and other non-commercial birds;
- Ban on fairs, exhibitions and other gathering of birds;
- Ban on duck hunting and general hunting in wetlands;
- Mandatory clinical examinations of turkeys and ducks before loading for transport;
- Mandatory clinical examinations ante-mortem for ducks and turkeys at slaughterhouses;
- Specific biosecurity measures (including: covering bedding and litter, applying hygiene protocols);
- Increasing awareness.

Housing order was implemented after experts on Avian Influenza belonging to an official Commission on Animal Diseases assessed the risk of infection and spread of AI. The housing order was triggered by the confirmation of HPAI A(H5N6) in poultry.

Other biosecurity measures included the registration of people visiting poultry farms, and the ban on getting in contact with reared birds. Furthermore, the Government stipulated an agreement with companies, in order to being able to deliver cleaning and disinfection supplies and equipment within four hours from an alert by the Dutch Government.

The ban on hunting, provided following the detection of HPAI A(H5N6) virus in the duck farm, was lifted as of 9 January 2018. Annex A reports in detail the prevention and control measures applied in the Netherlands in the period of interest.

4.2.2. In Italy

Only four HPAI A(H5N8) cases were reported in Italy in the reference period (16 November 2017 – 15 February 2018). Most of the control measures applied in this period were already in force during the second epidemic wave in Italy, and were extended accordingly to the evolution of the epidemiological situation.

On 21 November 2017 the Ministry of Health published a Provision³ defining a Further Restricted Zone (FRZ) which was further classified in High and Medium poultry density. In the FRZ the measures applied included:

- Census of industrial poultry holdings;
- Housing order, to reduce the risk of direct/indirect contact with wild birds;
- Pre-movement clinical inspection and virological testing;
- Increased biosecurity measures regarding the vehicles and the personnel entering and exiting farms;
- Ban on bird fairs and exhibitions, and of live bird markets;
- Ban on restocking of fattening turkey farms;
- A derogation was granted to restock turkey farms, following an assessment made by the Local Veterinary Authorities on biosecurity;

³ Ministerial Provision No 26651 of 21 November 2017 - Influenza aviaria ad alta patogenicità H5N8 – Dispositivo dirigenziale recante modifica e sostituzione del Dispositivo dirigenziale DGSAF prot. n. 24016 del 20 ottobre 2017 e successive modifiche;

The Ministerial Provision of 19 February 2018⁴, classified some Italian regions as High Risk Regions, accounting for:

- Epidemiological situation (occurrence of HPAI cases during the current epidemic);
- Risk factors for HPAIV introduction (location in proximity to wetlands);
- Risk factors for HPAIV spread (density of poultry farms, with a particular focus on species and production types considered at higher risk, as fattening turkeys, or domestic ducks);
- Outcome of the National Surveillance Plan (indicating where AI cases were recorded in the past years).

In the defined regions measures similar to those applied in the FRZ were applied.

Preventive culling was applied in Italy, after assessing the potential risk of AI spread from detected outbreak (i.e. location in close proximity to the outbreak, contacts via vehicles, sharing of personnel and equipment). Nevertheless, most of the farms that underwent preventive culling were related to outbreaks that occurred before the period of reference (see Annex B for more details). In fact, only three farms were preventively slaughtered following the epidemiological situation of period 16 November 2017 – 15 February 2018.

The Ministerial Provision No 4122 of 19 February 2018 extended the application of control and prevention measures on the defined area from 28 February until 30 April 2018; amendments could be issued to further prolong the period, according to the evolution of the epidemiological situation.

4.2.3. In Bulgaria

Bulgaria reported four HPAI A(H5N8) outbreaks since 18 October 2017, with the last being confirmed on 2 November, and being considered resolved as of 31 December 2017. Annex C reports in detail the prevention and control measures applied in Bulgaria in the period of interest.

On 25 October 2017 a housing order was enforced on the whole National territory, together with the ban on fairs, exhibitions and other gathering of domestic birds. In the same provisions, also other measures were included:

- Enhanced active surveillance in poultry (with a particular focus on backyard farms);
- Enhanced passive surveillance in wild birds;
- Strengthening of biosecurity measures, which were also regularly assessed by official veterinary authorities.

After the confirmation of the third and fourth outbreaks, a ban on moving and restocking was also issued for waterfowl farms, with exceptions for the transport of birds to the slaughterhouse. Derogations were granted to farms that tested negative to serological exams and that satisfied specific criteria for biosecurity, as provided in amendment to the national legislation on biosecurity in waterfowl. Duck and goose farms needed to be able to meet the biosecurity standard by 10 January 2018.

Furthermore, a series of weekly meetings were scheduled with poultry and hunting associations between 3 November and 20 December 2017. In the same period also informative campaigns were held with farmers at a regional level to increase awareness on the risk of AI introduction and spread.

⁴ Ministerial Provision No 4122 of 19 February 2018 - influenza aviaria ad alta patogenicità. Applicazione misure di riduzione del rischio e di biosicurezza.

4.3. AI situation in other continents between 16 November 2017 and 15 February 2018 (TOR4)

4.3.1. HPAI A(H5N1)

4.3.1.1. Domestic and wild birds

Detections

Outbreaks of the Asian lineage HPAI A(H5N1) in poultry have been observed in several African countries, the Middle East and Asia throughout the year 2017 and beginning 2018. From 16 November 2017 to 15 February 2018 only Bangladesh, Cambodia and Indonesia reported new outbreaks of HPAIV A(H5N1) in backyard poultry and commercial farms. The only cases so far in 2018 were reported from Cambodia in January (see Figure 11).

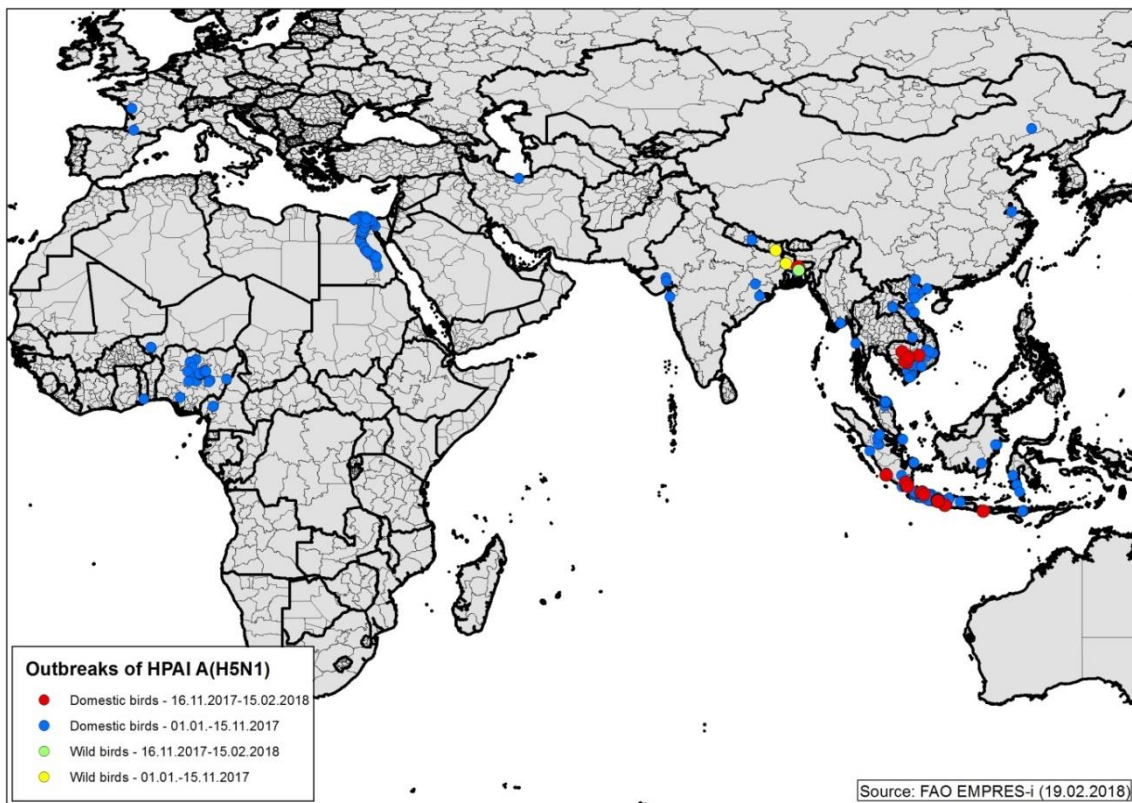


Figure 11: Distribution of confirmed HPAI A(H5N1) outbreaks in birds by place of reporting between 1 January 2017 and 15 February 2018 (FAO, online-a)

Genetic information

No new relevant information was published during the reporting period.

Phenotypic characterisation

Information extracted from scientific literature published during the reporting period:

A high level of co-circulation of A(H5), A(H7) and A(H9) viruses was demonstrated in live bird markets (LBMs) surveyed all-year-round in Cambodia in 2015 pointing to LBM as critical in maintenance and dissemination of AIV in the region (Horwood et al., 2018).

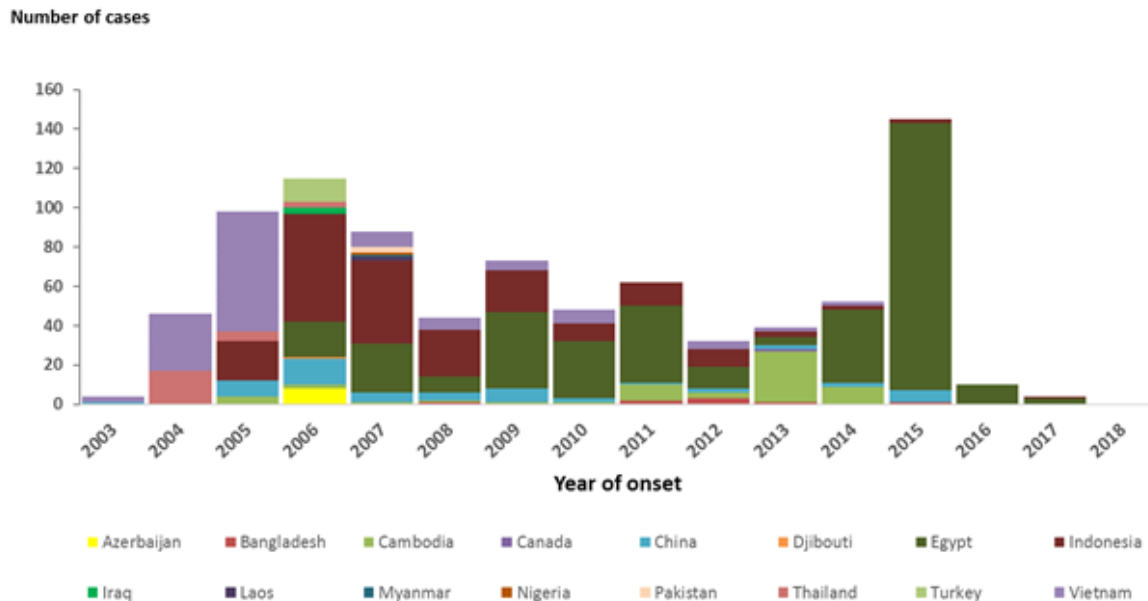
Pathogenicity of a local Egyptian strain of A(H5N1) clade 2.2.1.2 was assessed in domestic Sudani ducks (derivative of Muscovy duck) with the ducks showing an early onset of severe clinical signs (before 32 hours post infection) including ruffled feathers, recumbence, respiratory problems, neurological signs (tremors, circling, loss of balance) and high mortality. The virus was distributed systemically (Samir et al., 2018).

A(H5N1) in mammals (excluding humans)

Dogs experimentally inoculated with avian-origin A(H5N1) clades 1.1.2 and 2.3.2.1c exhibited mild respiratory signs and developed antibodies to avian influenza virus detected by nucleoprotein-based ELISA (Lyoo et al., 2017).

4.3.1.2. Human infections due to A(H5N1)

Since 2003 and as of 1 March 2018, 860 laboratory-confirmed cases of human infection with avian influenza A(H5N1) virus, including 454 deaths, have been reported from 16 countries globally. The latest case was reported in September 2017 by Indonesia (WHO, 2017a, 2018c). This was the first case reported in Indonesia since 2014 (Figure 12).



Source: Data used from WHO and Hong Kong Centre for Health Protection (CHP, 2018; WHO, 2018b).

Figure 12: Distribution of confirmed human cases of A(H5N1) by country of reporting 2003 – 2018 (n=860)

4.3.2. HPAI A(H5N6)

4.3.2.1. Domestic and wild birds

Detections

Besides the novel zoonotic reassortant HPAI A(H5N6) belonging to clade 2.3.4.4c, which was detected in domestic and wild birds in China, Japan, Myanmar, the Philippines, the Republic of South Korea, Taiwan and Vietnam since 2016, another novel reassortant HPAI A(H5N6) closely associated to clade 2.3.4.4b mainly circulating in Eurasia was isolated in December 2017 in Chungnam and Gyeonggi province from faecal samples of mallards (*Anas platyrhynchos*) (Kim et al., 2018). In the relevant time period for this report the Republic of South Korea confirmed 25 outbreaks of A(H5N6) HPAIV in large poultry and duck farms until February 2018, but no new cases of the zoonotic reassortant of HPAI A(H5N6) (2.3.4.4c) were reported from China. Single outbreaks of A(H5N6) HPAIV (clade 2.3.4.4c) were recently also reported from a backyard farm in Hong Kong Special Administrative Region (SAR) and a large chicken farm in Japan (see Figure 13). Between 16 November 2017 and 15 February 2018, Japan reported cases of HPAI A(H5N6) in northern goshawks (*Accipiter gentilis*), tufted ducks (*Aythya fuligula*) and mute swans (*Cygnus olor*), but the virus was also detected in oriental magpie-robin (*Copsychus saularis*; Hong Kong SAR), black-headed gull (*Chroicocephalus ridibundus*; Hong Kong SAR) and black-faced spoonbill (*Platalea minor*; Taiwan) (see Figure 14). Furthermore, Iran

notified to OIE the detection of A(H5N6) HPAIV in gadwalls (*Anas strepera*) related to a die-off event in wild ducks in Boujagh Natural Park, Gilan province, starting in January 2018.

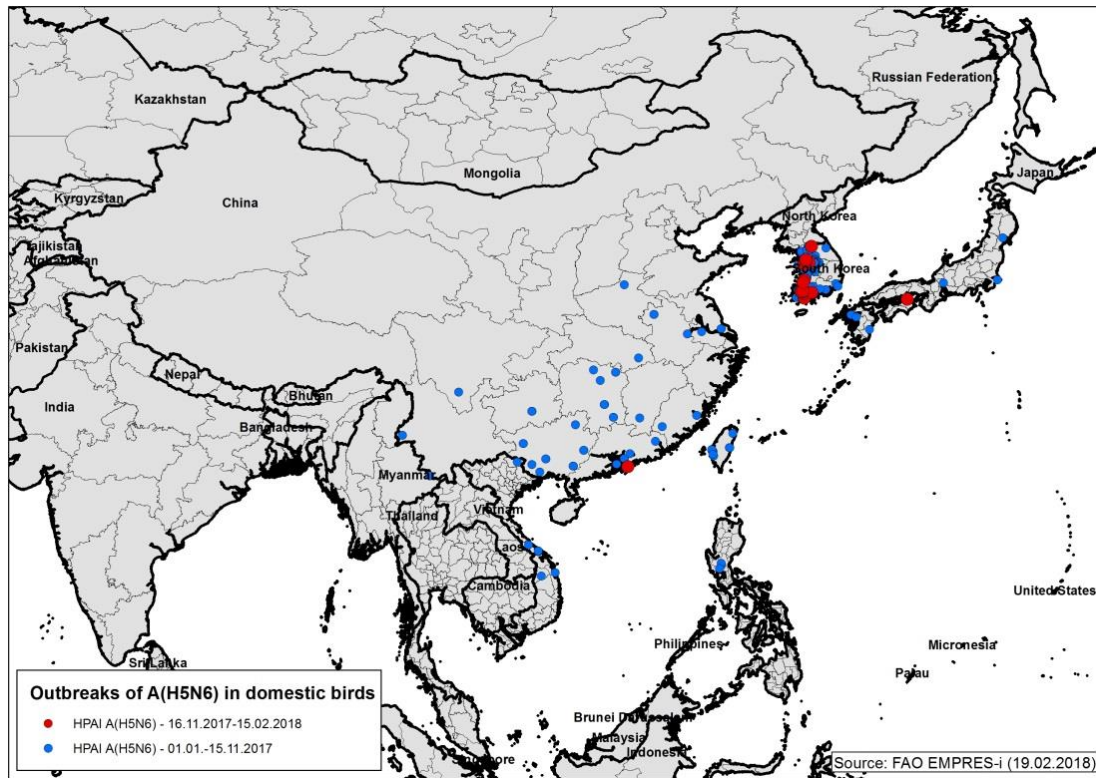


Figure 13: Outbreaks of A(H5N6) HPAIV in domestic birds between 1 January 2017 and 15 February 2018 (FAO, online-a)

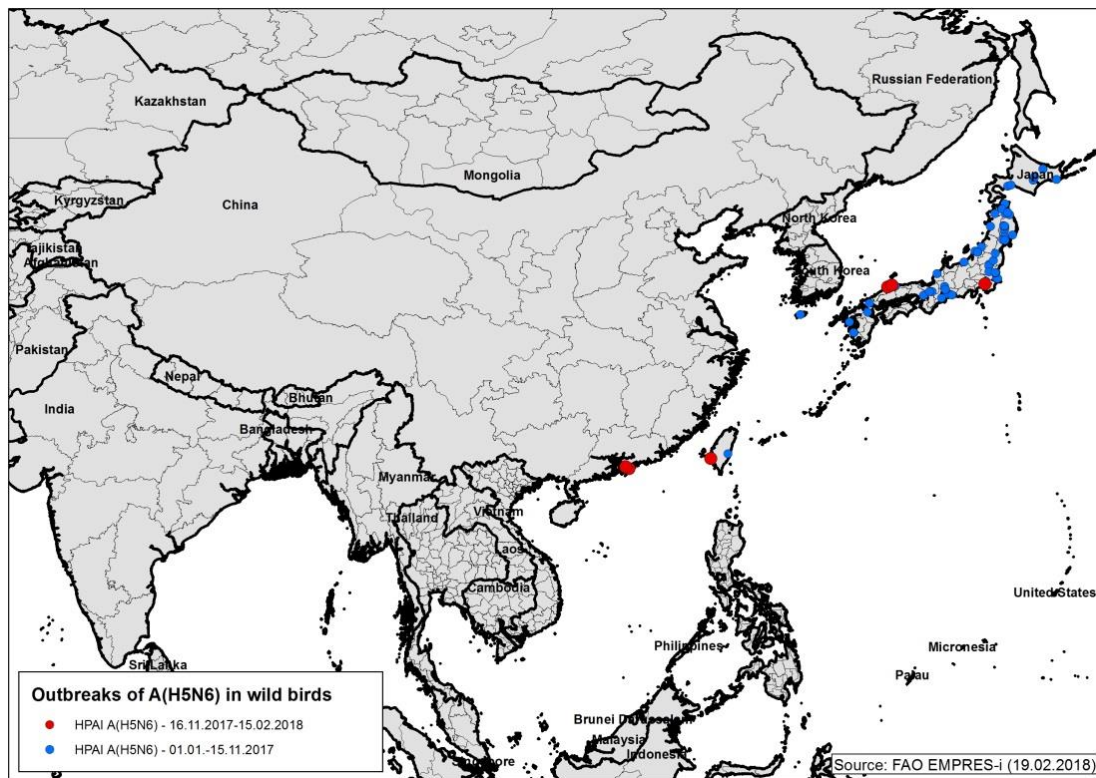


Figure 14: Outbreaks of A(H5N6) HPAIV in wild birds between 1 January 2017 and 15 February 2018 (FAO, online-a)

Genetic characterisation

Information extracted from scientific literature published during the reporting period:

A full-genome characterisation of recently detected A(H5N6) viruses from Korea (2017/2018) revealed the involvement of multiple Eurasian LPAIV subtypes and genetic relationship with Group B A(H5N8) clade 2.3.4.4 viruses, recently circulating in Eurasia (Kim et al., 2017).

Recent analyses of sequences available in public databases since the first detection in 2013 have revealed an increasing genetic diversity of A(H5N6) that continue to evolve into multiple genotypes and gradual geographical expansion of A(H5N6) in China and other countries in the region (Gao et al., 2017; Zhang et al., 2017b).

A retrospective study conducted in China confirmed that the A(H5N6) clade 2.3.4.4 had circulated in wild birds in southern China in 2013, the year of the first isolation of this subtype from poultry in the region (Luo et al., 2018).

Lu et al. (2018) reported the first case of detection of A(H5N6) in wild migratory birds sampled during active surveillance in western China at the end of 2015. The following species of birds were positive: Northern Shoveler, Common Teal, Ferruginous Pochard, Eurasian Wigeon, Ruddy Shelduck, Falcated Teal, Gadwall, and Great Crested Grebe. The authors identified that internal genes and NA gene were related to LPAIV while H5 gene clustered in clade 2.3.4.4.

A comprehensive whole-genome analysis of 89 A(H5N6) viruses detected in wild birds and poultry in Japan during the epidemic in winter 2016-2017 provided evidence for great genetic diversity exemplified by the existence of at least 5 genotypes (Takemae et al., 2017).

An A(H5N6) virus from wild waterfowl in South Korea (isolated in 2016) was genetically most similar to A(H5N6) virus detected in chickens, ducks, Pallas's sandgrouse, cats and the environment in China in 2014-2015 (Lee et al., 2017).

The analysis of the whole genome sequence of two quail-derived A(H5N6) from Vietnam in 2015 revealed the presence of triple-reassortant AIV with genes coming from viruses A(H5N2) (HA, PB1, NP, PA, M, and NS), A(H6N6) (PB2 gene), and A(H10N6) (NA gene) (Thanh et al., 2018).

Impact on risk assessment: Repeated reports on detections and genetic characterisations of multiple genotypes of A(H5N6) generated with the involvement of European and Asiatic gene pool of AI underlies the constant risk of intercontinental spread by wild birds into Europe.

Phenotypic characterisation

Information extracted from scientific literature published during the reporting period:

Pathogenicity of a novel reassortant A(H5N6) detected in wild birds in South Korea in December 2017 was evaluated in chickens and ducks (age, species and breed not specified) (Kim et al., 2018). Animals were infected with 10^7 – 10^2 egg infectious dose (EID)₅₀/mL by intranasal inoculation. The IVPI score in chickens was 2.76. The virus at the dose 10^6 EID₅₀/mL caused rapid death and replicated in all tested organs of chickens. No mortality was observed in ducks but the virus also replicated systemically (with the exception of brain) and seroconversion was observed. The 50% chicken lethal dose (CLD₅₀) was established at 2.83 log₁₀EID₅₀/mL. Since no mortality was observed in ducks following infection with 10^7 EID₅₀/mL (the highest dose used in the study), the duck lethal dose could not be calculated.

Pathogenic properties of three non-waterfowl A(H5N6) clade 2.3.4.4 viruses isolated in 2014/2015 from apparently healthy oriental magpie-robin, common moorhen and Pallas's sandgrouse in China was carried out in 6-week-old SPF leghorn chickens, 1-week-old Muscovy ducks and 6-to 7-week old SPF mice. The viruses were highly lethal and replicated systemically in chickens. The organ-wide distribution of viruses was also found in ducks, but no illness or mortality was observed. Mortality and systemic replication of viruses was demonstrated in mice (Kang et al., 2018).

Pathogenicity and transmission of an A(H5N6) 2.3.4.4 (group C) virus isolated from apparently healthy domestic goose in Guangdong province (China) was evaluated in 6-week-old chickens, 3-week-old domestic geese and 6-week-old pigeons. The virus caused 100% mortality in chickens and spread systemically. Infected geese showed clinical signs (depression), mortality (1/3 infected geese and 2/3

contact geese) and organ-wide replication. Pigeons remained healthy throughout the experiment but replication in various organs was demonstrated. The virus was transmitted through direct contact between chickens and geese but not between pigeons (Xiang et al., 2017).

Three captive-bred Mandarin ducks showed neither mortality nor clinical signs after experimental infection with A(H5N6) of Korean origin but the virus replicated efficiently in tissues, was shed from oral cavity and cloaca and was transmitted to contact birds (Son et al., 2017).

Impact on risk assessment: subclinical course of experimental infection with a recent A(H5N6) virus in ducks indicates that silent infections in domestic waterfowl are possible thus decreasing the value of passive surveillance as an early detection system in these poultry species. However, none of the studies on experimental infections cited above specifically used *Anas platyrhynchos domesticus*, which is the main species of domestic duck in the EU. Therefore, they are not informative for domestic ducks in the EU.

4.3.2.2. A(H5N6) in mammals (excluding humans)

Information extracted from scientific literature published during the reporting period:

Cao et al. (2017) performed the whole-genome characterisation of A(H5N6) viruses isolated from two cats in eastern China in 2016 and found that they were reassortants composed of gene segments derived from A(H5N6) subtype (PA, HA, NA), A(H9N2) subtype (PB2, M, NS) and A(H7N9) subtype (PB1, NP) of AIV.

Mild respiratory signs (sneezing and nasal discharge), shedding and seroconversion was observed in dogs experimentally infected with A(H5N6) virus (Lyoo et al., 2017).

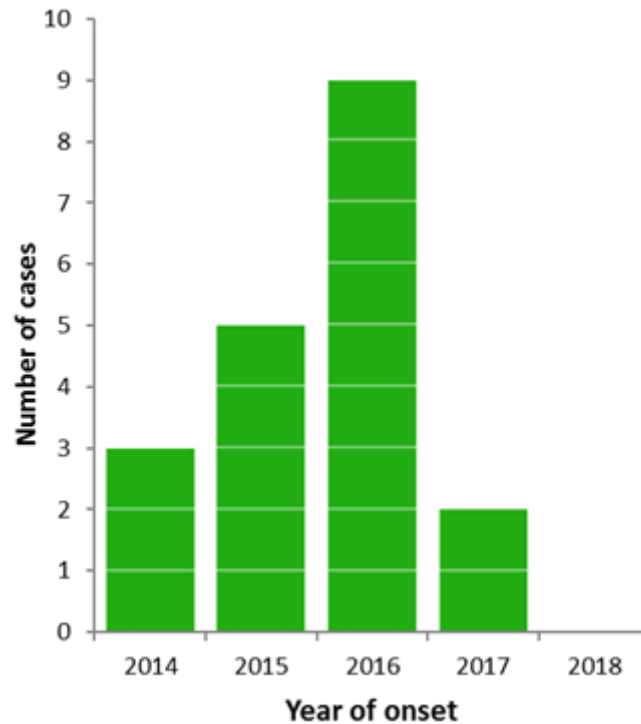
A human-derived A(H5N6) isolate (G1 genotype of clade 2.3.4.4) possessing a few amino acid substitutions (including E627K in PB2 protein), recognized previously as mammalian adaptation markers, was used for experimental inoculation of ferrets. The virus replicated to high titres in the respiratory tract (following intranasal inoculation) and additionally caused severe pneumonia (after intratracheal inoculation) but no airborne transmission between ferrets was demonstrated. Infected animals presented with inappetence, ruffled fur, watery eyes and weak hind legs (Herfst et al., 2018). In another experiment, an A(H5N6) of Chinese origin was transmissible by direct contact but not via aerosol between guinea pigs (Zhao et al., 2017).

4.3.2.3. Human infections due to A(H5N6)

Since 2014 and as of 1 March 2018, 19 laboratory-confirmed cases of human infection with avian influenza A(H5N6) virus, including six deaths, have been reported globally (WHO, 2018c). All cases occurred in mainland China. The latest case was reported in January 2018 with onset date 19 December 2017 (CHP, 2018; WHO, 2018a). According to an article in 2017, 12 deaths due A(H5N6) have been reported since 2014 (Jiang et al., 2017) (Figure 15).

A(H5N6) viruses are not transmissible via air between ferrets although the virus replicates to high titres in the respiratory tracts after intranasal inoculation and ferrets develop severe pneumonia after intratracheal inoculation.

A new highly pathogenic avian influenza virus A(H5N6) has recently emerged in Europe originating from reassorted A(H5N8) viruses of clade 2.3.4.4 with Eurasian low pathogenic viruses. It is different from A(H5N6) viruses causing human infection in China (Beerens et al., 2018). No human case due to the new emerging reassorted A(H5N6) viruses has been observed.



Source: Data used from WHO, the Hong Kong Centre for Health Protection of the Department of Health of the Government of Hong Kong SAR and Jiang et al. 2017 (Jiang et al., 2017; CHP, 2018; WHO, 2018a)

Figure 15: Number of human cases due to A(H5N6) infection by year of onset, 2014 – 2018 (n=19)

4.3.3. HPAI A(H5N8)

4.3.3.1. Domestic and wild birds

Detections

Further outbreaks of HPAI A(H5N8), clade 2.3.4.4b, from poultry and ostrich farms were reported between 16 November 2017 and 15 February 2018 primarily from the Western Cape Province, South Africa. In the same province HPAI A(H5N8) was also detected in Egyptian goose (*Alopochen aegyptiaca*), common tern (*Sterna hirundo*) and greater crested tern (*Thalasseus bergii*). The last outbreak in Nigeria from a large chicken farm in Nasarawa province was notified to OIE in February 2018 (see Figure 16).

Since November 2017 the Iraq and Saudi Arabia were hit by a wave of outbreaks of HPAI A(H5N8) in medium-sized to very large poultry farms. But no further outbreaks were officially reported from Iran despite media reports of culled chicken and economical losses in the poultry industry and a growing shortage of table eggs. Israel reported the death of a Eurasian eagle-owl (*Bubo bubo*) by HPAI A(H5N8) in February 2018 (see Figures 16 and 17).

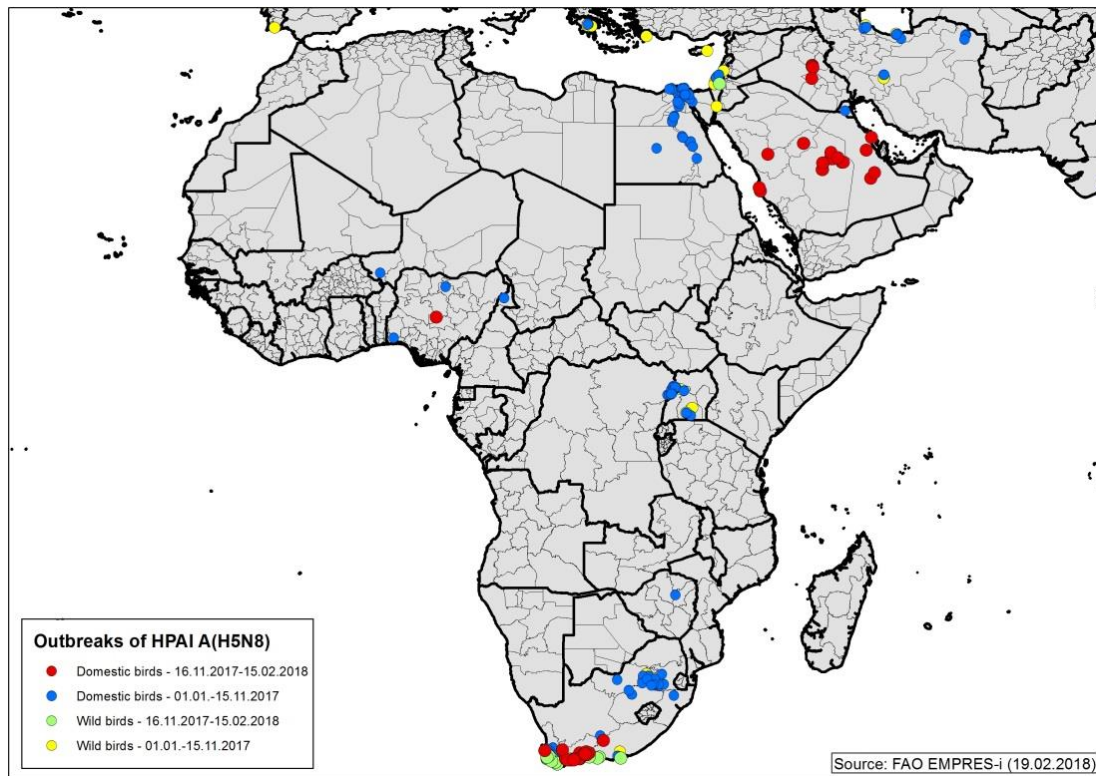


Figure 16: Distribution of confirmed HPAI A(H5N8) outbreaks in birds by place of reporting in Africa and the Middle East between 1 January 2017 and 15 February 2018 (FAO, online-a)

Between 16 November 2017 and 15 February 2018 outbreaks of HPAI A(H5N8) in Asia were notified by India, South Korea and Taiwan and several subtypes of HPAI A(H5) viruses are co-circulating in the domestic and wildlife populations of these countries (see also Section 4.3.1 and 4.3.2). The cases were mainly detected in backyard chicken and one duck farm (Taiwan), but no cases in wild birds were confirmed during this time period in Asia (see Figure 17).

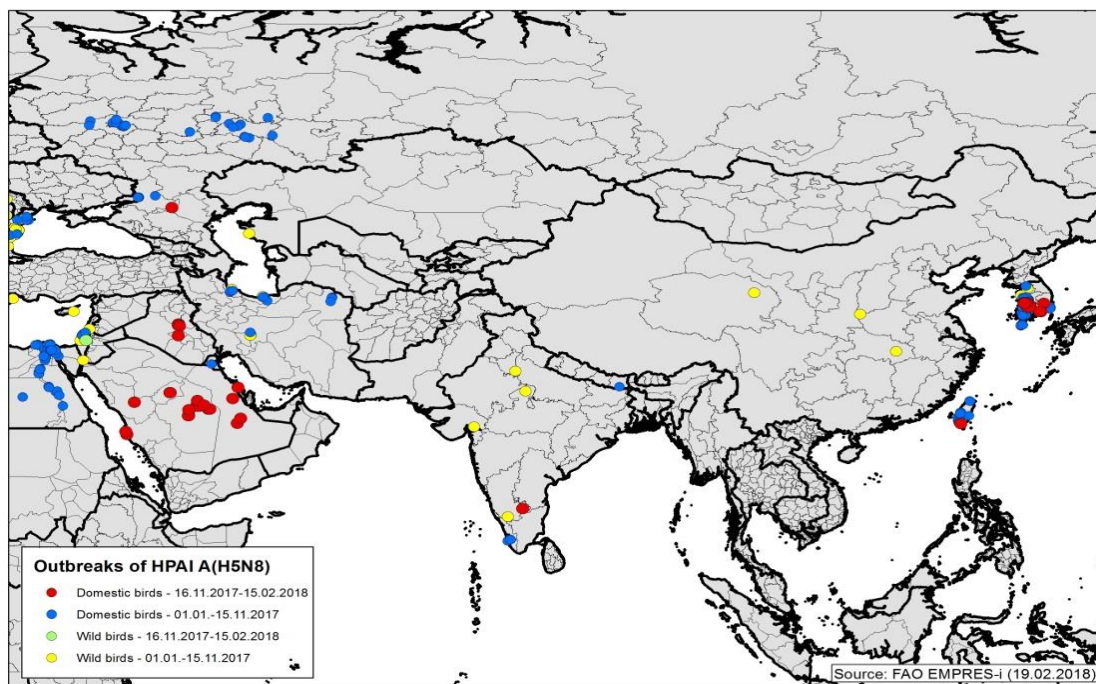


Figure 17: Distribution of confirmed HPAI A(H5N8) outbreaks in birds by place of reporting in Asia and the Middle East between 1 January 2017 and 15 February 2018 (FAO, online-a)

Genetic characterisation

Scientific groups continue to genetically characterize reassortant A(H5N8) viruses detected in recent years outside of Europe. The analysis of A(H5N8) isolated from wild birds and poultry in Egypt proved that HPAI in 2016-2017 was caused by multiple incursions of genetically similar genotypes of A(H5N8) originating from Central Asia (Yehia et al., 2017). The authors point at critical role of wild birds in the long-distance and multidirectional worldwide spread of A(H5N8) and underline the threat associated with the increased diversity of the AIV genetic pool and potential generation of novel reassortants with A(H5N1) clade 2.2.1.2 and A(H9N2), already endemic in Egypt.

The analysis of two reassortant A(H5N8) viruses detected in China (Hubei province) in 2016-2017 winter season from a dead swan goose (*Anser cygnoides*) and two dead black swans (*Cygnus atratus*) showed a relationship of genome segments with AIV detected in Far East, Central Asia and Europe. The authors suggest that wetlands intersecting East Asian-Australasian and Central Asian flyways constitute the starting point for intercontinental spread of A(H5N8) viruses (Ma et al., 2018).

An A(H5N8) isolate detected in January 2017 in South Korea possessed genome segments related to viruses from Western Siberia (Uvs-Nuur Lake), China (Qinghai Lake), Europe and India detected during the 2016-2017 epidemic (Woo et al., 2017).

Phenotypic characterisation

Mandarin ducks (*Aix galericulata*) experimentally infected with "group B" A(H5N8) clade 2.3.4.4 showed neither morbidity nor mortality but the virus replicated in different tissues and was excreted from inoculated birds. Transmission to contact ducks was also observed. The ducks infected with A(H5N8) strain shed more virus than those infected with A(H5N6) in a parallel experiment (Son et al., 2017).

4.3.3.2. A(H5N8) in mammals (excluding humans)

Ferrets experimentally infected with three A(H5N8) viruses isolated in South Korea in 2014-2015 showed no mortality and only mild respiratory signs. The viruses replicated exclusively in the respiratory tract (Lee et al., 2018).

4.3.4. Human infection due to A(H7N4)

On 13 February 2018, the first human case due to avian influenza A(H7N4) was notified from China (The Government of Hong Kong, online; WHO, online). The case is a 68-year-old female patient living in Liyang in Changzhou of Jiangsu Province who developed symptoms on 25 December 2017. She was admitted to hospital for medical treatment of severe pneumonia on 1 January 2018 and was discharged on 22 January 2018. The individual had slaughtered chickens prior to illness onset and LPAI A(H7N4) viruses were detected in ducks and chickens on the premises (WHO, 2018c). All her close contacts were under medical observation and have been tested negative.

Genetic sequencing of this A(H7N4) virus shows that all the virus segments originated from avian influenza viruses and the virus is sensitive to adamantanes and neuraminidase inhibitors based on genetic sequencing. No A(H7N4) virus was reported previously in China, based on surveillance of Ministry of Agriculture and the surveillance on poultry related environmental samples. LPAI A(H7N4) virus has been detected in the backyard poultry of the patient, but not in other poultry. Therefore, wild birds might be a possible source of introduction. A(H7N4) has not been described to be present in the poultry population in China, however, reassortment events between different avian influenza viruses with the emergence of new viruses in wild birds have been documented before.

In 1997, an outbreak of a different, unrelated avian influenza A(H7N4) occurred in New South Wales, Australia (Selleck et al., 2003). The viruses isolated from chickens on two commercial chicken farms during this outbreak were identified as A(H7N4) viruses, with hemagglutinin cleavage site amino acid sequences of RKRKRG and intravenous pathogenicity indices of 2.52 and 2.90, respectively. A virus with an identical nucleotide sequence, but with an intravenous pathogenicity index of 1.30, was also isolated from cloacal swabs collected from asymptomatic emus kept on a third property.

Another sequence of an avian influenza A(H7N4) virus, which was detected in a chicken in the Netherlands in 2010, has been deposited in GenBank (NCBI, online-a).

4.3.5. HPAI-LPAI A(H7N9)

4.3.5.1. Domestic and wild birds

Detection

Between 16 November 2017 and 15 February 2018, the Chinese authorities reported the detection of 10 LPAI A(H7N9) positive samples from chicken, ducks or the environment. In December 2017 and January 2018, out of 126,677 virology samples collected from 27 provinces, 12 samples (8 chickens, 2 duck, 1 quail, and 1 environmental sample) tested positive for LPAI A(H7N9) in Fujian, Anhui, Yunnan and Hunan Provinces, and Tibet Autonomous Region. With two exceptions in Anhui province and Lhasa city, where the virus was identified on backyard farms, all other positive samples were detected on live bird markets (see Figures 18, 19 and 20) (FAO, online-c). No HPAI A(H7N9) was detected during the relevant time period of this report. The results of the surveillance campaigns are published monthly by the Chinese Ministry of Agriculture (MoA, online) and also are available on the EMPRES-i website of the Food and Agriculture Organization (FAO) (FAO, online-a). The Chinese Ministry of Agriculture started a A(H7) vaccination programme for poultry in early July 2017 in Guangdong and Guangxi provinces. The nationwide A(H7N9) vaccination campaigns of poultry with influenza A(H5) and A(H7) bivalent inactivated vaccines, produced using reverse genetics, started extensively in September 2017. With exception of poultry in AI-free zones and export farms, all domestic birds will be vaccinated. Recently the Chinese Ministry of Agriculture published that 87.30% of poultry samples taken after the vaccination campaigns in 28 provinces in January 2018 achieved the required immunity level. Furthermore, new guiding principles on the prevention and control of A(H7N9) Flu in poultry were released focusing on live bird market management and biosecurity (FAO, online-c). Furthermore, Japan reported now officially about isolation and genetic sequencing of HPAI A(H7N9) virus from an illegally imported duck meat product confiscated from a flight passenger at Tokyo airport in November 2017 (FAO, online-c; NCBI, online-b).

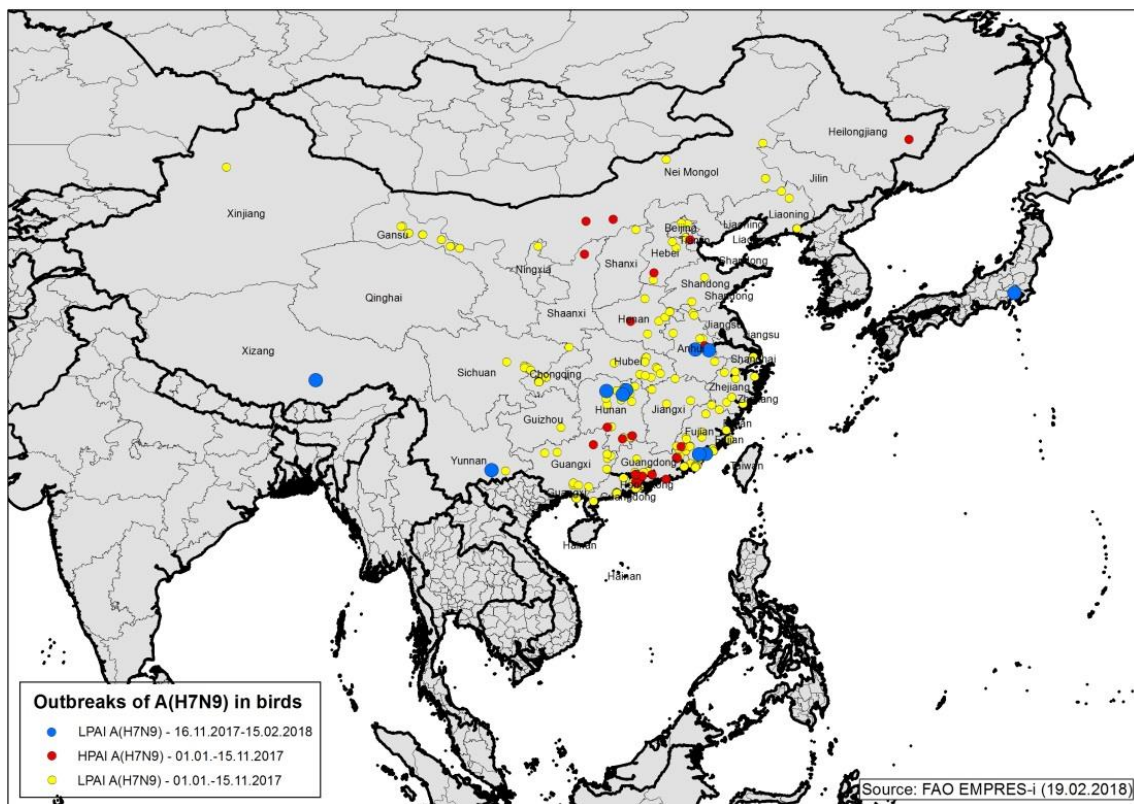


Figure 18: Distribution of confirmed LPAIV and HPAIV A(H7N9) in birds and environmental samples by place of reporting between 1 January and 15 February 2018 (FAO, online-a)

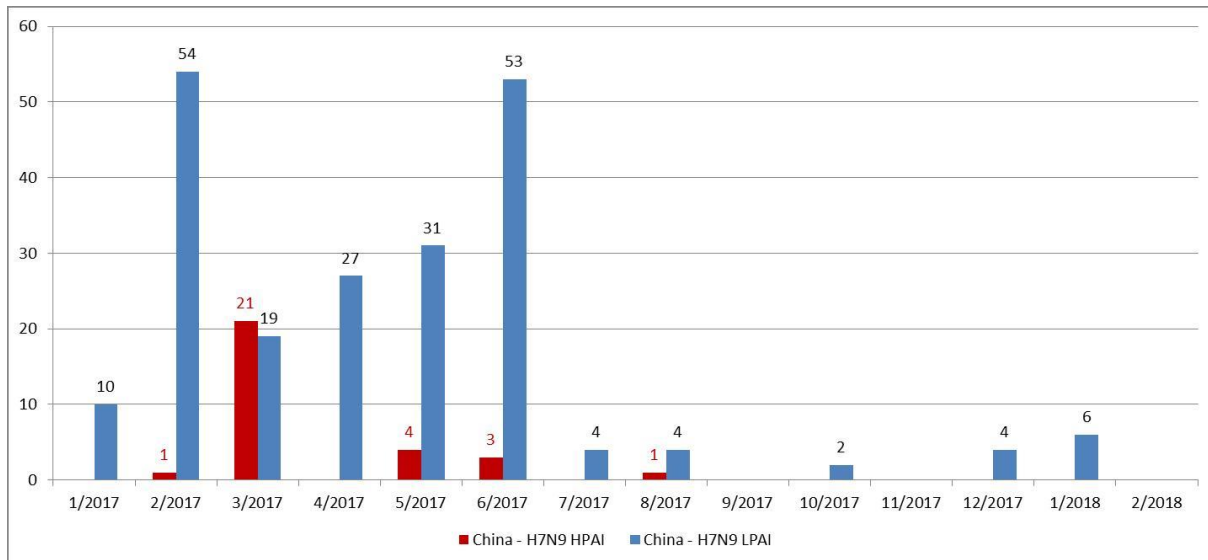


Figure 19: Number of confirmed LPAI and HPAI A(H7N9) outbreaks in birds and environmental samples in China since January 2017 (status: 19.02.2018)

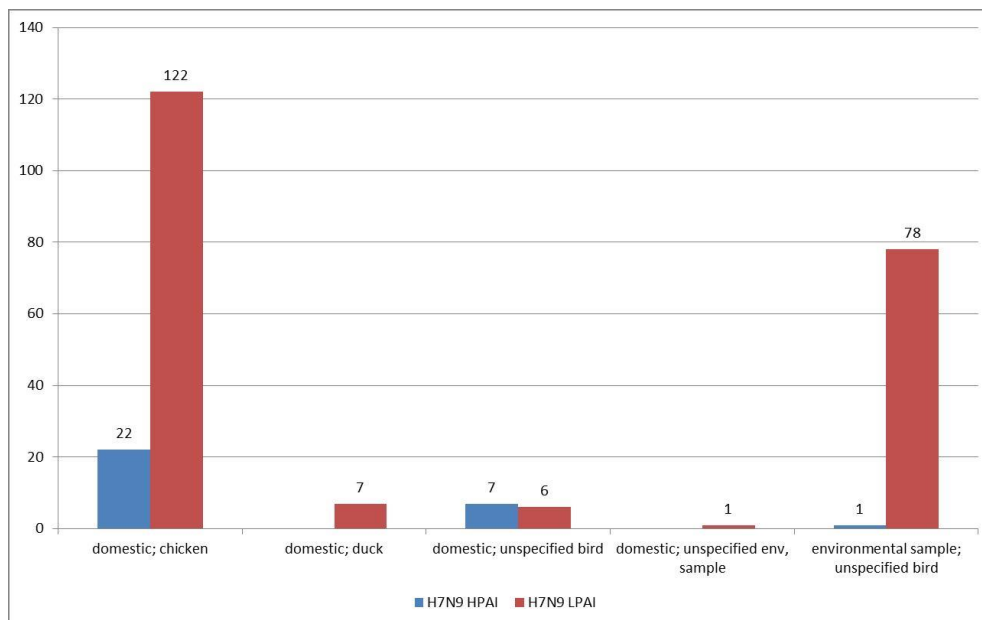


Figure 20: Number of confirmed LPAI and HPAI A(H7N9) outbreaks by species and environmental sample type in China since March 2013 (status: 19.02.2018)

Phenotypic characterisation

During the reporting period, a number of scientific publications have been published describing phenotypic features of newly-emerged HPAI A(H7N9) virus. The intravenous pathogenicity index (IVPI) of two chicken-derived A(H7N9) isolates with two different HA amino acid motifs was 2.54-3.00. The same isolates exhibited low- to high virulence in experimentally infected mice, depending on the strain (Liu et al., 2018a). Chickens infected experimentally with three HPAI A(H7N9) isolates detected in Guangdong province died within 2-4 days post infection and the virus was distributed in various organs. Contact chickens died within 4-7 days post contact (Wang et al., 2017a). Upon experimental infection of ferrets, a chicken-lethal A(H7N9) virus acquired two mutations in the PB2 segment (627K and 701N) and became highly lethal in ferrets and mice as well as transmissible via droplets in ferrets (Shi et al., 2017).

Genetic characterisation

There is a lot of genetic variation among A(H7N9) strains isolated from poultry. In the study performed by Shi et al. (2017), twenty-three different genotypes of A(H7N9) have been distinguished in poultry and the environment in China in 2013-2017, seven of which were found exclusively in ducks. Wang et al. (2017a) provided description of double and triple reassortants of A(H7N9) in chickens with the contribution of gene segments from A(H5), A(H7) and A(H9) subtypes. The study on the possible origin and spread of the novel highly pathogenic A(H7N9) has indicated that the ancestral virus of this pathotype emerged in the Yangtze River Delta region and spread, possibly through poultry trade, to other provinces of China. Within a few months the viruses reassorted with LPAI viruses of subtypes A(H7N9) and A(H9N2) (Yang et al., 2017).

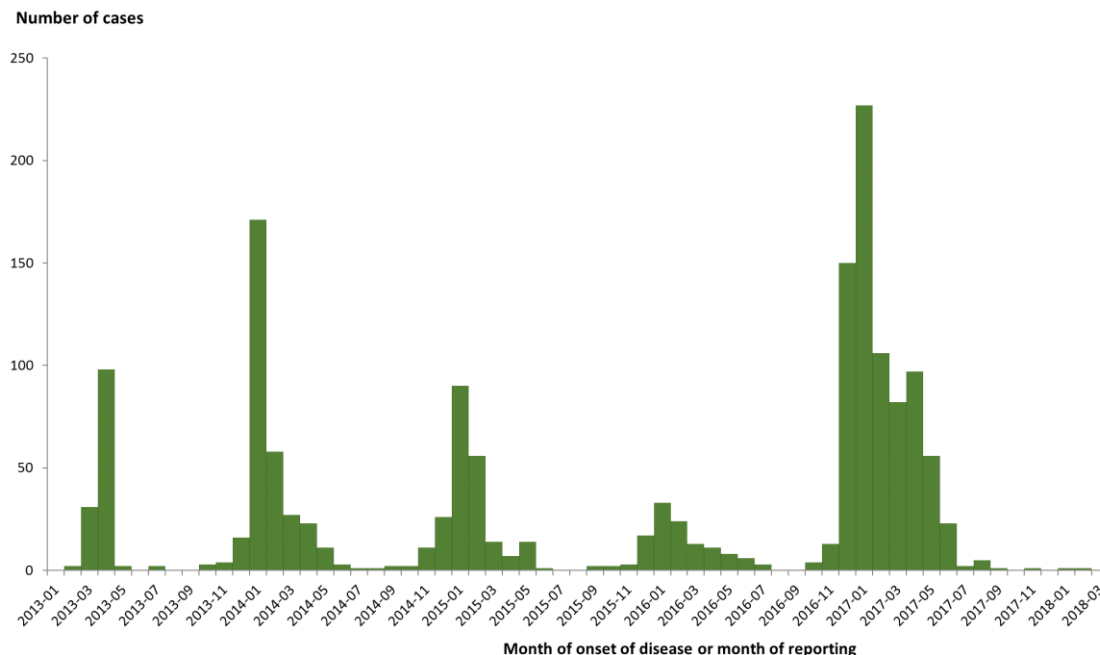
4.3.5.2. Human infections due to A(H7N9)

In March 2013, a novel avian influenza A(H7N9) virus was detected in patients in China. Since then and up to 1 March 2018, 1,567 cases have been reported globally, including 569 deaths (Table 5). During the winter 2017/18 three human cases have been reported (CHP, 2018; WHO, 2018c). No autochthonous cases have been reported outside China. Most cases are isolated, and zoonotic transmission from poultry to humans is the most likely explanation for the outbreak.

The outbreak shows a seasonal pattern. The first wave in spring 2013 (weeks 2013-7 to 2013-40) resulted in 135 cases, the second wave (weeks 2013-41 to 2014-40) led to 320 cases, the third wave (weeks 2014-41 to 2015-40) caused 223 cases, 120 cases were reported as a result of the fourth wave (weeks 2015-41 to 2016-40), 766 cases were reported as part of the fifth wave (weeks 2016-41 to 2017-40), and three cases during the sixth wave (weeks 2017-41 to 2018-6) (Figure 21).

The 1,567 cases were reported from Zhejiang (310), Guangdong (259), Jiangsu (253), Fujian (108), Anhui (101), Hunan (95), Shanghai (56), Jiangxi (50), Sichuan (38), Beijing (35), Guangxi (32), Hubei (31), Hebei (29), Henan (28), Shandong (27), Hong Kong (21), Guizhou (20), Xinjiang (14), Chongqing (9), Gansu (5), Shaanxi (7), Yunnan (8), Taiwan (5), Tianjin (5), Liaoning (5), Jilin (3), Tibet (3), Shanxi (3), Inner Mongolia (2), and Macau (2). Three imported cases were reported in Canada (2) and Malaysia (1) (Figure 22).

On 5 September 2017, China Center for Disease Control (CDC) reported one additional human case with highly pathogenic avian influenza A(H7N9) virus (changes in the hemagglutinin gene indicating a change to high pathogenicity in poultry) during the fifth wave (since October 2016), bringing the number of human cases with HPAI A(H7N9) virus to 28 (CNIC, 2017). These 28 cases were from Guangdong, Guangxi, Hebei, Hunan, Shaanxi and Taiwan (the case had travel history to Guangdong) with illness onset date before July 2017. FAO however, reports of 32 human cases due to HPAI A(H7N9) (FAO, online-c). No increased transmissibility or virulence to human cases has been detected related to the HPAI A(H7N9) virus, however, mutations have been described in a human HPAI A(H7N9) isolate that contribute to increased viral polymerase activity leading to enhanced replication and pathogenicity in the human host (Yamayoshi et al., 2018).



Source: Data used from WHO and Hong Kong Centre for Health Protection (WHO, 2017c; CHP, 2018)

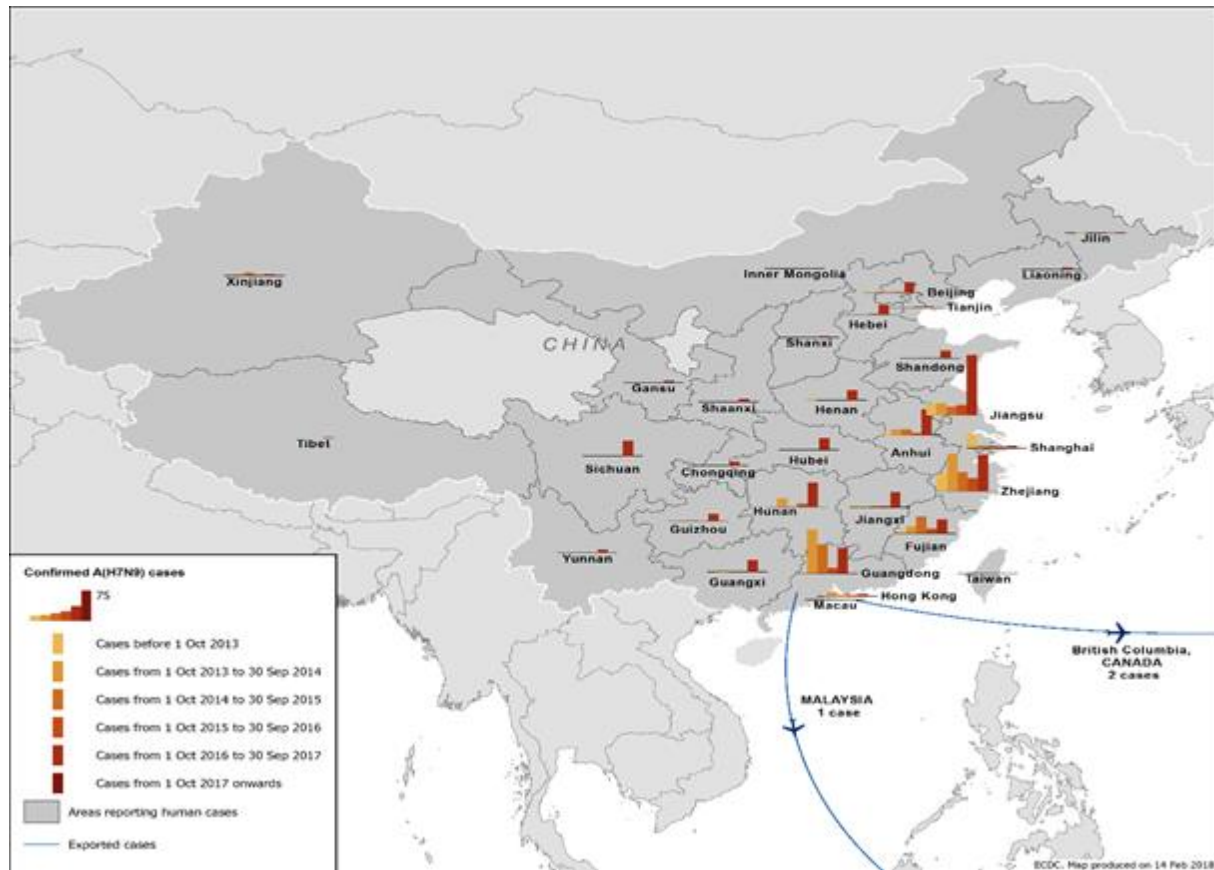
Figure 21: Distribution of confirmed human cases of A(H7N9) by first available month of onset of disease or month of reporting, February 2013 – 1 March (n= 1,567)

Table 5: Number of reported human cases and fatalities due to A(H7N9) infection up to 1 March 2018

	First wave (02/2013 – 09/2013)	Second wave (10/2013 – 09/2014)	Third wave (10/2014 – 09/2015)	Fourth wave (09/2015 – 10/2016)	Fifth wave (10/2016 – 10/2017)	Sixth wave (10/2017 – 3/2018)	Cumulativ e number of cases
Cases	135	320	223	120	766	3	1,567
Deaths *	43	134	98	45	248	1	569
CFR (%)	32%	42%	44%	38%	32%	33%	36%

Source: WHO and Hong Kong Centre for Health Protection (WHO, 2017c; CHP, 2018)

*The estimates in the table are based on the information available at the time of notification. Therefore, case fatality ratio (CFR) may be affected by completeness of information about outcome at time of notification.



Source: WHO and Hong Kong Centre for Health Protection (WHO, 2017c; CHP, 2018)

Figure 22: Distribution of confirmed human cases of A(H7N9) by first available month, February 2013 – 1 March 2018 (n = 1,567)

4.3.6. LPAI A(H9N2)

4.3.6.1. Domestic and wild birds

Detection

A(H9N2) remains the most commonly detected non-notifiable subtype of influenza viruses in poultry in Asia, Middle East and North Africa. Despite reports to OIE of an outbreak in western Ghana in January 2018 and a recent publication regarding the situation in Burkina Faso (Zecchin et al., 2017), the epidemic situation is greatly unknown due to underreporting. The endemic status of these regions continued between 16 November 2017 and 16 February 2018. Reports from Ghana of an A(H9N2) virus displaying highly pathogenic properties were not confirmed so far; while natural A(H9N2) viruses with HP characteristics have never been described, mixed infections with e.g. velogenic Newcastle Disease virus or Infectious Bronchitis virus may provoke a clinical picture resembling HPAI. No further information that would affect any risk estimation has been received.

Phenotypic characterisation

Two ostrich A(H9N2) reassortant viruses isolated in 2013-2014 had an intravenous pathogenicity index (IVPI) ranging from 0.4 to 0.63. The viruses showed low replication and transmission efficiency in guinea pigs and mice (Wang et al., 2018). The geese-derived A(H9N2) viruses from China (2011-2012) showed various level of replication efficiency in experimentally infected chickens and geese (Zhu et al., 2018).

Genetic characterisation

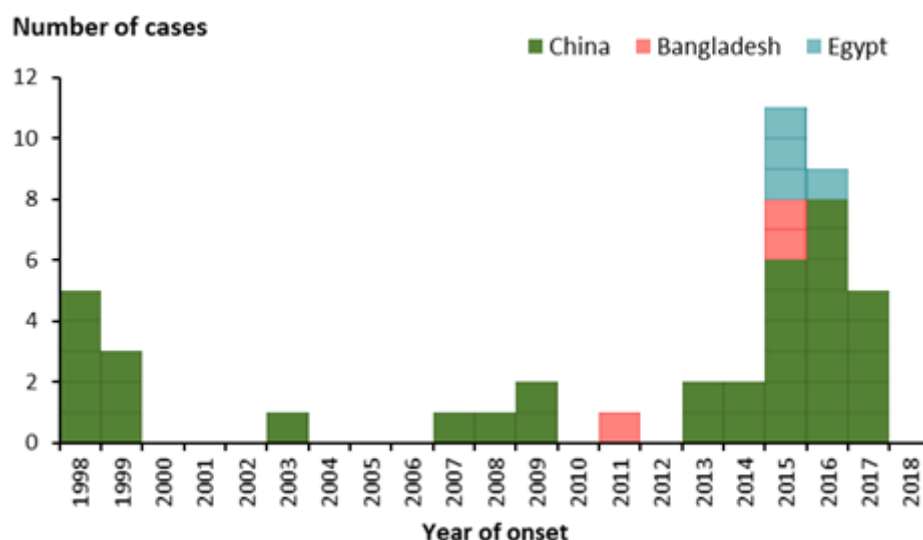
Reports on the occurrence of inter-subtype, inter-clade and intra-clade reassortant A(H9N2) viruses circulating in China in the past few years have been published in recent weeks. Yang et al. (2017) provided new data on the possible origin and transmission pathways of a newly emerged HPAI A(H7N9) virus together with phylogenetic evidence that at some stage the A(H7N9) acquired internal gene cassette from A(H9N2) viruses. Full-genome characterisation of two A(H9N2) isolates derived from domestic geese in 2011-2012 showed the presence of double and triple reassortants emerged from local A(H9N2) strains circulating in the region (Zhu et al., 2018). Molecular characterisation of seven A(H9N2) isolates from sick ostriches in China in 2013-2014 revealed the existence of quadruple reassortants between various lineages of A(H9N2), α -2, 6-linked sialic acid receptors binding affinity ("human-like") and some other mammalian host specific markers in PB1, M1, M2 and NS1 (Wang et al., 2018). A close relationship between internal genes of A(H9N2) virus isolated from a mink farm and A(H7N9) virus has been described recently in China (Xue et al., 2018). Internal genes of A(H9N2) (genotype S) were carried by three A(H5N6) viruses isolated from chickens in LBM in China in 2015-2016 (Liu et al., 2018b). The A(H9N2) strains isolated from aerosol samples in LBM in Zhongshan (China) showed close genetic relationship with human A(H9N2) strains (Wu et al., 2018). A novel reassortant subtype A(H9N6) identified in samples of poultry collected at LBM in Jiangxi Province, China, in 2014, most likely emerged as a result of reassortment between A(H9N2) and A(H6N6) (Zhang et al., 2017a).

Hu et al. (2017) performed hierarchical classification of A(H9N2) viruses through analysis of all HA and NA genes available in NCBI Influenza Virus Resource and proposed the division into three main lineages: Worldwide lineage, Asia-Africa lineage, and China lineage. Additionally, the authors reconstructed the possible pathways of A(H9N2) spread using the Bayesian phylogeography approach.

Gradual accumulations of mutations in the genome of the European A(H9N2) viruses isolated from turkeys in Poland in 2013-2014 was observed, including a substitution in the PA protein that can enhance activity of viral polymerase in mammalian cells. However, *in vivo* studies showed low pathogenicity of the European A(H9N2) in mice (Świętoń et al., 2017).

4.3.6.2. Human infections due to A(H9N2)

Since 1998 and as of 4 March 2018, 43 laboratory-confirmed cases of human infection with avian influenza A(H9N2) virus, including one death, have been reported globally (WHO, 2017c; CHP, 2018; WHO, 2018c). Cases occurred in China (36), Egypt (4) and Bangladesh (3). The latest case was reported in December 2017 from China (Figure 23).



Source: WHO and Hong Kong Centre for Health Protection (WHO, 2017c; CHP, 2018)

Figure 23: Distribution of confirmed human cases of A(H9N2) by country of reporting 1998 – 2018 (n=43)

4.3.7. Scientific analysis of AI spread from Third countries to poultry in the EU

In comparison to the last report, sections 4.3.1–4.3.6 showed in the time period of this report from 16 November 2017 to 15 February 2018 an increasing number of reported outbreaks in poultry and wild birds in Asia, Northern Africa and particular the Middle East. The outbreaks of clade 2.3.2.1c, A(H5N1) continued in Asia, but no further outbreaks were reported in the relevant time period from Africa or the Middle East. In contrast clade 2.3.4.4b, A(H5N8) outbreaks were notified in Africa, Asia and several new outbreaks were reported from the Middle East. Interestingly, despite the endemic presence of A(H5N1) and A(H5N8) virus in Africa and Middle East, no introduction from Africa or the Middle East to Europe has been observed in the last 10 years and it is estimated that the probability of entering the EU via this route is lower than the north-east route, a fact that can be linked to the unique ecology of migratory birds at the European-African interface (EFSA AHAW Panel et al., 2017). But uncertainty is still high and close collaboration with ornithologists is recommended in order to provide scientific ground for the explanation of this phenomenon.

The outbreaks of clade 2.3.4.4, A(H5N6) in poultry and wild birds are still confined to Asia, but a novel reassortant closely associated to clade 2.3.4.4b mainly circulating in Eurasia was detected in migratory wild birds in South Korea showing the continued circulation of this lineage in multiple geographical regions and likely wild bird mediated spread. There is considerable uncertainty regarding the real geographical distribution of these viruses. The A(H7N9) and A(H5N1) virus has not been detected on a large scale in wild waterfowl in the relevant time period. This might be attributable by the high degree of adaptation to gallinaceous poultry. The risk associated with the incursion of this subtype by means of wild birds is currently low but constant monitoring is warranted.

HPAIV remains still in the environment and possible incursion from contaminated environment into poultry holdings cannot be excluded. But the environmental stability of AIV will likely decrease with the higher temperatures and increase UV radiation in the coming months. Nevertheless 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 spreading the infection.

The multiple pathways through which AIV can be brought to the EU include trade and illegal movements of poultry and poultry products, contaminated fomites and wild birds.

The risk of avian influenza viruses being transported to Europe through poultry trade is negligible as live poultry, day-old chicks and semen have been identified as the only non-wild bird pathways via which AIV introduction is non-negligible and suitable risk management measures are in place, such as testing and quarantine (EFSA AHAW Panel et al., 2017). EU legislation (Regulation (EC) No 798/2008⁵) prohibits the importation of live poultry, day-old chicks and hatching eggs, semen and other birds (captive birds such as parrots, finches and ornamental birds for trade) from countries which cannot provide suitable health guarantees to comply with the certification. The list of approved countries is therefore limited (for reference see Table F5 of Appendix F, EFSA AHAW Panel et al., 2017).

Illegal movement of captive birds (in particular passerines) is a viable pathway for spread of the viruses, in particular A(H5Nx), but the risk is difficult to assess due to the paucity of data.

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

4.3.8.1. Surveillance in the EU

As already outlined in the previous report (EFSA et al., 2017a), human infections with A(H7N9), A(H5N6), A(H5N8) and other novel influenza subtypes are notifiable under EU legislation and the International Health Regulations (IHR) through the Early Warning and Response System (EWRS) and the IHR notification system (Decision No 1082/2013/EU⁶) (WHO, 2005). Agreed protocols for clinical

⁵ Regulation (EC) No 798/2008 of the European Parliament and of the Council of 8 August 2008 laying down a list of third countries, territories, zones or compartments from which poultry and poultry products may be imported into and transit through the Community and the veterinary certification requirements.

⁶ Decision (EC) No 1082/2013 of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health and repealing Decision No 2119/98/EC.

investigations have been prepared by the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) (ISARIC, online). Contacts of confirmed cases should be followed-up and tested. International recommendations for the use of post-exposure prophylaxis differ.

Diagnosis

With routine diagnostic laboratory assays, the novel A(H5Nx) or A(H7Nx) viruses should be detected as positive for influenza A virus, and negative for influenza B, A(H1), A(H1)pdm09 and A(H3) viruses.

Influenza A(H5Nx) or A(H7N9) viruses are expected to be classified as un-subtypeable influenza A if no-specific H5 or H7 diagnostic test is performed. It is standard procedure in diagnostic laboratories to send influenza A virus isolates or clinical samples that cannot be subtyped to the national reference laboratory (National Influenza Centres; NICs), and further to a World Health Organization (WHO) Collaborating Centre for Reference and Research on Influenza for characterisation, as was undertaken in China for the first influenza A(H7N9) isolates.

In October 2017, WHO reviewed and updated the recommendations regarding RT-PCR testing (WHO, 2017b).

According to Chinese Centers for Disease Control and Prevention (CDC), the current A(H7N9) H7 primer/probe sets can detect this A(H7N4) virus, although this virus clusters in a different branch within the HA tree of A(H7N9) viruses.

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

It is suggested that travellers to China and other countries where avian influenza viruses have been reported transmissible to humans e.g. A(H5N1), A(H5N6), A(H7N9) are asked to avoid visiting live bird markets, direct contact to poultry or poultry products and should adhere to general hygiene measures like hand washing. It is also suggested that travellers that experience respiratory symptoms within 10 days after return should include travel history and possible bird contacts in their report to the practitioner.

Routine vaccination with seasonal influenza vaccine is recommended in most countries for workers having contact with birds and poultry to minimise the possibility of co-infection with human and avian influenza viruses thereby reducing the risk of reassortment.

Protective measures are the best option to prevent transmission from infected birds to humans and have been recommended in accordance with national guidelines for HPAI. It is important to remain vigilant, identify any possible early transmission events to humans. Local health authorities may consider ensuring active or passive surveillance of exposed people with direct contact to infected birds for human health complaints (e.g. influenza-like symptoms, fever or conjunctivitis) following national guidelines, particularly during and 10 days after culling operations.

Information about national recommendations regarding avian influenza can be found at European Centre for Disease Control (ECDC) webpage (ECDC, 2006). Persons exposed to the virus are asked to report any symptoms to the municipal health service and in the event that they develop conjunctivitis or influenza-like-illness, sampling material will be obtained for diagnostic testing according to the national recommendations. Active and passive monitoring measures have been recommended by the US CDC during HPAI A(H5N1), A(H5N2) and A(H5N8) outbreaks in the US in 2015 (CDC, online). The FAO also raised awareness regarding HPAI A(H5N8) providing general recommendations as well as those pertaining to poultry producers, hunters and national authorities (FAO, online-b).

Considering the severity of the disease, the fact that limited human-to-human transmission cannot be excluded in some clusters, that no vaccine is available on the market against A(H5Nx), A(H7Nx) or A(H9N2) and the favourable safety profile of the anti-viral drugs of choice, it is likely that the benefits of post-exposure chemoprophylaxis of close contacts with neuraminidase inhibitors outweigh the risks (ECDC, 2017).

Healthcare workers managing symptomatic exposed (or possible) cases should follow standard, contact and respiratory precautions, depending on the local risk assessment according to their national guidelines.

4.3.8.3. Vaccines

The most important intervention in preparing for the pandemic potential of influenza viruses is the development and use of human vaccines, therefore the situation is constantly monitored and assessed by WHO. Following the vaccine composition meeting in March 2018, WHO published an updated overview of recommended candidate vaccine viruses (CVVs) and status of development (WHO, 2018c). Currently 33 different CVVs for different A(H5) clades are listed as available, while for five CVVs with the most recently circulating viruses including A(H5N1) clade 2.3.2.1c and A(H5N6) clade 2.3.4.4, availability is pending. Representative viruses of the HA lineage of clade 2.3.4.4. reacted less well with postinfection ferret antiserum, which was raised against the available CVVs. Therefore, a new CVV has been proposed (A/Fujian-Sanyuan/21099/2017-like A(H5N6)) (WHO, 2018c). Fourteen currently developed and available A(H7N9) CVVs have been assessed appropriate based on the current antigenic, genetic and epidemiologic data and no additional CVVs have been recommended. The same is true for the seven A(H7) and A(H9N2) CVVs.

CVVs based on an attenuated influenza A/Puerto Rico/9/1934 virus backbone showed less severe disease and reduced virulence without extrapulmonary spread in the ferret model compared to wild type viruses (Belser et al., 2017).

4.3.9. ECDC risk assessment for the general public in the EU

Currently the risk of travel-related importation of human cases due to avian influenza particularly from Asia is low. This is based on the fact that a very low number of human cases are currently reported from China indicating a low level of human exposure to e.g. A(H7N9) viruses in poultry markets and the environment. This could also serve as an indicator for low level circulation in poultry although human infections with new, yet unknown avian influenza viruses like the recent A(H7N4) case cannot be ruled out. Also an upsurge of human cases due to lower ambient temperature over the next few months comparable to previous waves is possible. According to FAO, the "likelihood of a human being exposed to the Chinese-origin influenza A(H7N9) virus through contact with infected live birds, during LBM visits within affected areas of China from January to May 2018"...is considered moderate with medium uncertainty (FAO, 2018)

The first human case of a new avian influenza virus, A(H7N4), in China is of concern. Despite large ongoing investigations following the emergence of the highly pathogenic avian influenza virus A(H7N9) in 2016/17 and the introduction of a comprehensive vaccination programme in poultry with rigid follow-up studies, this virus has so far not been described in poultry or wild birds except in the birds at the backyard farm of the patient. Further genetic analyses are required to characterise the relationship and origin of the new virus as well as the potential to transmit to humans.

The risk of zoonotic transmission to the general public in Europe is considered to be very low. Monitoring and testing of wild birds and poultry in the EU plays an important role in the detection of further virus spread among birds and consequently reduces the possible risk for exposure of humans to infected birds. A lack of mammalian adaptation markers was found as outlined in section 4.1.2.

The number of outbreaks or wild bird detections due to A(H5N8) or A(H5N6) has been decreased over the last few months. No human infection due to A(H5N8) or the newly emerged A(H5N6) viruses representing a reassortment of A(H5) clade 3.2.4.4 viruses with local European viruses donating the N6 gene, has ever been reported. The A(H5N8) and new A(H5N6) viruses are considered to be predominantly avian-adapted according to the EU Reference Laboratory for Avian Influenza and Lee et al. 2018 (2018). Poultry outbreaks and wild bird findings of A(H5N8) and A(H5N6) continue in Europe and with the high capability of the virus to reassort with other local avian influenza viruses, the threat to transmit to humans after adaptation processes or through the acquisition of new characteristics via reassortment remains. Given the uncertainty of the likelihood of zoonotic transmission, the use of personal protective measures for people being exposed to avian influenza viruses will minimise the remaining risk.

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Abbreviations

AI	Avian Influenza
AIV	Avian Influenza virus
CDC	Center for Disease Control
CVET	Community Veterinary Emergency Team
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
EFSA	European Food Safety Authority
EWRS	Early Warning and Response System
FAO	Food and Agriculture Organization
FRZ	Further restriction zone
HPAI	Highly pathogenic avian influenza
IHR	International Health Regulations
ISARIC	International Severe Acute Respiratory and Emerging Infections Consortium
LBM(s)	Live bird market(s)
LPAI	Low pathogenic avian influenza
MS(s)	Member State(s)
OIE	World Organisation for Animal Health
PAFF Committee	The Standing Committee on Plants, Animals, Food and Feed
SAR	Special Administrative Region
WHO	World Health Organization

Appendix A –Term of References

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 HP AI 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, legislation⁷, 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 HP AI 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. 178/2002⁸, EFSA should provide the technical and scientific assistance to the Commission based on the following Terms of Reference:

⁷ 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.

⁸ 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 TORs 1 and 2, this scientific report gives an overview of the HPAI and LPAI outbreaks in poultry and captive birds as well as HPAI events in wild birds detected in Europe between 16 November 2017 and 15 February 2018, mainly based on data submitted by Member States (MSs) and neighbouring countries via the Animal Disease Notification System (ADNS). A phylogenetic characterisation of the circulating viruses is included as well as a brief genetic characterisation to explain how related/distant viruses are. MSs where HPAI outbreaks occurred in poultry submitted additional epidemiological data to EFSA, which have been used to analyse the characteristics of poultry holdings affected between 16 November 2017 and 15 February 2018.

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

A description of the applied prevention and control measures (TOR3) is reported based on a case report provided by representatives of Bulgaria, Italy and the Netherlands and attached as Annex A, B and C, respectively, to this report. The main topics covered are increasing awareness, release and repeal of housing order, strengthening biosecurity, preventive culling, and implementation of regional stand still, hunting and derogations on restriction zone implementation after a risk assessment.

The monitoring of the avian influenza (AI) situation in other continents (TOR4) focuses on HPAI A(H5N1), HPAI A(H5N6), HPAI A(H5N8), A(H7N4), HPAI/LPAI A(H7N9) and LPAI A(H9N2). Background and epidemiology, detections, phenotypic and genetic characterisations are described based on information from confirmed human and poultry cases as well as wild bird events. To provide a full picture of the situation, the reported AI human cases cover the full period of time since the first human case has been reported. Data on AI infection in birds cover the period between 1 September 2017 and 15 November 2017. Possible actions for preparedness in the EU are discussed.

The report mainly describes information that became available since the publication of the previous report (EFSA et al., 2017a) and that might affect the interpretation of risks related to AI introduction and/or spread.

Appendix B –Data and methodologies

B.1. Data on animals

B.1.1. Overview of AI outbreaks in Europe (TOR 1 and TOR 2)

The data on the AI outbreaks submitted by MSs from 16 November 2017 to 15 February 2018 to the Animal Disease Notification System (ADNS) (EC, online-b) were taken into account for this report. In addition, Bulgaria, the Netherlands and Italy were asked to provide more detailed epidemiological data (see Table A.1, Appendix A in EFSA et al., 2017a) directly to EFSA on the AI outbreaks that occurred in the same period. The data model has been discussed with representative appointed by the MS during a teleconference. The only implemented change in the EFSA data model used for this data collection was the following: MSs have been asked to report information on the presence/absence of signs of HPAI infection (mortality, clinical signs, drop in egg production and feed/water intake, non-clinical indicators), regardless these signs were or not the driver for the outbreak detection. The collection of data was carried out by exchanging Excel files via email to the representative appointed by the MS.

The slide presentations, which EU MSs affected by AI presented to the Standing Committee on Plants, Animals, Food and Feed (PAFF Committee), were consulted to extract information on the mortality rates and clinical signs of different species of domestic and wild birds from HPAIV infections, both in single species and multiple species holdings. The PDFs of these slide presentations are available on the European Commission website (EC, online-a).

Information on Phenotypic characterisation of AI viruses circulating in the EU were extracted from the scientific literature performing a search on 2 March 2018 in the PubMed database using the keywords 'avian influenza' and for the period of publication between 16 November 2017 and 15 February 2018. Obtained articles were subsequently screened for information on phenotype of relevant avian influenza virus infections in poultry, wild birds, or both. Studies which results had limited value given the missing data on species, breed, age of infected birds, and on clinical signs or given the inoculation of the virus in bird species whose phenotypic characterisation is not comparable either free-living mallards (*Anas platyrhynchos*) or domestic duck breeds (*Anas platyrhynchos domestica*) such as the Pekin duck were excluded.

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

Bulgaria, the Netherlands and Italy expressed the interest in supporting the analysis of the AI outbreaks from 16 November 2017 to 15 February 2018 and submitted a case report on the AI prevention and control measures based on the template that was generated for the previous report (EFSA et al., 2017a). The case reports provided to EFSA can be consulted in Annex A, B and C.

B.1.3. Overview of AI outbreaks in other continents (TOR 4)

For the information extracted from scientific literature on genetic and phenotypic characterisation a literature search was performed continuously until 15 February 2018 in the PubMed database with the key words: 'H5N1', 'H5N6', 'H5N8', 'H7N9', 'H9N2' [Title/Abstract] and '2017/11/16 to 2018/02/15' [Date of publication].

B.2. Data on humans

The collection of numbers of human cases due to infection with AIVs has been performed by experts at the ECDC. Multiple sources are scanned regularly to collect information about laboratory-confirmed human cases within epidemic intelligence activities at ECDC. Data were extracted and line lists have been developed to collect case-based information on virus type, date of onset of disease, 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 are laboratory-confirmed cases. Double entries and validity of data are continuously checked by ECDC duty experts. The data on human cases covers the full period of time since the first human case has been reported. Therefore, data on human cases refer to different time periods and are included irrespective if new human cases during the reporting period occurred.

Literature searches were performed continuously until 19 February 2018 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'. The literature search was not systematic or comprehensive.

Annex A – Applied prevention and control measures on avian influenza in The Netherlands

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Scope

This document provides a brief overview of specific prevention and control measures applied in The Netherlands during the autumn-winter (November 2017 - February 2018) in relation to avian influenza. There is only information provided that is relevant to the implementation of the following selected measures: increasing awareness of stakeholders and the general public, housing order, strengthening biosecurity measures (other than poultry confinement), preventive culling, regional stand still, derogations on restriction zone implementation after risk assessment and hunting. This document is made to support the EFSA working group in generating an overview on the application of the selected measures at EU level.

Timing of the applied prevention and control measures

Table 1 provides a timeline on the main events that triggered actions in relation to the selected prevention and control measures. More information on the actions taken is provided in the sections below.

Table 1: Overview of main communication actions

Date	Event that triggered action	Type of action taken	Target audience (if applicable)
08/12/2017	First outbreak HPAI serotype H5N6 positive commercial poultry holding (fattening ducks)	Measurements for protection and surveillance zone- As of 8th of December Culling HPAI positive commercial poultry holding, implement protection and surveillance zones around HPAI positive commercial poultry holding with transport restrictions for all bird inclusive commercial poultry and poultry products, sperm, manure and feed as well transport restrictions for domestic mammals, feed, sperm, milk and manure of these domestic mammals.	e.g. poultry associations, general public, etc.
13/12/2017	HPAI positive wild bird finding	Measurements for the whole country- As of 8th of December: housing order commercial poultry confinement and housing order hobby birds and other non-commercial captive birds confinement. As of 8th of December next measures were also implemented: 1. ban for visit commercial poultry holdings and other holdings or locations where birds are held; 2. mandatory visitors registration; 3. ban races and exhibitions with birds; 4. ban hunting ducks or to hunt in general in wet areas with waterfowl; 5. mandatory clinical examination of birds for transport to or from ducks and turkey holdings; 6. mandatory intensive clinical examination ante mortem of ducks and turkeys at slaughterhouses; 7. measures regarding cover and application of litter on duck holdings; 8. using a hygiene protocol for visiting of commercial poultry holdings; 9. increasing awareness, repeal housing order (commercial poultry confinement), strengthening biosecurity, intensified wild bird monitoring	
20/12/2017	HPAI positive captive bird finding		
19/12/2017	HPAI positive wild bird finding		
23/12/2017	HPAI positive wild bird finding		
22/01/2018	HPAI positive captive bird finding		

Thirty days after cleansing and disinfection of the HPAI positive culled holding all the measures were lifted as 9 January 2018 with exception of measures valid for the whole country 1. ban for visit commercial poultry holdings and other holdings or locations where birds are held, 2. mandatory

visitors registration, 3. ban races and exhibitions with birds, 4. housing order commercial poultry confinement and housing order hobby birds and other non-commercial captive birds confinement, 5. measures regarding cover and application of litter on duck holdings, 6. using a hygiene protocol for visiting of commercial poultry holdings.

Increasing awareness of the stakeholders and the general public

Development of biosecurity measures during crisis in contact with poultry sector. Communication both by Ministry and poultry sector like as follows: Directly published on government website (www.rijksoverheid.nl): Legal information/Information to Parliament / Information for press / Questions & Answers / Phone center for questions from both poultry owners and general public, in direct contact with poultry advisors / Communication department in close contact with press / Meeting for all stakeholders and communication by media with general public.

Housing order

The housing order was implemented in mandatory national legislation on 8 December 2017 after an executed risk assessment by the Commission of animal disease experts which consists of this matter of Avian Influenza experts. This Commission advise the Chief Veterinary Officer and The Minister to introduce measures against HPAI. The trigger of implementing the housing order was the HPAI H5N6 outbreak on the commercial poultry holding in Biddinghuizen on 8 December 2017. The lifting of the housing order will be considered after an execution of a risk assessment by the Commission of animal disease experts coming month March 2018.

Strengthening biosecurity measures (other than housing order)

We have concluded multiple years service level agreements with suppliers who can deliver cleaning and disinfection equipment 24H/7days within 4 hours after calling by Dutch government for culling on every location in the whole country.

Preventive culling

It was applied but there were no other commercial poultry holdings in the one kilometer radius zone around the index holding.

Regional stand still (beyond the restriction zones specified in the EU Regulation)

No, only the 1km/ 3km and 10 km zones (protection and surveillance zones).

Derogations on restriction zone implementation after risk assessment

No

Hunting

From 9 January 2018 the ban hunting ducks or to hunt in general in wet areas with waterfowl was lifted.

Annex B – Applied prevention and control measures on avian influenza in Italy

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Istituto Zooprofilattico Sperimentale delle Venezie

• Scope

This document provides a brief overview of specific prevention and control measures applied in Italy between 16 November 2017 and 15 February 2018 in relation to avian influenza. There is only information provided that is relevant to the implementation of the following selected measures: increasing awareness of stakeholders and the general public, housing order, strengthening biosecurity measures (other than poultry confinement), preventive culling, regional stand still, derogations on restriction zone implementation after risk assessment and hunting. This document is made to support the EFSA working group in generating an overview on the application of the selected measures at EU level.

Timing of the applied prevention and control measures

Table 1 provides a timeline on the main events that triggered actions in relation to the selected prevention and control measures. More information on the actions taken is provided in the sections below.

Table 1: Overview of main communication actions

Date	Event that triggered action	Type of action taken	Target audience (if applicable)
21/11/2017	Ministerial Provision n 2665, which amend and replace the Ministerial provision 24016 of October 20 th , 2017	Modification of the Further Restricted Zone, with distinction of measures to be applied in high and medium poultry density areas. Definition of biosecurity measures, and of laboratory tests to be performed	Regional veterinary services; Poultry Companies
22/11/2017	80 th H5N8 HPAI poultry outbreak in housed broiler farm (Brescia)	3km PZ and 10km SZ in place, with all associated visits and testing.	Poultry and backyard/captive bird keepers in the restriction zone only; Poultry Companies
23/11/2017	81 st H5N8 HPAI poultry outbreak in a backyard flock (Treviso)	Authority derogations from the establishment of the protection and surveillance zones (Art. 16(2) of the Council Directive 2005/94/EC)	-
01/12/2017	82 nd H5N8 HPAI poultry outbreak in mixed species farm (Treviso)	3km PZ and 10km SZ in place, with all associated visits and testing.	Poultry and backyard/captive bird keepers in the restriction zone only; Poultry Companies
11/12/2017	83 rd H5N8 HPAI poultry outbreak in housed fattening turkey farm (Ravenna)	3km PZ and 10km SZ in place, with all associated visits and testing.	Poultry and backyard/captive bird keepers in the restriction zone only; Poultry Companies
31/01/2018	Ministerial Provision n 2307, which extend the duration of measures indicated in the Provision 26551 of November 21 st , 2017	Extension of the duration of control measures previously indicated in the Provision 26551	Regional veterinary services; Poultry Companies

31/01/2018	Ministerial Provision n 2309, which extend the measures indicated in the Provision 19967 of August 31 st , 2017	Extension of the duration of risk reduction and biosecurity adopted with the Ministerial Provision 19967	Regional veterinary services; Poultry Companies
19/02/2018	Ministerial Provision n 4122, which defines measures to reduce the risk of AI infection, and biosecurity	Identification of regions exposed ad higher risk of H5 and H7 AI introduction; Definition of measures to prevent or reduce the risk; Definition of potential derogations	Regional veterinary services

Increasing awareness of the stakeholders and the general public

Details on Avian Influenza outbreaks occurred in Italy and on the epidemiological situation at the European level are provided and updated through the website of Istituto Zooprofilattico Sperimentale delle Venezie, where the National Reference Laboratory for Avian Influenza and Newcastle Disease has dedicated sections: <http://www.izsvenezie.it/temi/malattie-patogeni/influenza-aviaria/situazione-epidemiologica-HPAI/>; <http://www.izsvenezie.it/temi/malattie-patogeni/influenza-aviaria/situazione-epidemiologica-hpai-europa/>.

Other websites at the local/national level from various stakeholder groups and association (e.g. associations of poultry farmers, National and Regional veterinary associations, etc) link directly to the IZSVE website for updates on AI epidemiological situation, allowing to reach a broader audience.

Official communications by Competent Authority (Ministry of Health) on a new outbreak is forwarded for information to poultry farmer unions, poultry production companies, and veterinary associations.

Housing order

In accordance with Ministerial provision n. 2304 of 31 January 2018, measures provided by Ministerial Provision n. 26651 of 21 November 2017, which updated the Further Restricted Zone accordingly to the epidemiological situation, defining a Densely Populated Poultry Area and a Medium Populated Poultry Area, were extended to 28 February 2018.

Measures applied at farm-level within the Further Restricted Zone:

Census of industrial poultry holdings

Birds shall be kept inside closed buildings and measures should be taken to reduce the risk of direct/indirect contact with wild birds

- Pre-movement clinical inspection and virological testing
- Enforcement of increased biosecurity measures regarding the vehicles and the personnel entering and exiting farms
- Gathering of domestic birds for fairs, exhibitions and live-bird markets is banned
- Re-stocking of meat turkey farms is prohibited - A derogation to this measure can be authorized only whether an official veterinarian has verified the compliance with new biosecurity standards (these requirements have been recently defined and applied to strengthen the level of biosecurity considering also the risk of AIV introduction from the wild reservoir) and IZSVE has evaluated the geographical risk of the farm according to the poultry density in the area and the proximity to other poultry premises.

Strengthening biosecurity measures (other than housing order)

Ministerial provision n. 19967 of 31 August 2017 was extended to 28 February 2018 (Ministerial Provision n. 2309 of 31 January 2018).

In accordance with Ministerial provision n. 4122 of 19 February 2018, Piedmont, Lombardy, Emilia-Romagna, Friuli Venezia Giulia, Veneto, Umbria, and Lazio have been defined as high-risk regions, by taking into account:

- Epidemiological situation;
- Risk factors for HPAIV introduction
- Risk factors for HPAIV spread
- Outcomes of AI surveillance plan

High risk areas have been defined within the high risk Regions, by taking into account the Ministerial provision of 26 August 2005.

Specific biosecurity measures were applied within the high-risk regions by means of:

- ban of free-range poultry rearing
- ban on using superficial water reservoirs (sources that can be accessed by wild birds)
- feed and bedding materials stocks must be protected from wild birds or other animals
- ban on exhibitions, fairs, and live-bird markets - A derogation to this measure can be authorized by the Regions and Autonomous Provinces following a risk-based evaluation
- ban on using live-decoy birds and/or rearing them in such conditions that allow them to have contact with wild birds

Fattening turkey housing in the high risk areas is allowed only after favourable assessment of biosecurity requirements. Such evaluation is carried out by local veterinary authorities, through the administration of a check list (Annex V of Ministerial provision n. 4122 of 19 February 2018) purposely created to assess the application of biosecurity measures at a structural and managerial level.

Preventive culling

As provided for in art.15 and art.17 in Council Directive 2005/94/EC, preventive culling was applied in 12 industrial poultry farms, with an amount of 426,500 culled birds. Criteria used to decide which holdings should be depopulated were: i) proximity to infected farms (within 500-1000 mt radius); ii) potential contacts (sharing of personnel, farms belonging to the same owner, farms belonging to familiars of the owner).

Most of the farms that were preventively culled after 15 November 2017, were related to outbreaks confirmed before the period of interest for the current case report (see table below, Outbreak confirmation).

Outbreak	Preventive culling – productive type	Culled birds	End of culling	Related outbreak	Outbreak confirmation
BRESCIA	LAYING HENS	31,800	15/11/2017	66 th	03/11/2017
BRESCIA	LAYING HENS	25,000	16/11/2017	66 th	03/11/2017
BRESCIA	LAYING HENS	39,900	15/11/2017	66 th	03/11/2017
BRESCIA	LAYING HENS	21,200	16/11/2017	66 th	03/11/2017
BRESCIA	BROILER	51,000	17/11/2017	67 th	03/11/2017
BRESCIA	BROILER	13,500	17/11/2017	67 th	03/11/2017
BRESCIA	LAYING HENS	39,000	15/11/2017	75 th	10/11/2017
BRESCIA	LAYING HENS	100,000	20/11/2017	77 th	10/11/2017
BRESCIA	LAYING HENS	4,475	18/11/2017	79 th	10/11/2017
BRESCIA	BROILER	3,030	23/11/2017	80 th	22/11/2017
BRESCIA	BROILER	86,605	29/11/2017	-	-
TREVISO	LAYING HENS	10,990	04/12/2017	82 nd	01/12/2017

The broiler farm preventively culled on 29 November 2017, was not evidently connected to a single outbreak: the Regional Veterinary Services of Lombardy region proposed to cull the birds as the premise was located in a high risk area, where lateral spread was profusely observed

Regional stand still (beyond the restriction zones specified in the EU Regulation)

In accordance with Ministerial provision n. 26651 of 21 November 2017, fattening turkey housing is prohibited inside the Densely Populated Poultry Area defined within the FRZ. A derogation to this measure can be authorized by the Regions following a risk-based evaluation made by the National

Reference Laboratory for Avian Influenza and favourable assessment of biosecurity requirements carried out by the official veterinary service.

Derogations on restriction zone implementation after risk assessment

In the restriction zones of all the cases, bird movement and housing derogations were applied as follows:

- i. in Protection Zones (PZ), derogations were discussed in the context of the Central Crisis Unit (UCC);
- ii. in Surveillance Zones (SZ): derogations were discussed in the context of the UCC if the farm was located within a Densely Populated Poultry Area (DPPA); in the case the farm was located outside of the DPPA, derogations were granted by Local Veterinary Service (the approval of more than one Regional Authority was needed, in case the derogation would affect more than one region). Derogations on poultry housing restrictions were granted in case of severe welfare issues: e.g. ready-to-lay pullets, and breeders belonging to small companies and needing to be moved in premises within the SZ (and which could have been culled due to the impossibility of being moved to the new farms).

Derogations were granted for the definition of PZ and SZ for the 81st outbreak (confirmation date: 23 November, 2017) according to Art. 16(2) of the Council Directive 2005/94/EC, as the backyard farm was located in a scarcely populated poultry area, and affected farm resulted not having risk contacts in the previous weeks.

Hunting

Ministerial provision n. 26551 of 21 November 2017 prohibits the use of live-decoy birds and/or rearing them in such conditions that allow them to have contact with wild birds.

References

Besides the National Provisions of the Ministry of Health discussed in the main text of the report, the

Provision of the Ministry of Health of 26 August 2005: '*Control measures to reduce the risk of transmission for infectious poultry diseases*' laid the bases for the application of biosecurity measures

Annex C – Applied prevention and control measures on avian influenza in Bulgaria

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• Scope

This document provides a brief overview of specific prevention and control measures applied in Bulgaria during the autumn-winter (November 2017- February 2018) in relation to avian influenza. There is only information provided that is relevant to the implementation of the following selected measures: increasing awareness of stakeholders and the general public, housing order, strengthening biosecurity measures (other than poultry confinement), preventive culling, regional stand still, derogations on restriction zone implementation after risk assessment and hunting. This document is made to support the EFSA working group in generating an overview on the application of the selected measures at EU level.

Timing of the applied prevention and control measures

Table 1 provides a timeline on the main events that triggered actions in relation to the selected prevention and control measures. More information on the actions taken is provided in the sections below.

Table 1: Overview of main communication actions

Date	Event that triggered action	Type of action taken	Target audience (if applicable)
18.10.2017	Confirmation of first HAPI poultry outbreak (in duck farm)	Measures on eradication of disease, epidemiological investigation , restriction zones established, Increasing awareness and strengthening passive surveillance in the whole country, notification EU, MSs, other Competent Authority in the country (MAF, Ministry of Health, Forestry Agency)	Official Vets, poultry associations, general public
20.10.2017	Confirmation of second HAPI poultry outbreak (in back yard)	Same as above	Official Vets, poultry associations, farmers
25.10.2017		<ul style="list-style-type: none"> Housing of poultry (particular focus on back yards) Ban of live poultry markets and exhibitions of birds on whole territory of the country. Enhancing the active surveillance in poultry – clinical examination in poultry farms (special focus on back yards). Enhancing the passive surveillance in wild birds. Strengthening biosecurity in poultry farms and regularly inspection to control it. Restocking of wild-feathered game was forbidden in the on the entire territory of the country, including gatherings and restocking of game in January 03, 2017. 	Official Vets, poultry associations, farmers
03.11.2017	Confirmation of third HAPI poultry outbreak (in back yard)	Eradication measures mentioned above.	Official Vets
	Confirmation of forth HAPI poultry outbreak (in duck farm)	Eradication measures mentioned above.	Official Vets,

	Confirmation of HPAI outbreaks	Ban for movement of waterfowl (except slaughtering) and repopulation of waterfowl farms	poultry associations, farmers
07.11.2017		Enhancing the active surveillance –serological surveillance in all duck farms in the country	Official Vets, poultry associations, farmers
10.11.2018		Derogation for movement and repopulation for those waterfowl farms in which serological investigation was negative and were met the enhanced biosecurity measures laid down in the new Ordinance for veterinary and sanitary requirement in farms (amendment of the legislation and new rules in terms of biosecurity in waterfowl farms has been enforced in response to the epidemic October 2016-April 2017. The transition period to meet these rules ended on 10.01.2018. Due to HPAI emergency, the Bulgarian CA decided to enforce their implementation and allowed repopulation of farms which were able to meet them)	
03.11.2018 – 20.12.2018	Confirmation of HPAI outbreaks	Increasing awareness through regular meetings (weekly basis) with poultry associations , hunting associations , informative campaigns with farmers at regional level	poultry associations, hunters

Increasing awareness of the stakeholders and the general public

As mentioned in the table 1 regular meetings (weekly basis) with poultry associations, hunting associations, informative campaigns with farmers at regional level were conducted for the purpose of increasing awareness. Moreover the opportunity of other meeting with stakeholders dedicated on different animal health topics are also being used in terms of enhancing awareness, keeping up to date with the AI epidemiological situation in Europe and in Bulgaria (present and past), measures taken and lessons learnt.

Housing order

Based on the outcomes and concern raised during the last HPAI epidemic (the season 2016-2017), precautionary measures as keeping poultry indoors, taking steps to separate them from wild birds and ensuring feed and water is not accessible to wild birds was also required. Special focus was given in backyards, due to lack of biosecurity measures applied.

Strengthening biosecurity measures (other than housing order)

The national legislation related to minimum requirements for farm animals and poultry was amended resulting in strengthening the biosecurity in waterfowl (white/black zones; density, capacity to keep indoor the poultry if necessary etc.

Preventive culling

Preventive culling was applied in holdings around two of the outbreaks based on the epidemiological investigation and in accordance with Art.17, paragraph 3 of Directive 2005/94.

Regional stand still (beyond the restriction zones specified in the EU Regulation)

No

Derogations on restriction zone implementation after risk assessment

No

Hunting

Hunting was not forbidden as it during the last epidemic season. In restricted zones established around the outbreaks a restocking of wild feathered game was forbidden only.