SCIENTIFIC REPORT

European Union Reference Laboratory for Avian Influenza

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Avian influenza overview August – November 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 August and 15 November 2018, 14 highly pathogenic avian influenza (HPAI) A(H5N8) outbreaks in poultry establishments in Bulgaria and seven HPAI A(H5N6) outbreaks, one in captive birds in Germany and six in wild birds in Denmark and the Netherlands were reported in the European Union (EU). No human infection due to HPAI A(H5N8) and A(H5N6) viruses have been reported in Europe so far. Seroconversion of people exposed during outbreaks in Russia has been reported in one study. Although the risk of zoonotic transmission to the general public in Europe is considered to be very low, appropriate personal protection measures of people exposed will reduce any potential risk. Genetic clustering of the viruses isolated from poultry in Bulgaria suggests three separate introductions in 2016 and a continuing circulation and transmission of these viruses within domestic ducks. Recent data from Bulgaria provides further indication that the sensitivity of passive surveillance of HPAI A(H5N8) in domestic ducks may be significantly compromised. Increased vigilance is needed especially during the periods of cold spells in winter when aggregations of wild birds and their movements towards areas with more favourable weather conditions may be encouraged. Two HPAI outbreaks in poultry were reported during this period from western Russia. Low numbers of HPAI outbreaks were observed in Africa and Asia, no HPAI cases were detected in wild birds in the time period relevant for this report. Although a few HPAI outbreaks were reported in Africa and Asia during the reporting period, the probability of HPAI virus introductions from non-EU countries via wild birds particularly via the north-eastern route from Russia is increasing, as the fall migration of wild birds from breeding and moulting sites to the wintering sites continues. Furthermore, the lower temperatures and ultraviolet radiation in winter can facilitate the environmental survival of any potential AI viruses introduced to Europe.

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

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Amendment: An editorial correction was carried out that does not materially affect the contents or outcome of this scientific output. Figure 8 was amended: In the legend, 'HPAI (H5N1) outbreaks in birds' was changed to 'HPAI outbreaks in birds'; 'the figure title 'Geographical distribution of HPAI outbreaks in Europe, Asia and Africa by virus subtype and affected subpopulation, 16 August – 15 November 2018 (n=36)' was changed to 'Geographical distribution of HPAI outbreaks in Europe, Asia and Africa by virus subtype and affected subpopulation, 16 August – 15 November 2018 (n=39)'. To avoid confusion, the older version has been removed from the EFSA Journal, but is available on request, as is a version showing all the changes made.

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1. Introduction

The present document gives an overview of highly pathogenic avian influenza (HPAI) outbreaks detected in poultry, captive and wild birds and low pathogenic avian influenza (LPAI) outbreaks in poultry and captive birds, as well as human cases due to avian influenza (AI) reported in and outside Europe between 16 August and 15 November 2018. The background, terms of reference (TORs) and their interpretation are reported in Appendix A; data and methodologies are reported in Appendix B.

2. Conclusions

Avian Influenza outbreaks in European countries and in other countries of interest between 16 August and 15 November 2018

2.1. Main observations

- No human infections with HPAI or related LPAI viruses of the same genetic composition as those currently detected in domestic and wild birds have been reported from Europe. However seroreactivity to A(H5N8) clade 2.3.4.4. and A(H5N1) clade 2.3.2.1c viruses in people exposed to infected or dead birds has been reported from Russia.
- In Europe, between 16 August and 15 November 2018 (based on the Animal Disease Notification System (ADNS)):

– 14 HPAI A(H5N8) outbreaks were reported in poultry in Bulgaria;

– seven HPAI A(H5N6) outbreaks were reported: four in Denmark in wild birds, two in the Netherlands in wild birds, and one in captive birds in Germany; the wild bird species involved were present in the revised list of target species for passive surveillance.

- Genetic clustering for the HA gene from viruses isolated from Bulgarian poultry suggests three separate initial introductions. Additional genetic diversity could be explained by the continued circulation and transmission of these viruses within domestic ducks.
- In Bulgaria the evolution of the epidemiological situation prompted the adoption of enhanced active surveillance measures. An increase of the sampling frequency, the introduction of pre-movement polymerase chain reaction (PCR) testing in poultry in high risk areas, strict veterinary controls on duck farms, and extended virological surveillance in force-fed duck establishments were some of the measures introduced.
- Two HPAI A(H5Nx) outbreaks were reported in poultry in this time period from Russia via OIE.
- In the reporting period, a low number of HPAI outbreaks were observed in Africa and Asia, and no new outbreaks were reported from some previously affected areas. Furthermore, no cases of HPAI A(H5Nx) in wild birds were detected in the relevant time period for this report.

2.2. Conclusions

- The risk of zoonotic transmission of AI viruses to the general public in European countries is considered to be very low.
- The mortality events due to HPAI virus A(H5N6) reported in wild birds in Denmark and the Netherlands underlines the potential for HPAI virus A(H5N6) to remain present in free-living wild birds for several months after the peak of the outbreaks, and emphasises the need for continued vigilance regarding incursion into poultry establishments.
- Recent data from Bulgaria provide further indication that the sensitivity of passive surveillance for HPAI A(H5N8) in domestic ducks may be significantly compromised.
- In the period of this report in EU/EEA, there is no evidence of a new HPAI virus incursion from Asia. However, passive surveillance systems may not be sensitive enough to detect the virus if the prevalence of infection and/or case fatality in wild birds is very low. Increased vigilance is

needed especially during the periods of cold spells in winter that may encourage aggregations of wild birds and their movements towards areas with more favourable weather conditions.

- The continued presence of HPAI A(H5Nx) in the western parts of Russia spatially associated with fall migration routes of wild water birds is of concern for the possible spread of the virus via wild birds migrating to the EU/EEA.
- The probability of AI virus being introduced from non-EU countries via wild birds is increased as the migration of wild birds from breeding and moulting sites to the wintering sites continues.
- The environmental survival of AI viruses potentially introduced to EU/EEA can be facilitated by the low temperatures and low ultraviolet radiation during winter.

3. Suggestions

- Continued surveillance for AI virus in wild birds and poultry in Europe and worldwide combined with timely generation of complete viral genome sequences and data sharing among European countries and between animal and human health sectors are crucial to be able to detect and early respond to threats that are relevant to animal and public health. It is particularly important that information on the genetic composition and possible origins of recently detected new variants are shared and communicated in a timely manner. If HPAI virus A(H5) persists in the EU/EEA in wild birds or poultry, rapid (as real-time as possible) and detailed genetic analyses become even more important to distinguish persisting infections from new incursions.
- It is critical that maximal efforts are made to stamp out outbreaks in poultry before the next fall migration begins.
- Given the increased probability of new outbreaks among poultry and wild birds in Europe in the forthcoming period, enhanced surveillance for HPAI A(H5) is recommended in EU/EEA; this surveillance should also include cases of single sick or dead wild birds of the target species.
- People exposed to birds who may potentially be infected with AI should take appropriate personal protection measures following national guidelines.

4. Results

4.1. HPAI and LPAI outbreaks in Europe, 16 August – 15 November 2018 (TOR 1 and TOR 2)

4.1.1. Description of the AI detections in time and space

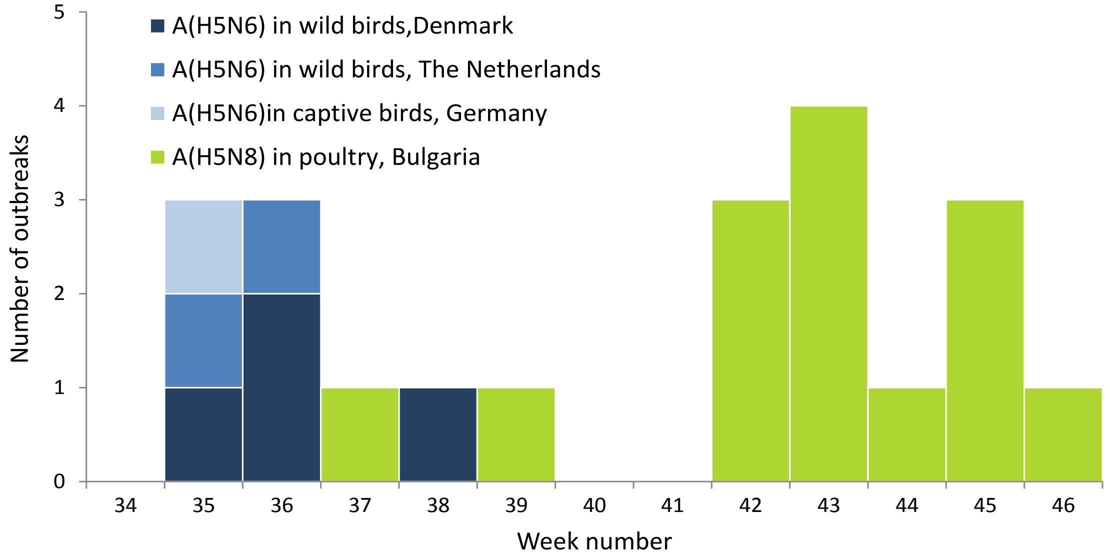
4.1.1.1. HPAI and LPAI in poultry, other captive birds, and wild birds

From 16 August to 15 November 2018, 21 HPAI outbreaks, seven A(H5N6) and 14 A(H5N8), occurred in European countries reported via the ADNS, as presented in Table 1. No LPAI outbreaks were detected during this time period in Europe. The timeline, location and affected subpopulation of the AI outbreaks are reported Figures 1 and 2. The characterisation of HPAI- affected poultry establishments[1] is reported in Section 4.1.2.1. For wild birds, Table 1 displays the number of outbreaks, whereas the description of cases by outbreak is reported in Section 4.1.2.2. Furthermore two HPAI A(H5Nx) outbreaks occurred in western Russia; as those outbreaks are not reported via ADNS but via OIE, they are described in section 4.4.

Table 1: Number of AI outbreaks in Europe by virus subtype and country, 16 August – 15 November 2018. Data Source: ADNS (07.12.18)

Country	HPAI			LPAI	All AI
	A(H5N6) in wild birds	A(H5N6) in captive birds	A(H5N8) in poultry		
Bulgaria		–	14	–	14
Denmark	4	–	–	–	4
Germany		1(a)	–	–	1
Netherlands	2(b)	–	–	–	1
Total (four countries)	6	1	14	–	21

(a) Chicken, domestic duck and domestic goose.
(b) The Information on one of these two outbreaks is from Wageningen University Research (WUR, online).



Data Source: ADNS (07.12.18).

Figure 1: Distribution of the HPAI outbreaks in Europe by week of suspicion, virus subtype, affected subpopulation and country, 16 August – 15 November 2018 (n=21)

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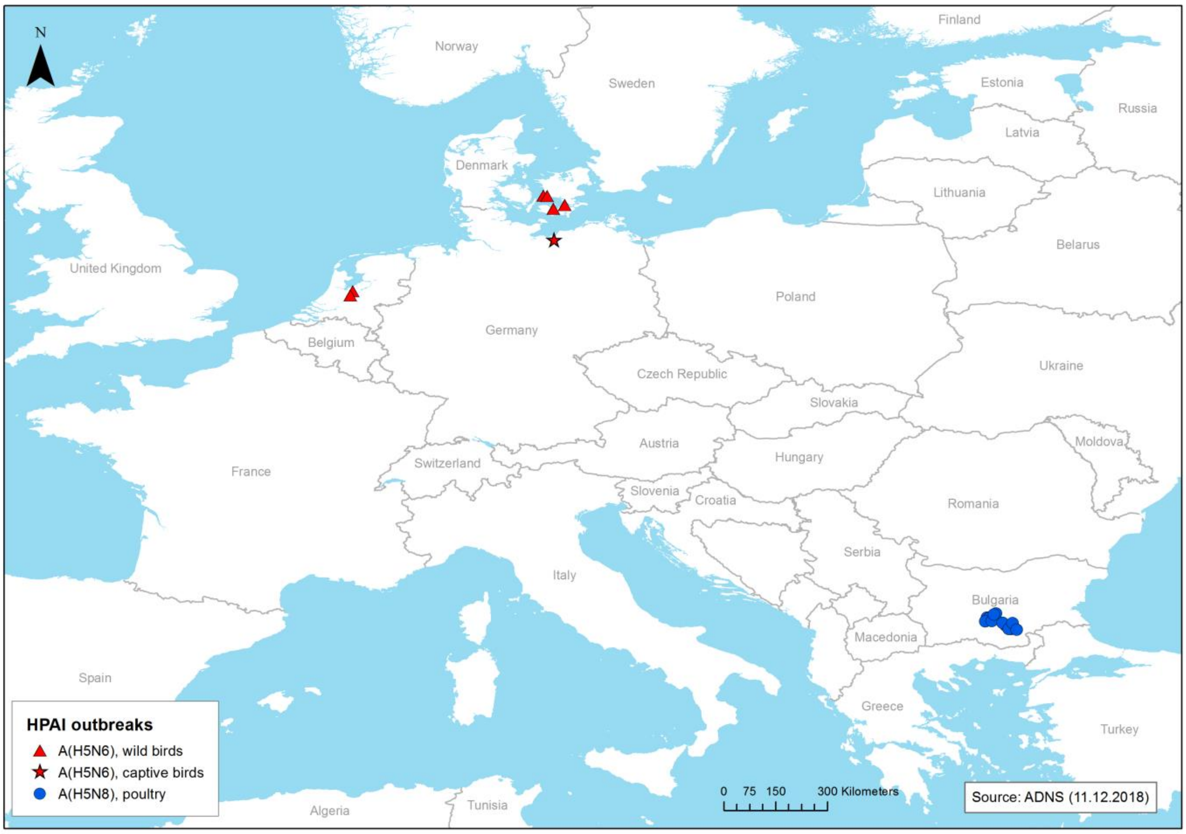
[1] According to Regulation (EU) 2016/429 'establishment' means any premises, structure, or, in the case of open-air farming, any environment or place, where animals or germinal products are kept, on a temporary or permanent basis, except for: (a) households where pet animals are kept; (b) veterinary practices or clinics.



Source: ADNS (11.12.2018)

Figure 2: Geographical distribution of HPAI outbreaks in Europe by virus subtype and affected subpopulation, 16 August – 15 November 2018 (n=21)

4.1.2. Phenotypic characterisation of AI viruses circulating in Europe

4.1.2.1. HPAI in domestic birds

Characterisation of the HPAI-affected poultry establishments in Bulgaria

From 16 August to 15 November 2018, 14 HPAI outbreaks were notified in the poultry sector in the EU, all caused by A(H5N8) viruses and reported from Bulgaria (Figure 3). Six outbreaks occurred in establishemnts rearing domestic ducks (mulard ducks) for foie gras production; three in laying hens; two in fattening turkey; one in broiler; two in multiple species estabishemnts (rearing laying hens and domestic turkey). Since April 2018 Bulgaria has been the only country in the EU/EEA experiencing HPAI outbreaks in poultry. The situation prompted the adoption of additional measures, described in section 4.3.1, to prevent, early detect and eradicate HPAI outbreaks. Up to 15 November 2018, a total of 26 HPAI A(H5N8) outbreaks have been detected in poultry and captive birds as shown in Figure 3. Six out of the 26 outbreaks were reported in establishments previously affected in 2017. Since February 2017, no AI positive wild birds have been reported in Bulgaria.

Most of the HPAI outbreaks reported in 2018 in poultry (20/26) and in domestic duck (11/14) holdings and all the ones occurred in the referring period are located in the Plovdiv and Haskovo regions (Figure 3). Those two regions host togheter 172 out of 739 poultry and 149 out of 277 of domestic duck etablishments present in Bulgaria. The vast majority of the domestic ducks bred are mulard ducks for foie grass production.

Concerning the reporting period of this report, from 16 August to 15 November 2018, the outbreaks affecting chicken, turkeys and mixed species establishments were detected by mean of passive surveillance as animals reared showed signs of HPAI virus infection. Among the six outbreaks occurring in domestic duck establishments, one was detected via outbreak related surveillance while five were identified via enhanced active surveillance (virological surveillance in force-fed duck before movement to slaughteraouse). With the exception of the outbreak detected via outbreak related surveillance where dead ducks were found (331 out of 16 183), no signs of HPAI infection were detected in the affected ducks in the other five establishments. The frequency of the different signs of HPAI infection in the affected animal species is reported in Figure 4; an overview of the characteristics of the affected establishments and species reared is reported in Table 2.

The epidemiological findings (i.e. any findings of wild bird cases, location of the outbreaks in high density poultry farm regions (particularly duck farms), life cicle and management/housebandry of foie gras ducks) coupled with the results of the genetic analysis of the HPAI A(H5N8) viruses isolated in Bulgaria in 2017 and 2018 (Secion 4.1.3) indicate that HPAI virus is persisting in the country without being re-introduced via wild birds. The main possible source of infection in poultry establishment is considered to be breaches of biosecurity measures applied in the farms, as well as during the transport in mulard production cycle (staff and equipment and vehicles involved in the transport).

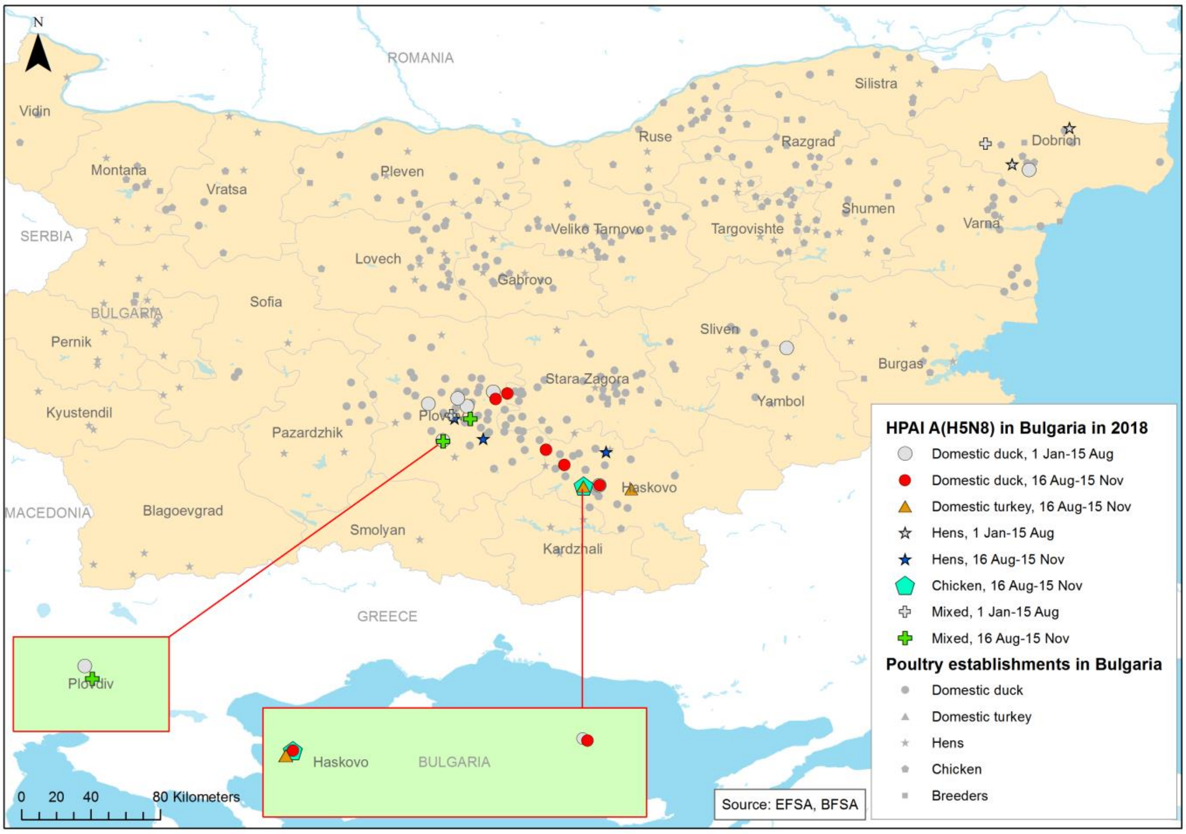
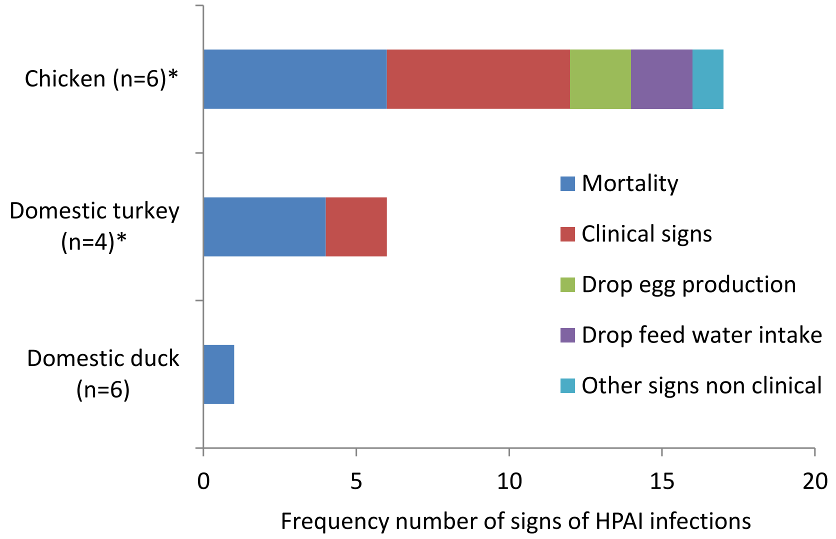


Figure 3: Geographical distribution of HPAI A(H5N8) outbreaks by affected subpopulation, 1 January – 15 November 2018 (n=26), and of pultry establishments by subpopulation (n=739) in Bulgaria



*Two outbreaks were identified in establishments rearing laying hens and fattening ducks.

Figure 4: Frequency of number of signs of HPAI infection by affected subpopulation in Bulgaria, 16 August – 15 November 2018 (n=16)

Table 2: Characteristics of the A(H5N8) HPAI affected poultry establishments in Europe, 16 August – 15 November (n=14). Data Source: ADNS and EFSA

Country	Poultry species	Production category	Surveillance stream	Presence of signs due to HPAI infection	Outdoor access	Date of suspicion$^{(a)}$	Number of susceptible animals$^{(b)}$	Number of people exposed
Bulgaria	Domestic duck	Foie gras	Outbreak related	Yes	Yes	16/10/2018	16 183	12
			Active$^{(c)}$	No	Yes	23/10/2018	12 797	7
					No	23/10/2018	1 000	3
					No	27/10/2018	7 020	6
					Yes	05/11/2018	3 500	5
					No	13/11/2018	1 973	2
	Chicken	Egg	Passive	Yes	No	15/09/2018	44 083	7
					No	26/10/2018	43 377	10
					No	05/11/2018	37 403	12
		Fattening	Passive	Yes	No	16/10/2018	130 000	18
	Domestic turkey$^{(d)}$	Fattening	Passive	Yes	Yes	29/10/2018	150	1
						07/11/2018	243	2
	Mixed$^{(d-e)}$	Mixed	Passive	Yes	Yes	18/10/2018	85	2
						28/09/2018	456	2
Total							**298 270**	**89**

(a) Date of confirmation is provided when the date of suspicion is not available.
(b) Based on the number of susceptible domestic birds reported to EFSA.
(c) Enhanced active surveillance: virological testing before transport to slaughterhouse in force feeding duck farm for foie gras production.
(d) Non-commercial establishment.
(e) Laying hens and domestic turkey for fattening.

An HPAI outbreak was confirmed outside the reporting period for this report, on 22 November, in the course of AI surveillance activities and control programme in a non-commercial establishment located in Bulgaria, Yambol region (Pravdino village).

Information extracted from the scientific literature

No new relevant information was published during the reporting period.

4.1.2.2. HPAI in wild birds

Pathogenicity in the affected species

From 16 August to 15 November 2018, the only HPAI virus subtype that was identified in carcasses of wild birds submitted for AI virus testing was A(H5N6) (six outbreaks in two countries) (Table 3). This is similar to the number of cases compared with the previous 3-month period (EFSA et al., 2018b), when three outbreaks were reported in two countries. Despite the low number of outbreaks, this does underline the potential for HPAI virus A(H5N6) to remain present in free-living wild birds for several months after the peak of the outbreak, necessitating continued vigilance regarding incursion into poultry establishments.

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

OIE report number	Country	Number of outbreaks by country	Number of cases by outbreak	Number of wild bird species involved by outbreak	List of wild birds species involved in the country	Total wild bird cases by country
27906[(a)]	Denmark	4	4, 2, 1, 3	2, 2, 1, 1	Mallard (*Anas platyrhynchos*), common pheasants (*Phasianus colchicus*), mute swan (*Cygnus olor*), common eider (*Somateria mollissima*), greylag goose *(Anser anser*)	10
26949[(b)]	The Netherlands	2	1, 1	1, 1	Mallard (*Anas platyrhynchos*), marsh harrier (*Circus aeruginosus*)	2
Total	**(2)**	**6**	**-**	**-**	**(6)**	**12**

(a) The third and the fourth outbreaks involving a greylag goose and three common pheasants, respectively, are not described in the OIE report 27906; information on these outbreaks are from ADNS.

(b) The second outbreak involving the marsh harrier is not described in the OIE Report No. 26949; information on this outbreak is from Wageningen University Research (WUR, online).

Information extracted from the scientific literature

HPAI A(H5N8) characterisation (virulence, replication)

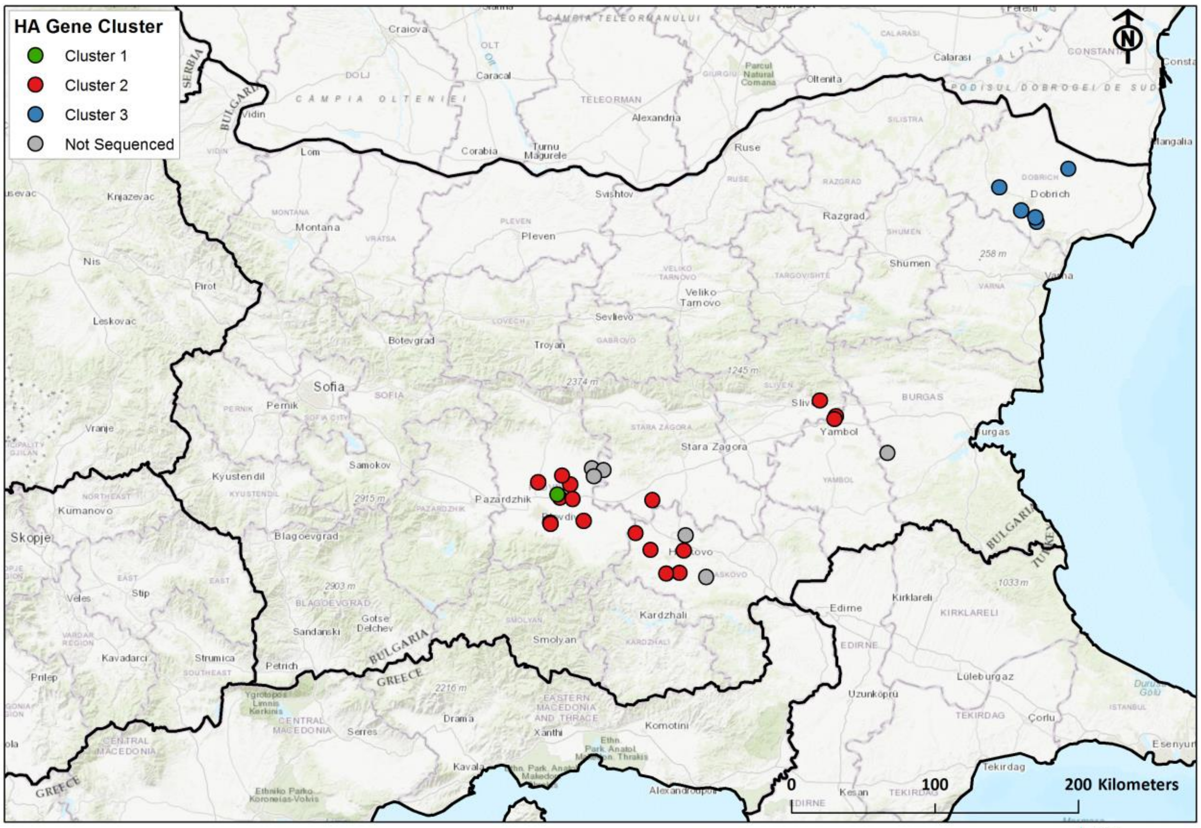
One article (Krone et al., 2018) reported the virulence of HPAIV H5N8 clade 2.3.4.4b for white-tailed eagles (*Haliaeetus albicilla*). Between November 2016 and April 2017, HPAIV H5N8 clade 2.3.4.4b infection was detected in oropharyngeal and/or cloacal swabs of 17 white-tailed eagles (14 dead, three alive) in northern Germany. Eleven were juvenile, two were subadult, and three were adult. The live birds displayed neurological signs including torticollis, opisthotonus, ataxia, and circling. At autopsy, no gross lesions were detected, but by histopathology, there was inflammation and necrosis in the brain, colocalised with influenza virus antigen expression. Lead poisoning was ruled out. It is likely that white-tailed eagles became infected because they predated on or scavenged infected waterfowl. Because 0/19 white-tailed eagles found dead during the HPAIV H5N1 clade 2.2 were diagnosed positive for HPAIV in the same area in 2006, it cannot be ruled out that HPAIV clade 2.3.4.4b was more virulent for this species. The implication from this study is that white-tailed eagles may act as a sentinel for the presence of HPAIV H5Nx clade 2.3.4.4b in waterfowl in their range, and that this virus is a new threat to the protected white-tailed eagle across its range in Eurasia.

4.1.3. Genetic characterisation of AI viruses circulating in the Europe

25 of the 32 2.3.4.4b A(H5N8) viruses isolated from domestic birds in Bulgaria since from October 2017 through to November 2018 have been sequenced by the EURL at APHA-Weybridge, UK. Three clusters have been identified for the HA gene which is the primary target of the immune response (Figure 5).

Cluster 1 consisted of a single strain sampled on 17 October 2017 from a duck with the closest genetic relative being viruses from wild birds in Hungary in the previous year. No further detections of this cluster have occurred since October 2017. Cluster 2 is the largest cluster by number of isolates and has circulated throughout the above time period. The cluster 2 isolates are from outbreaks in several locations in Central Bulgaria including Haskovo, Plovdiv and Yambol in chickens, ducks and partridge. Cluster 3 consists of strains from chickens in Dobrich in the North-East of Bulgaria. Representatives of this cluster have only been detected in March, June and July 2018.

At the whole genome level we see three different gene constellations mirroring the above HA patterns. However, within the cluster 2 viruses there is additional diversity in the MP gene through reassortment. The cluster 3 viruses are similar in gene constellation to the cluster 2 viruses only for NS, PA, PB1 and PB2. This suggests three separate initial introductions/variants followed by additional diversity generated in the cluster 2 viruses through reassortment of the MP gene. Given that cluster 2 is circulating in a number of domestic species including ducks and ducks are ancestral on a number of phylogenetic tree nodes, it is likely that continued circulation and transmission within domestic ducks is contributing additional genetic diversity. Estimated time to most recent common ancestor for these three introductions are Cluster 1: September 2016 (95% HPD July 2016 – December 2016), Cluster 2: April 2016 (95%HPD April 2016 – September 2016), Cluster 3: November 2016 (95% HPD May 2016 – December 2016).



H5N8 HPAI Avian Influenza events in Poultry in Bulgaria Since 17/10/2017 (n=32)

Created by: EURL Dec 2018

Figure 5: HPAI A(H5N8) outbreaks in poultry in Bulgaria, 17 October – 15 November 2018 (n=32)

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

No human infection related to A(H5N6) or A(H5N8) viruses detected in wild birds and poultry in Europe has been reported so far (Adlhoch et al., 2018). Bulgaria reported to EFSA that a total of 89 people were exposed to poultry infected with HPAI A(H5N8) during the outbreaks that occurred in the country from 16 August to 15 November (Table 2).

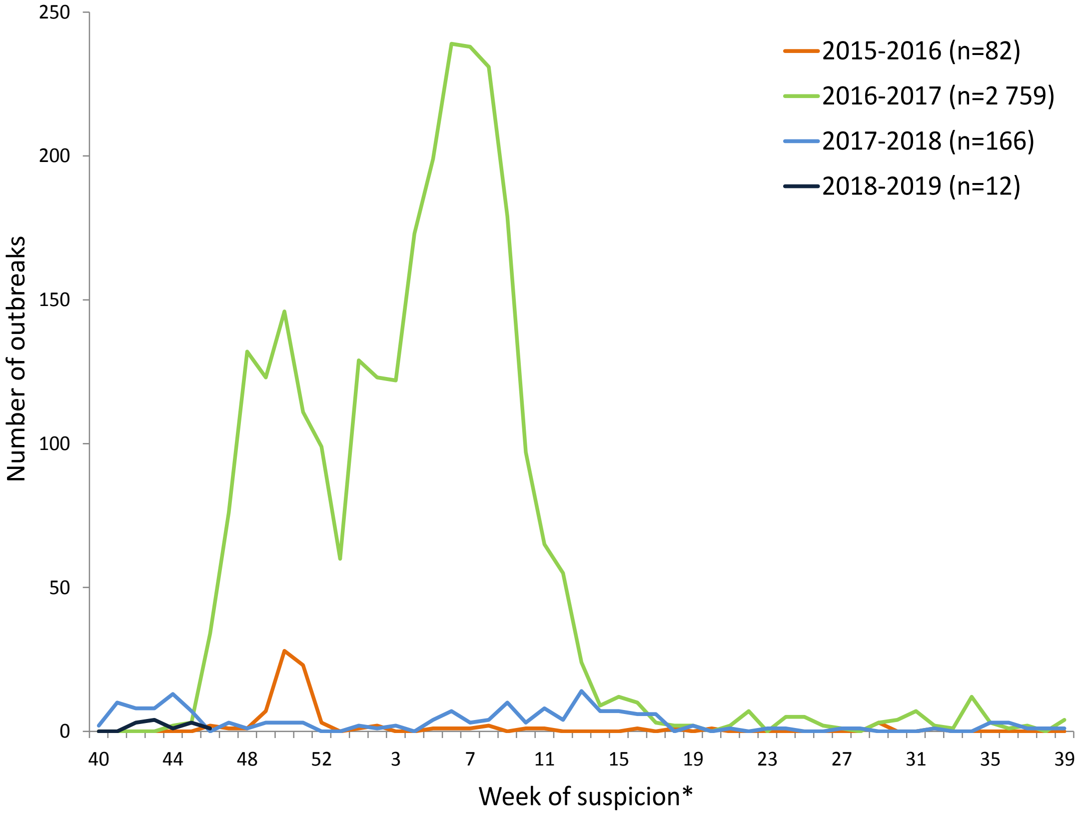
Four genetic groups (a, b, c, d) of clade 2.3.4.4 have been proposed by Lee et al. (2018a) based on the HA sequences. A(H5N8) and A(H5N6) viruses detected in birds and poultry in Europe cluster in clade 2.3.4.4.b. One human case in China was infected with A(H5N6) of the 2.3.4.4.b clade in 2017. All viruses circulating and causing outbreaks in European domestic and wild birds since 2016 also cluster within this clade 2.3.4.4.b (Globig et al., 2017; Pohlmann et al., 2018). However, there is a high variability within the gene segments within the A(H5N6) viruses world-wide and the overall gene composition of the European viruses in birds differs from the human case detected in China (DEFRA, 2018; GISAID, online).

In a study from Russia, 760 sera from people having had contact to infected or perished birds during the AI outbreaks between November 2016 and March 2017 showed the presence of antibodies to A(H5N1) clade 2.3.2.1c and A(H5N8) clade 2.3.4.4. (Ilyicheva et al., 2018). In this study, 4 979 serum specimens collected from October to November 2016 were sero negative for A(H5N8) and A(H7N9) viruses by HI test. No illness in humans due to avian influenza was registered between November 2016 and March 2017. Of 760 nasopharyngeal swabs taken from all personnel with contact with infected or perished birds, two were PCR positive for A(H5N8), but the workers did not have any symptoms and their paired blood samples were negative in HI and neutralisation tests. Paired sera were taken during the outbreaks and 21 days later and tested by HI test. Of 760 sera, 28 paired samples were reactive to A/rook/Chany/32/2015 (H5N1) and 60 paired samples were reactive to A/chicken/Sergiyev Posad/38/2017 A(H5N8). In one instance, antibodies were only present in the second serum three weeks after the outbreak. All HI-reactive sera were analysed in a neutralisation assay with 40% also showing positive neutralisation. Positive sera with antibodies agains A(H5N8) derived from people in the Republic of Kalmykia, Astrakhan region, Nizhniy Novgorod region, Moscow region and Krasnodar Krai.

This is the first description of a seroconversion related to A(H5N8) clade 2.3.4.4. viruses. However, as the serum specimens taken on day 1 of the outbreaks were already positive, it remains inconclusive when this exposure to the virus and subsequent seroconversion occurred.

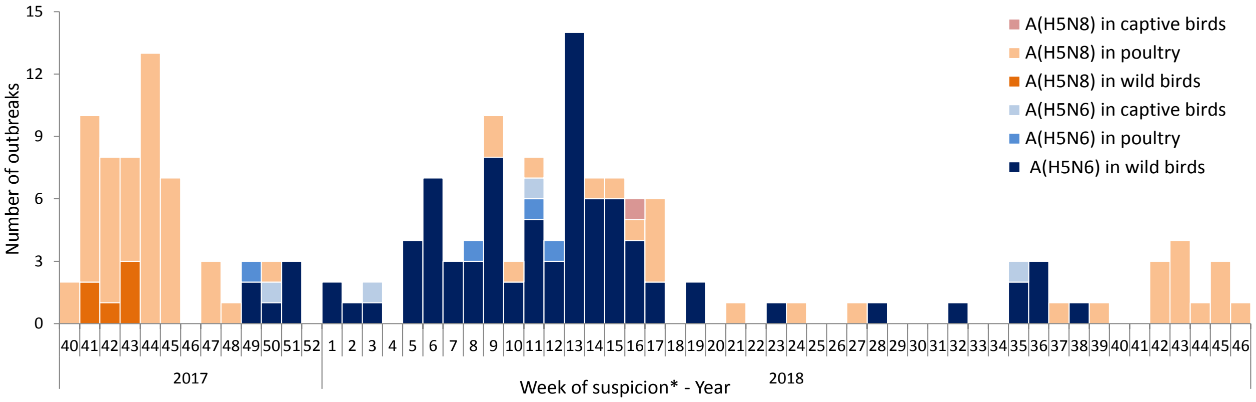
4.2. Overview of HPAI outbreaks in Europe in the current and previous seasons

Figure 6 and Figure 7 show the HPAI outbreaks detected in Europe and reported via ADNS in the previous and current season, considering a season as starting on week 40 and ending on week 39 of the following year.



* When the week of suspicion is not available then the week of confirmation is provided.
Data Source: ADNS, EFSA.

Figure 6: Distribution of HPAI outbreaks in Europe by week of suspicion and seasons, 28 September 2015 – 15 November 2018 (n=3 019)



* When the week of suspicion is not available then the week of confirmation is provided.
Data Source: ADNS, EFSA.

Figure 7: Distribution of the HPAI outbreaks in Europe by week of suspicion, virus subtype and affected subpopulation, 2 October 2017 – 15 November 2018 (n=178)

4.3. Applied prevention and control measures in Europe, 16 August – 15 November 2018 (TOR 3)

4.3.1. Bulgaria

The evolution of the epidemiological situation prompted the adoption of enhanced active surveillance measures in poultry farms (chicken breeders and layers) and domestic waterfowl, starting from 16 August. Measures included an increased frequency of sampling.

The confirmation of primary outbreaks since September 2018 lead to the extension of the measures already applied and described in the report for May to July 2018 (EFSA et al., 2018a) including:

1. housing order on the National level;
2. ban on exhibitions and live bird markets;
3. enhancement of surveillance activities in poultry;
4. enhancement of passive surveillance in wild birds;
5. strengthening of biosecurity measures in poultry farms, and regular controls to assess the maintenance of adequate level of biosecurity;
6. ban on restocking game birds in the protection and surveillance zones.

Awareness was increased in stakeholders and the generic public, through regular meetings with representatives of the poultry associations, and publishing information on dedicated websites.

On 30 October 2018, surveillance measures were further enhanced in high-risk areas, by requesting premovement PCR testing on poultry, before loading for transport to other farms or to slaughterhouses. Strict veterinary controls were to be performed on duck farms, with a particular focus on premises dedicated to force feeding, due to the high frequency of poultry movements. High-risk areas were defined according to the epidemiological situation (i.e. number of outbreaks), density of poultry farms and other risk factors.

An extended virological surveillance in force-fed duck farms lead to the detection of five out of 14 HPAI outbreaks identified in the reference period.

Details on the control measures applied in Bulgaria are given in Annex A.1.

4.3.2. Germany

On 1 September 2018 a backyard farm was confirmed as infected with a A(H5N6) HPAI virus. Following a risk assessment, the competent authority decided to use the derogation and refrain from establishing protection and surveillance zones around this outbreak. Disease control measures were applied and the birds were culled and disposed of on 1 September 2018.

Increased surveillance activities were implemented at the national level, together with strict movement controls and traceability of poultry and poultry products.

4.3.3. Denmark

On 31 August 2018 two mallards (*Anas platyrhynchos*) and two common pheasants (*Phasianus colchicus*) found dead on 27 August on a small island between the southern Zealand and Lolland-Falster, were confirmed as infected with an A(H5N6) HPAI virus. The pheasants were released for hunting from a game bird farm on 1 July 2018.

Following the confirmation, an expert meeting was held, leading to a press release focused on increasing bio-exclusion measures in the affected area, suggesting the use of roofs, horizontal fabric or nets.

Three other wild birds were found positive in the following weeks, with the latest being confirmed on 25 September 2018. Consequently, the Danish Veterinary and Food Administration contacted the

Danish Hunters Association and informed them about the importance of biosecurity in connection with hunting and how to report finding of dead wild birds using the app 'Fugleinfluenza Tip', already described in the first EFSA report on HPAI monitoring (EFSA et al., 2017).

Details on the control measures applied in Denmark are given in Annex A.2.

4.3.4. The Netherlands

The confirmation of a HPAI H5N6 virus in a sample taken from a mallard duck found dead led to an increase in biosecurity at the national level, including a mandatory logbook and the adoption of strict hygiene protocols for visitors. An information campaign was performed to increase awareness in the stakeholders and the general public.

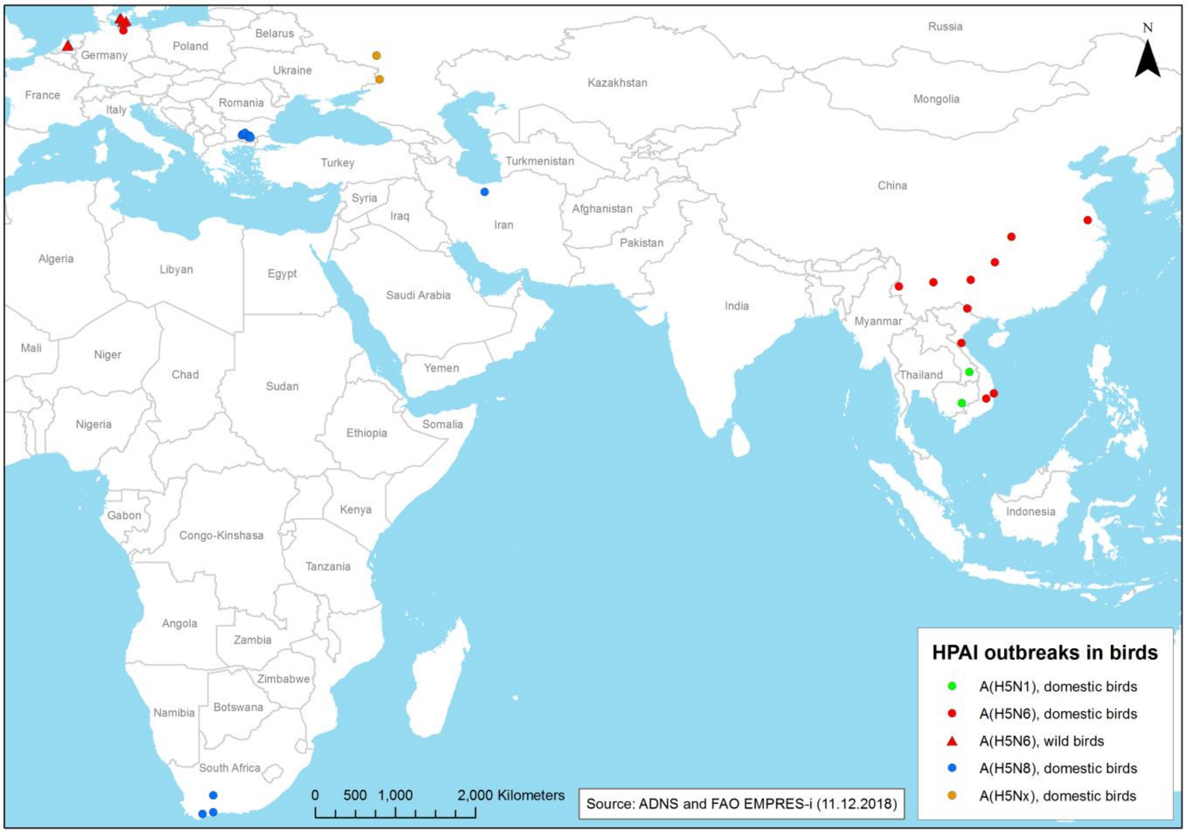
Details on the control measures applied in the Netherlands are given in Annex A.3.

4.4. The AI situation in other countries not reporting via ADNS, 16 August – 15 November 2018 (TOR 4)

An overview of the HPAI outbreaks reported from other countries not reporting via ADNS but via OIE from 16 August to 15 November 2018 is presented in Table 4 and Figure 8. For the purpose of this report findings of HPAI A(H5N1), A(H5N6), A(H5N8), A(H5Nx), HPAI and LPAI A(H7N9) and LPAI A(H9N2) viruses occurring in countries that are considered of epidemiological interest for the EU/EEA are described.

Table 4: Number of HPAI outbreaks in other countries not reporting via ADNS by virus subtype and country, 16 August – 15 November 2018 (n=18)

Region	**Country**	**HPAI A(H5N1)**	**HPAI A(H5N6)**	**HPAI A(H5N8)**	**HPAI A(H5Nx)**	**All HPAI**
		Domestic birds	Domestic birds	Domestic birds	Domestic birds	
Asia	**Cambodia**	1	–	–	–	1
	Lao People's Democratic Republic	1	–	–	–	1
	China	–	6	–	–	6
	Viet Nam	–	4	–	–	4
	Iran	–	–	1	–	1
Europe	**Russia**	–	–	–	2	2
Africa	**South Africa**	–	–	3	–	3
Total	**(seven countries)**	2	10	4	2	18



Source: ADNS and FAO EMPRES-i (11.12.2018)

Figure 8: Geographical distribution of HPAI outbreaks in Europe, Asia and Africa by virus subtype and affected subpopulation, 16 August – 15 November 2018 (n=39)

4.4.1. HPAI A(H5N1)

4.4.1.1. Domestic and wild birds

Detections

From 16 August 2017 to 15 November 2018 only the Lao People's Democratic Republic and Viet Nam reported new outbreaks of HPAI virus A(H5N1) in a backyard poultry and in a commercial farm respectively. In this reporting period, still no outbreaks of HPAI virus A(H5N1) were reported from Africa or the Middle East (see Figure 9).

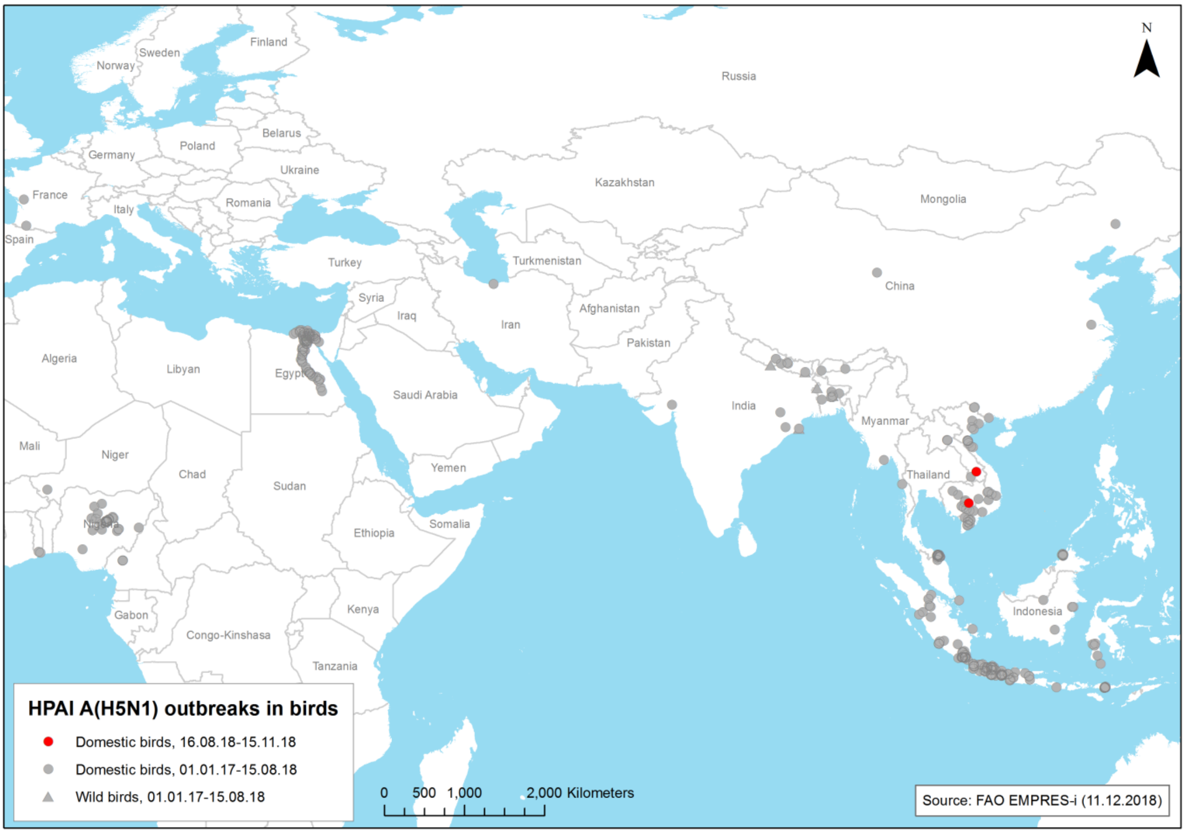


Figure 9: Distribution of confirmed HPAI A(H5N1) outbreaks in birds by place of origin, 1 January 2017 – 15 November 2018 (FAO, online-b)

Genetic information

An A(H5N1) clade 2.1.3.2a reassortant virus identified in Indonesia in 2012 with internal genome segments (PB2, PB1 and NS genes) acquired from an LPAIV progenitor was described (Dharmayanti et al., 2018). The virus showed attenuated infectivity and virulence in mice. An A(H5N1) virus detected from a backyard flock in Iran in 2015 belonged to clade 2.3.2.1c and possessed several mutations in NA gene that are associated with adaptation to galliforms and antidrug resistance (Yegani et al., 2018).

Phenotypic characterisation

Nooruzzaman et al. (2018) provided descriptive analysis of HPAI A(H5N1) clade 2.3.2.1 outbreaks on quail and duck farms in Bangladesh in 2011. Mortality of 100% within 2 days was observed in 6-month-old quail. Haemorrhages and congestion with necrotic/inflammatory lesions in the respiratory tract, liver, pancreas and kidneys were predominantly seen at necropsy and by histological examination. Nervous signs such as in-coordination, torticollis and head tremors were observed in 2-month-old sick ducks of Khaki Campbell breed, but mortality was approximately 10% at the time of investigation. No significant gross lesions were described and histopathological lesions concentrated in the central nervous system. Viral antigen was detected in multiple organs of both ducks and quail by immunohistochemistry.

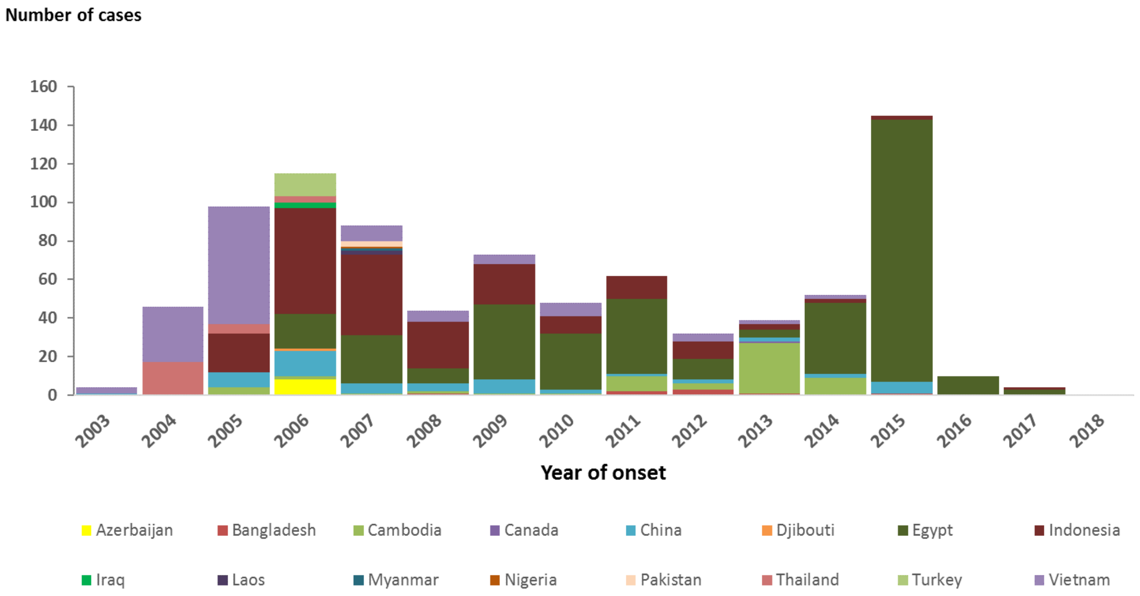
4.4.1.2. A(H5N1) in mammals (excluding humans)

No new relevant information was published during the reporting period.

4.4.1.3. Human infections due to A(H5N1)

No new human cases due to AI A(H5N1) have been reported worldwide in 2018 (CHP, 2018b; WHO, 2018b).

Since 2003 and as of 15 November 2018, 860 laboratory-confirmed cases of human infection with AI A(H5N1) virus, including 454 deaths, have been reported from 16 countries outside the EU/EEA. The latest case was reported in September 2017 by Indonesia (Figure 10).



Data Source: WHO and Centre for Health Protection Hong Kong (CHP, 2018b; WHO, 2018a, online-a).

Figure 10: Distribution of confirmed human cases of A(H5N1) by year and country of reporting, 2003 – 15 November 2018 (n=860)

4.4.2. HPAI A(H5N6)

4.4.2.1. Domestic and wild birds

Detections

While an updated nomenclature of clade 2.3.4.4 viruses is pending, the four genetic groups (a, b, c, d) of clade 2.3.4.4 introduced by Lee et al. (2018a) are used in this section to give a better insight onto the characteristics of the HPAI A(H5N6) viruses detected in domestic and wild birds.

As mentioned in the EFSA report for November 2017 – February 2018 (EFSA et al., 2018c), two novel HPAI A(H5N6) reassortants are cocirculating in Asia: (1) the zoonotic reassortant belonging to clade 2.3.4.4c that was detected in domestic and wild birds in China, Japan, Myanmar, the Philippines, South Korea, Taiwan and Viet Nam, and (2) a reassortant associated with clade 2.3.4.4b that is mainly circulating in Eurasia (Kwon HI et al., 2018; Lee et al., 2018a).

New cases of the zoonotic reassortant of HPAI A(H5N6) (2.3.4.4c) were reported from China and Viet Nam between 16 August and 15 November 2018 (Figure 11). The six outbreaks in medium-sized commercial poultry farms in China were detected in five different provinces. The last cases were confirmed at the end of the relevant time period for this report. Viet Nam notified an outbreak of HPAI A(H5N6) (2.3.4.4c) on a medium-sized mixed farm with chicken, ducks and geese in September 2018. Further outbreaks were detected on commercial poultry farms in three additional provinces in October 2018.

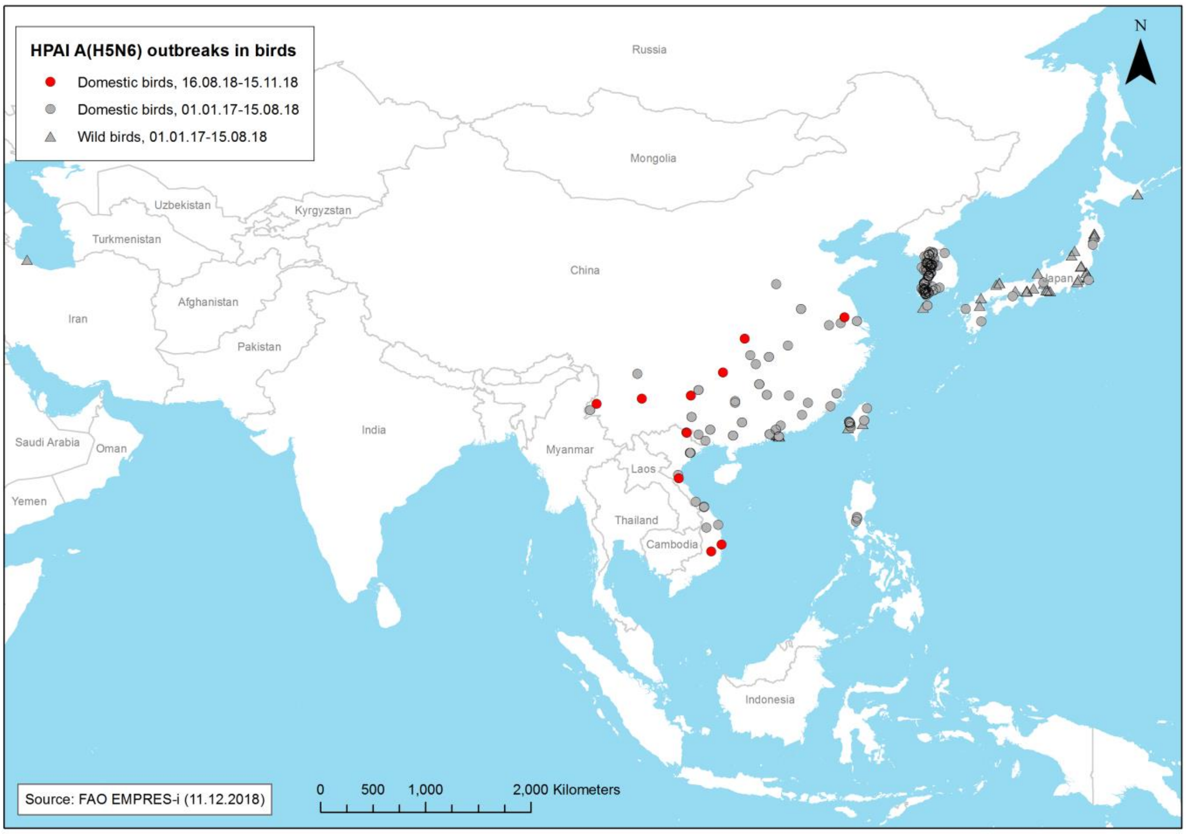


Figure 11: Distribution of confirmed HPAI A(H5N6) outbreaks in birds by place of origin, 1 January 2017 – 15 November 2018 (FAO, online-b)

Genetic characterisation

Whole-genome sequencing of 19 A(H5N6) viruses detected in wild birds and on duck farms in South Korea in 2017/2018 revealed the presence of at least two different genotypes of reassortants between A(H5N8) clade 2.3.4.4 and Eurasian LPAIV (Kwon et al., 2018; Lee et al., 2018c).

Phenotypic characterisation

No new relevant information has been published during the reporting period

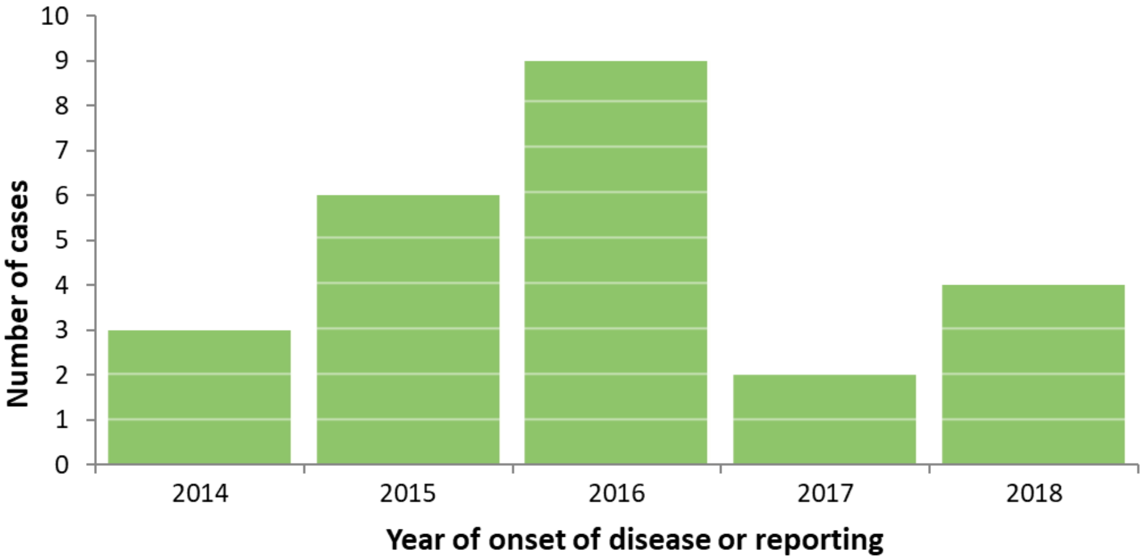
4.4.2.2. A(H5N6) in mammals (excluding humans)

During the epidemic of HPAI A(H5N6) in South Korea in 2016-17, A(H5N6) viruses were recovered from three carcasses of cats that died 4 days after onset of illness in which lethargy, salivation, convulsions and blood discharge from the mouth were observed (Lee et al., 2018b). At necropsy, congestion and oedema of the lungs, white-coloured foci in the liver, enlargement of spleen, pin-point foci and spotty haemorrhages in pancreas were seen. Severe histopathological lesions were noted in the brain (loss of neurons, perivascular cuffing, and gliosis), liver (necrosis and hepatitis), lungs (congestion, oedema, haemorrhages, interstitial pneumonia, thrombus in the alveolar capillaries). Phylogenetic analysis demonstrated close relatedness of the examined viruses to A(H5N6) clade 2.3.4.4c viruses detected in poultry nearby.

4.4.2.3. Human infections due to A(H5N6)

Three new human cases due to AI A(H5N6) have been reported since the last EFSA report and within the reporting period (WHO, 2018c). In September, a 22-year old male from Guangdong Province, China, was hospitalised with severe pneumonia in critical condition. Exposure to live poultry before onset of disease was reported for the case. In October, a 44-year-old male from Guangxi Zhuang Autonomous Region, China, was hospitalised and passed away. For this case, no exposure to live poultry was reported. In November 2018, the Hong Kong health authority posted a notification about a human case of AI A(H5N6) in China (The Government of the Hong Kong Special Administrative, 2018). The case is a 10-year-old girl from Suzhou in Jiangsu. She developed symptoms on 29 October and was hospitalised on 3 November in serious condition.

WHO lists 22 human cases of AI A(H5N6) (WHO, 2018c). However, one additional case from 2015 was described in a publication (Li et al., 2016) and has been added to ECDC's line list together with the most recent case reported by Hong Kong health authorities (The Government of the Hong Kong Special Administrative Region, 2018). Since 2014 and as of 15 November 2018, 24 laboratory-confirmed cases of human infection with AI A(H5N6) virus of clade 2.3.4.4 circulating in South-east Asia, including six deaths, have been reported globally (Figure 12). All the cases occurred in mainland China (WHO, 2018c). Twelve deaths due to A(H5N6) had been reported between 2014 and 2017 (Jiang et al., 2017).



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 (Li et al., 2016; Jiang et al., 2017; CHP, 2018a; The Government of the Hong Kong Special Administrative Region, 2018; WHO, 2018d, c).

Figure 12: Number of human cases due to A(H5N6), clade 2.3.4.4, infection by year of onset, China 2014 – 2018 (n=24)

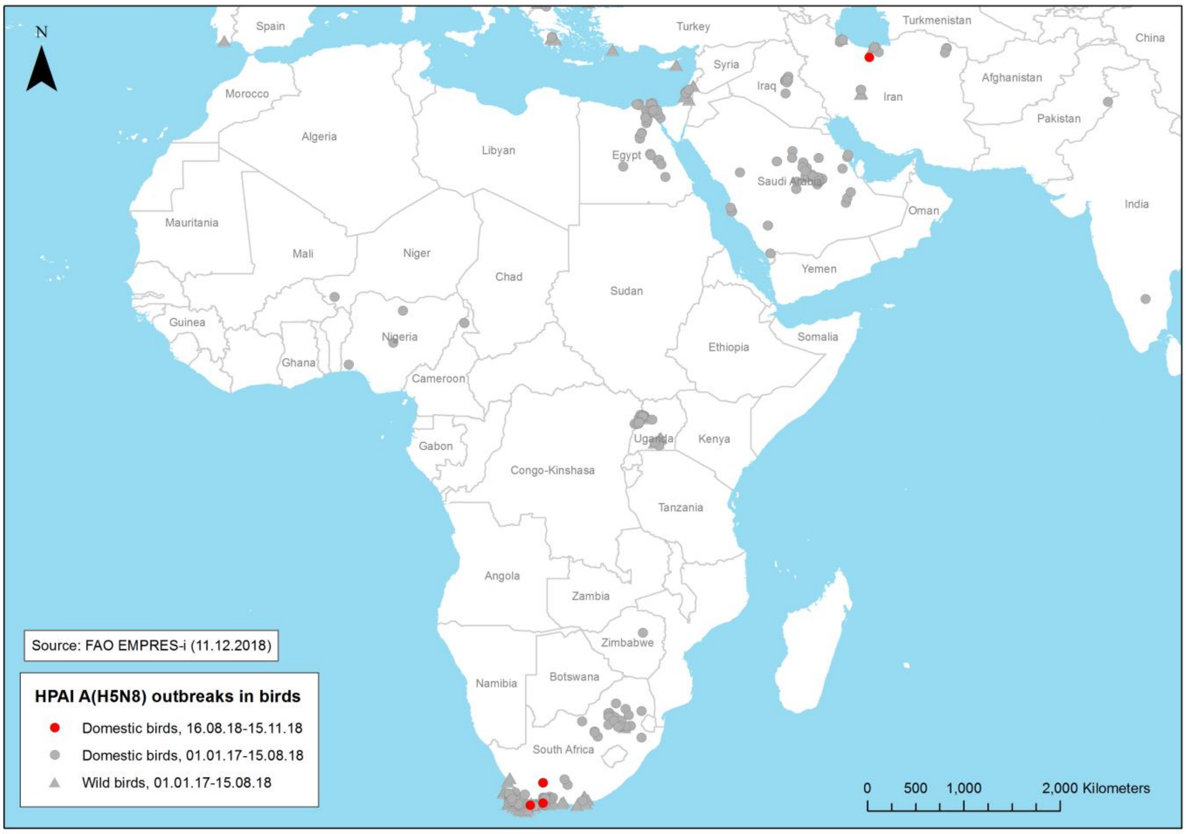
The genetic characterisation of a virus from a human case infected with HPAI A(H5N6) in Anhui Province, China, showed a high level of similarity of the HA gene to a chicken isolate belonging to clade 2.3.4.4. (He et al., 2018a). This virus was considered a triple reassortant with internal genes closely related to A(H9N2) and the NP and MP gene derived from A(H7N9) and A(H10N8) viruses.

4.4.3. HPAI A(H5N8)

4.4.3.1. Domestic and wild birds

Detections

In the relevant time period of this report, only South Africa and Iran notified outbreaks of HPAI A(H5N8), clade 2.3.4.4b. The cases were detected on three ostrich farms in the Northern and Western Cape Province, and in a small-sized non-commercial farm rearing multi species poultry in Tehran. Between 16 August and 15 November 2018, none of the other previously affected countries in Africa and the Middle East reported any outbreaks in domestic poultry or wild birds (see Figure 13).



Source: FAO EMPRES-i (11.12.2018)

Figure 13: Distribution of confirmed HPAI A(H5N8) outbreaks in birds by place of origin in Africa and the Middle East, 1 January 2017 – 15 November 2018 (FAO, online-b)

Furthermore, Russia reported further outbreaks of HPAI A(H5Nx) in two large-sized farms in the Rostovskaya and Voronezhskaya Oblast in September and October 2018 (OIE, online-a).

Genetic characterisation

The first genetic description of A(H5N8) viruses detected in wild and domestic birds in Uganda in early 2017 was provided by Ndumu et al. (2018). The spectrum of affected wild bird species included white-winged black terns, egrets and grey-headed gulls. Phylogenetic analysis revealed that the viruses belonged to clade 2.3.4.4b and clustered in the group with viruses from Democratic Republic of the Congo and West Africa.

Phenotypic characterisation

No new relevant information has been published during the reporting period.

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

No new relevant information has been published during the reporting period.

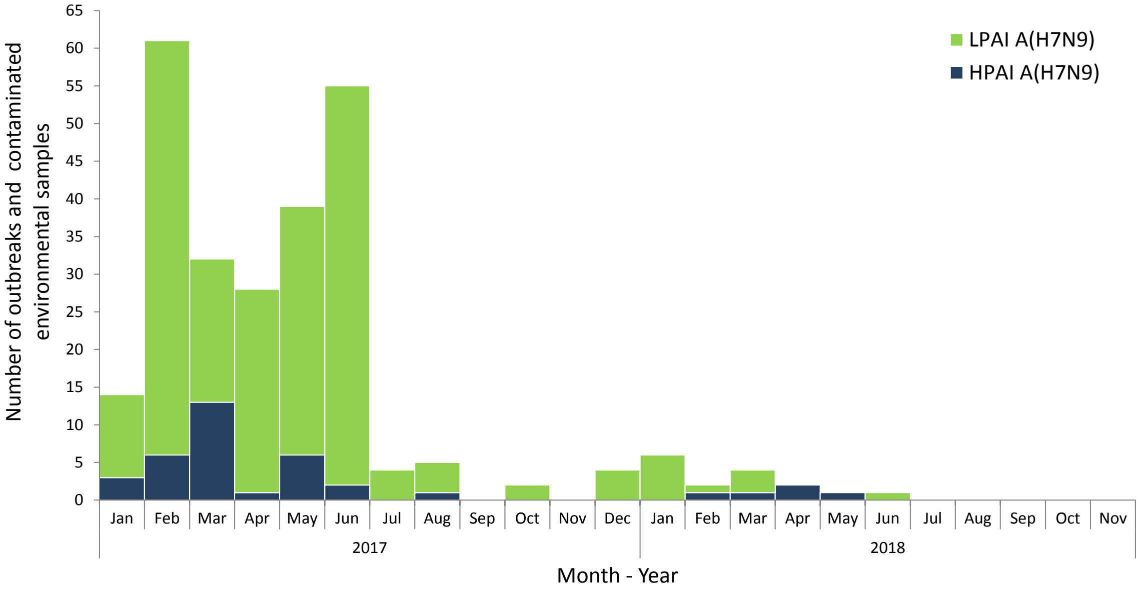
4.4.4. HPAI-LPAI A(H7N9)

4.4.4.1. Domestic and wild birds

Detection

No LPAI or HPAI A(H7N9) were detected in poultry and wild birds during the relevant time period for this report. The last case was reported from Anhui province on the 29 June 2018 (Figure 14). The results of the surveillance campaigns are published monthly by the Chinese Ministry of Agriculture and Rural Affairs (MoA, online) and are also available on the EMPRES-i website of the Food and Agriculture

Organization (FAO, online-b). But no new official information was reported by the Chinese Ministry of Agriculture and Rural Affairs since the last update at the end of June 2018 (MoA, online). The nationwide campaigns for A(H7N9) vaccination of poultry, with the exception of poultry in AI-free zones and export establishments, started extensively in September 2017 (FAO, online-a).



Data Source: FAO EMPRES-i (15.11.2018)

Figure 14: Distribution of confirmed LPAI and HPAI A(H7N9) outbreaks in birds and of contaminated environmental samples in China by month, 1 January 2017 – 15 November 2018 (n=260)

Phenotypic characterisation

Two novel reassortant highly pathogenic A(H7N9) viruses isolated from dead mule ducks in Southern China during June–August 2017 showed high virulence in chickens and ducks as expressed by intravenous pathogenicity index (IVPI) ranging from 1.86-1.91 (ducks) and 2.95-3.0 (chickens) (He et al., 2018b). In another study, two Chinese HPAIV A(H7N9) viruses originated from a chicken and a duck isolated in 2017 were intravenously inoculated into chickens and the IVPI was 2.86 and 2.68, respectively. Ducks experimentally inoculated with 10^6 EID_{50} of each virus remained asymptomatic during the 14-day observation period but the virus RNA was found in the brain, heart, liver, spleen, lung, intestine, kidney, tracheal and cloacal swabs of birds necropsied at days 3 and 5 post infection (Hou et al., 2018).

Genetic characterisation

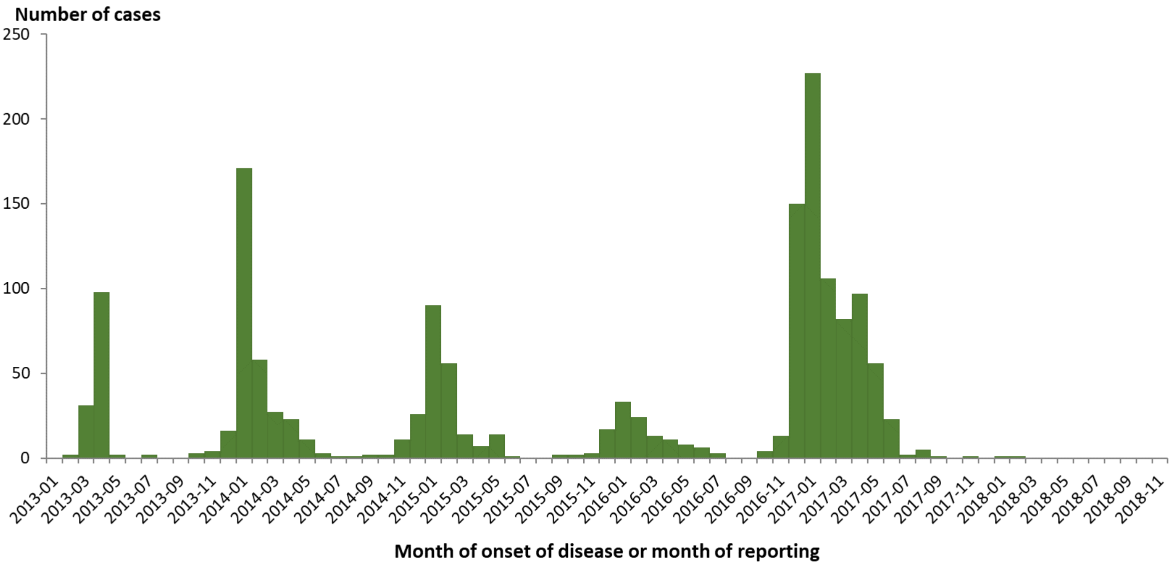
Reassortment between A(H7N9) and other AI virus subtypes was discovered in two mule duck-origin A(H7N9) isolates detected in Southern China in 2017 (He et al., 2018b). Genetic characterisation of 11 A(H7N9) HPAIV strains (eight from chickens and three from ducks) detected during routine surveillance in China in 2017 revealed the existence of four different motifs at the HA cleavage site and the HA receptor-binding sites (RBS), suggesting preferential binding to avian-like receptors.

4.4.4.2. Human infections due to A(H7N9)

No human cases due to AI A(H7N9) have ever been reported from Europe and no human cases have been reported globally since the last EFSA report published in October 2018 CHP, 2018b; WHO, 2018b). The latest case was reported from China in February 2018.

Since February 2013, a total of 1 567 human cases have been reported from outside of Europe, including at least 615 deaths (39%) (CHP, 2018a; WHO, 2018a, b, e, online-a); see Figure 15).

Thirty-two human cases have been due to infection with HPAI virus A(H7N9) according to the Chinese National Influenza Center (2018). The cases had onset of illness before October 2017. The viruses did not show increased transmissibility or virulence to humans.



Data Source: WHO and Centre for Health Protection Hong Kong (CHP, 2018b; WHO, 2018a, online-a).

Figure 15: Distribution of confirmed human cases of A(H7N9) by month of disease onset or month of reporting, February 2013 – 15 November 2018 (n= 1 567)

The introduction of control measures as well as a mass vaccination programme in poultry in China in relation to the large upsurge of human cases due to A(H7N9) and the emergence of the highly pathogenic variant in 2017 reduced the number of birds tested positive for A(H7N9) viruses since June 2018 (Figure 13). This has also reduced the human exposure to the virus and no human cases have been reported since March 2018 (Zeng et al., 2018).

4.4.5. LPAI A(H9N2)

4.4.5.1. Domestic and wild birds

Detection

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

Phenotypic characterisation

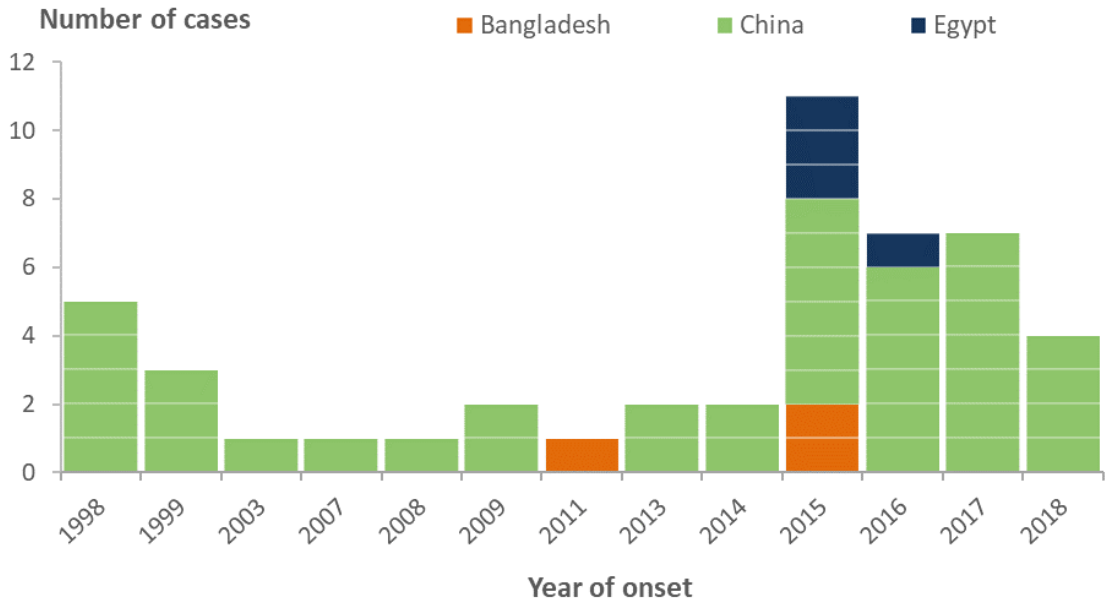
In an experiment in laying hens, it was demonstrated that a G1 lineage of A(H9N2) virus spread beyond respiratory and digestive tract, replicated in the infundibulum and caused lesions in the oviduct resulting in a long-term drop in egg production (Bonfante et al., 2018).

Genetic characterisation

The first report on the occurrence and genetic characterisation of A(H9N2) detected in Indonesia in 2016/17 demonstrated, that the detected viruses shared similarities with A(H9N2) viruses from China and Vietnam, and that they clustered in a novel lineage (tentatively designated CVI), diverging from BJ94 lineage (Jonas et al., 2018). Phylogenetic analysis of A(H9N2) viruses recovered from free-range poultry in China in 2014-15 revealed that they belonged to G57 genotype (F/98-like lineage) (Zhu et al., 2018).

4.4.5.2. Human infections due to A(H9N2)

No new human case has been reported since the last report (EFSA et al., 2018a). Since 1998 and as of 15 November 2018, 47 laboratory-confirmed cases of human infection with AI A(H9N2) virus, including one death, have been reported globally. Cases occurred in China (40), Egypt (4) and Bangladesh (3) (Figure 16).



Data Source: WHO (WHO, 2018a, b)

Figure 16: Distribution of confirmed human cases of A(H9N2) by reporting country, 1998 – 15 November 2018 (n=47)

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

The low number of AI outbreaks reported in the last report (EFSA et al., 2018a) continued in the time period of this report, from 16 August to 15 November 2018. Some outbreaks were reported in poultry in Europe (Russia), Asia and Africa, but no further cases were notified from the Middle East and previously affected areas. Furthermore, no cases of HPAI A(H5Nx) in wild birds were detected in the relevant time period for this report (Sections 4.4.1–4.4.5). Nevertheless, possible incursion into poultry establishments cannot be excluded due to the presence of HPAI virus in wild and domestic bird populations. Two outbreaks of clade 2.3.2.1c, A(H5N1) were reported from Lao People's Democratic Republic and Viet Nam, but no further outbreaks were reported in the relevant time period from Africa or the Middle East. Between 16 August and 15 November 2018 only four outbreaks of clade 2.3.4.4b, A(H5N8) were detected in South Africa and in Iran. Two outbreaks of HPAI A(H5Nx) were reported in the western parts of Russia. The continued presence of HPAI virus in Russia spatially associated with fall migration routes of wild water birds is of concern for the possible spread of the virus via wild birds migrating to the EU (EFSA AHAW Panel et al., 2017). However, uncertainty remains high and close monitoring of the situation is required. Furthermore, fall migration from breeding sites to wintering sites has started and will proceed into the next period. The low temperature and ultraviolet light in winter may facilitate the environmental survival of AI viruses potentially introduced to Europe. Aggregation before and during fall migration, as well as the mixing of wild birds from different geographic origins during migration, will increase the risk of the infection spreading. Outbreaks of novel zoonotic reassortant HPAI A(H5N6) belonging to clade 2.3.4.4c are still confined to Asia. Furthermore, during the relevant period for this report, A(H7N9) and A(H5N1) viruses have not been detected in wild waterfowl. Constant monitoring is warranted, despite the low risk associated with the incursion of these subtypes into poultry establishments at the moment.

As mentioned in the last reports, there are several possible pathways through which AI viruses can be brought into the EU, including legal and illegal trade of poultry and poultry products, contaminated fomites and wild birds. Nevertheless, the risk of AI 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 AI virus introduction is non-negligible, and as suitable risk management measures are in place, such as testing and quarantine (EFSA AHAW Panel et al., 2017). EU legislation (Regulation (EC) No. 798/2008[2]) prohibits the importation of live poultry, day-old chicks and hatching eggs and Regulation (EU) No. 139/2013[3] of other birds (captive birds such as parrots, finches and other ornamental birds for trade) from countries that cannot provide suitable health guarantees to comply with the required certification. The list of approved countries is therefore limited (for reference see Table F5 of Appendix F in EFSA AHAW Panel (2017)). Furthermore, the illegal movement of captive birds (passerines in particular) is a viable pathway for the spread of the viruses, notably A(H5Nx), but the risk is difficult to assess due to the paucity of data.

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

4.6.1.1. Surveillance in the EU

As outlined in the EFSA report for November 2017 – February 2018 (EFSA et al., 2018c), human infections with zoonotic and other novel influenza strains are notifiable under EU legislation[4] and the International Health Regulations (IHR) through the Early Warning and Response System and the IHR notification system, respectively (WHO, 2016).

4.6.1.2. Diagnosis

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

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

Options for public health control measures remain the same as outlined in the EFSA report for November 2017 – February 2018 and should follow national guidelines and recommendations (EFSA et al., 2018c). A new publication summarises the public health measures taken in 22 EU/EEA Member States and Israel during the A(H5N8) outbreaks in 2016–17 (Adlhoch et al., 2018). The use of personal protective measures for people exposed to birds that are infected with AI viruses will minimise the risk of transmission to humans.

4.6.1.4. Vaccines

WHO published a status update on available and recommended vaccines or candidate vaccine viruses (CVVs) for pandemic preparedness in September 2018 related to the vaccine composition meeting (WHO, 2018b). No new CVV for A(H7N9) virus, but new CVVs based on A/duck/Bangladesh/17D1012/2018-like A(H5N1) and A/Anhui-Lujiang/39/2018-like A(H9N2) were proposed.

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[2] Commission Regulation (EC) No. 798/2008 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. OJ L 226, 23.8.2008, pp. 1–94.

[3] Commission Implementing Regulation (EU) No. 139/2013 of 7 January 2013 laying down animal health conditions for imports of certain birds into the Union and the quarantine conditions thereof. OJ L 47/1, 20.02.2013, pp. 1-17.

[4] Decision No 1082/2013/EU 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. OJ L 293, 5.11.2013, pp. 1–15.

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

The risk of zoonotic influenza transmission to the general public in EU/EEA countries remains very low. Outbreaks due to AI viruses or detections of infected wild birds continued at a very low level during the recent months. Although no transmission of viruses detected in wild birds or poultry to humans has been observed in Europe, a Russian study identified sero-reactive antibodies to A(H5N8) clade 2.3.4.4 and A(H5N1) 2.3.2.1c viruses in people exposed to infected or dead birds during the AI outbreaks from November 2016 to March 2017 (Ilyicheva et al., 2018). However, the antibodies were present in both of the paired sera (day 1 and 21) and it remains inconclusive when these people were exposed to the virus and seroconverted. This study underlines that zoonotic transmission of viruses related to AI A(H5) clade 2.3.4.4 circulating in wild birds and poultry in Europe cannot be fully excluded, as these viruses are able to reassort and new viruses may emerge or be introduced e.g. via migratory birds. Avian influenza virus transmission to humans is a rare event overall and the risk is considered very low for viruses with an avian-adapted genetic makeup. The use of personal protective measures for people exposed to AI viruses will minimise any residual risk.

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

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Abbreviations

ADNS	Animal Disease Notification System
AI	Avian Influenza
BFSA	Bulgarian Food Safety Authority
CVV	Candidate vaccine virus
DVFA	Danish Veterinary and Food Administration
ECDC	European Centre for Disease Prevention and Control
EFSA	European Food Safety Authority
EEA	European Economic Area
EU	European Union
FAO	Food and Agriculture Organization
HPAI	Highly pathogenic avian influenza
IHR	International Health Regulations
IVPI	Intravenous pathogenicity index
LPAI	Low pathogenic avian influenza
MS	Member State
OIE	World Organisation for Animal Health
PCR	Polymerase chain reaction
SCOPAFF	Standing Committee on Plants, animals, food and feed
TOR	Terms of reference
WHO	World Health Organization
WUR	Wageningen University Research

Appendix A –Terms of Reference

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

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

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

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

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

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

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

There is knowledge, legislation[5], technical and financial tools in the EU to effectively deal with outbreaks of avian influenza in poultry and captive birds. However, the very wide virus spread by wild birds and the increased risk of direct or indirect virus introduction into poultry or captive bird holdings has led to the largest HPAI epidemic in the EU so far. This situation calls for a reflection and evaluation how preparedness, risk assessment, early detection and control measures could be improved.

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

Therefore, in the context of Article 31 of Regulation (EC) No. 178/2002[6], EFSA should provide the technical and scientific assistance to the Commission based on the following Terms of Reference:

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[5] 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.

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

1. Analyse the epidemiological data on highly pathogenic avian influenza (HPAI) and low pathogenic avian influenza (LPAI), where co-circulating or linked within the same epidemic, from HPAI disease affected Member States.

2. Analyse the temporal and spatial pattern of HPAI and LPAI as appropriate in poultry, captive birds and wild birds, as well the risk factors involved in the occurrence, spread and persistence of the HPAI virus in and at the interface of these avian populations.

3. Based on the findings from the points above, describe the effect of prevention and control measures.

4. Provide for regular quarterly reports updating on the avian influenza situation within the Union and worldwide, in particular with a view to describe the evolution of virus spread from certain regions towards the EU. In case of significant changes in the epidemiology of avian influenza, these reports could be needed more frequently. These reports should in particular closely follow the developments of zoonotic avian influenza viruses (such as HPAI A(H5N6) and LPAI A(H7N9)) in collaboration with the European Centre for Disease Prevention and Control (ECDC).

A.2. Interpretation of the Terms of Reference

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

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

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

Monitoring of the AI situation on other countries (TOR 4) was based on data submitted via OIE or reported to FAO. The description focuses on HPAI A(H5N1), HPAI A(H5N6), HPAI A(H5N8), A(H7N4), A(H5Nx), HPAI/LPAI A(H7N9) and LPAI A(H9N2). Background and epidemiology, detections, phenotypic and genetic characterisations are described based on information from confirmed human, poultry and wild bird cases that occurred between 16 August and 15 November 2018 and on information gather performing a literature search from papers published in PubMed from 16 August to 15 November 2018. Possible actions for preparedness in the EU are discussed.

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

Appendix B –Data and methodologies

B.1. Data on animals

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

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

The slide presentations, which EU MSs affected by HPAI and LPAI presented to the SCOPAFF meeting, and the evidences on HPAI and LPAI outbreaks provided in the INFO NOTEs by the affected MSs to the European Commission, were consulted to extract relevant information reported in Sections 4.2.1, 4.2.2 and 4.2.3. The PDFs of the SCOPAFF presentations are available on the European Commission website (European Commission, online-a). Information from the website of Wageningen Bioveterinary Research (Wageningen University and Research, online) was used to complement data on HPAI in wild birds occurred in the Netherlands.

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

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

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

Search The PubMed database was searched by using subject index terms and free-text terms combined with the appropriate Boolean operators. Scientific articles added to the database from 16 August to 15 November were searched; the search was run on 16 November 2018. Information regarding the search strategy (terms and search string) is provided in Appendix C.1.

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

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

Results The search retrieved 131 papers. The articles were subsequently screened against the relevance and eligibility criteria. One paper was in the end taken into consideration in the description of the phenotypic characterisation of HPAI viruses circulating in the EU in domestic and wild birds in the reporting period.

The search protocol and the results can be consulted at https://doi.org/10.5281/zenodo.2276657.

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

Bulgaria, Denmark and the Netherlands expressed an interest in supporting the analysis of the HPAI outbreaks from 16 August to 15 November 2018, and submitted case reports on the prevention and control measures that have been applied as consequences of the outbreaks. The case reports provided to EFSA can be consulted in Annex A.

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

Data from FAO EMPRES-i (FAO, online-b) on HPAI A(H5N1), A(H5N6), A(H5N8), A(H5Nx), HPAI and LPAI A(H7N9) in domestic, captive and wild birds, and environmental samples, were used to map the geographical distribution of AI cases in domestic and wild birds in Africa, Asia, the Middle East and Europe on the basis of the observation dates. With the purpose of avoiding over-complication of the maps, captive birds and environmental samples have been mapped as domestic birds. Despite the fact that some of these kept animals may be of wild species, in most of the cases captive birds, or, for environmental samples, the birds from which samples have been taken (mainly at live market places) will not move around and not spread the infection by migrating and for this reason have been considered as domestic birds in the maps provided in this report. Only when there was a strong discrepancy among the locality, the administrative regions and geo-coordinates, and the outbreaks were not officially reported to the OIE (e.g. national authorities), the confirmed outbreaks were not taken into account in the analysis.

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

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

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

Search The PubMed database was searched by using subject index terms and free-text terms combined with the appropriate Boolean operators. Scientific articles added to the database from 16 August to 15 November were searched; the search was run on 16 November 2018. Information regarding the search strategy (terms and search string) is provided in Appendix C.2.

Relevance criteria Scientific articles added to the database from 16 August to 15 November 2018 and reporting information on the presence or absence of clinical signs, pathological changes or mortality or genotypic characterisation due to HPAI infection with viruses circulating in Asia, Africa or the Middle East in domestic or wild birds or mammals other than humans.

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

Results The search retrieved 123 papers. After de-duplication against previous searches, 122 papers remained. The articles were subsequently screened against the relevance and eligibility criteria. Twelve papers were in the end taken into consideration in the description of phenotypic and genotypic characterisation of HPAI viruses circulating on other continents and regions (Africa, Asia, the Middle East) in domestic or wild birds or mammals (excluding humans) in the reporting period.

The search protocol and the results can be consulted at https://doi.org/10.5281/zenodo.2276657.

B.2. Data on humans

Numbers of human cases due to infection with AI viruses have been collected by ECDC. Multiple sources are scanned regularly as part of epidemic intelligence activities at ECDC to collect information about laboratory-confirmed human cases. Data were extracted and line lists developed to collect case-based information on virus type, date of disease onset, country of reporting, country of exposure, sex, age, exposure, clinical information (hospitalisation, severity) and outcome. All cases included in the line list and mentioned in the document are laboratory-confirmed. Data are continuously checked for double entries and validity. The data on human cases cover the full period of time since the first human case was reported. Therefore, data on human cases refer to different time periods and are included irrespective of whether there have been any new human cases during the reporting period.

Literature searches were performed until 15 November 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'; 'humans'; 'mammals'. The literature search was not systematic or comprehensive.

Annex A – Applied prevention and control measures on avian influenza

Scope

This document provides a brief overview of the specific prevention and control measures applied in Bulgaria, Denmark and the United Kingdom between 16 May and 15 August 2018 in relation to AI outbreaks in poultry and wild birds. Information is only provided if it is considered 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 from restriction zone implementation after risk assessment and hunting ban. 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

Tables A.1, A.2 and A.3 provide timelines for the main events that triggered actions in relation to the selected prevention and control measures in Bulgaria, Denmark and the United Kingdom, respectively. More information on the actions taken is provided in the sections below the tables.

A.1 Bulgaria

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Animal Health and Welfare, and Feed Control Directorate

Bulgarian Food Safety Agency

Table A1: Overview of main actions

Date	Event that triggered action	Type of action taken	Target audience
16/08/2018	Epidemiological situation in the country	Enhanced active surveillance in poultry farms (Galliformes (breeders and laying hens) and waterfowl (duck farms)), as follows: • Frequency of sampling- every 21 days for period of 3 months and then 50-60 days of age. • Sampling protocol - in accordance with Directive 2005/94. • Objectives: 1) surveillance and screening of the reared population and poultry farms; 2) enhanced control and engagement by the operators.	Official vets, poultry associations, Farmers

19/09/2018 03/10/2018 17/10/2018(a) 23/10/2018 26/10/2018(a) 29/10/2018(a) 31/10/2018 07/11/2018(a) 09/11/2018 15/11/2018	Confirmation of primary outbreak of HPAI in poultry	The same measures applied for the outbreaks occurred in the previous reporting period are in force: • Housing of poultry across whole territory of the country. • Ban on live poultry markets and exhibitions of birds across whole territory of the country. • Enhancing the active surveillance in poultry – clinical examination on poultry farms (special focus on backyards). • Poultry farm positive for antibodies against HPAI (even if negative for HPAI virus) sent for immediate slaughtering • Conducting epidemiological investigation, establishing restrictive zones, enforcing all restrictive measures according to Council Directive 2005/94/EC on Community measures for the control of AI and the National contingency plan for AI. • Enhancing the passive surveillance in wild birds. • Strengthening biosecurity on poultry farms and regularly inspection to control it. • Ban on restocking of wild-feathered game across the entire territory of the country, including gathering and restocking of game in 3 and 10 km restriction zones. • Six months repopulation ban in the farms where HPAI outbreaks were confirmed more than twice within 12 month.	
22/10/2018 – 15/11/2018	Epidemiological situation in the country	Enhanced active surveillance in duck farms – virological sampling in ducks kept in force feeding holdings (5 out of 14 HPAI outbreaks were detected in the framework of this active surveillance)	Official vets, poultry Farmers
30/10/2018	Epidemiological situation in the country	Additional to the serological testing every 50-60 days in poultry holding, in high risk areas the surveillance has been strengthen by: • a premovement sampling (by PCR) of domestic poultry (all species) for transport to other holdings, and of ducks for force feeding for transport to slaughterhouse; • enhanced veterinary control of duck farms, particularly those keeping ducks only for force-feeding (holdings with intensified poultry movement where the poultry are kept for 12-13 days only). High risk areas were identified based on the epidemiological situation (high number of outbreaks), high density of poultry population and other risk factors.	Official vets, poultry Farmers

* Two HPAI A(H5N8) outbreaks were confirmed on that date

Increasing awareness of the stakeholders and the general public

- Regular meetings with representatives of the poultry associations;
- Close cooperation with public health authority;
- Publishing information related to the epidemiological situation and prevention and control measures taken

http://www.babh.government.bg/bg/Page/influentza/index/influentza/%D0%98%D0%BD%D1%84%D0%BB%D1%83%D0%B5%D0%BD%D1%86%D0%B0%20%EF%BF%BD

Housing order

Continuing the enforcement of the measures as described in the scientific report IV.

Precautionary measures such as keeping poultry indoors, taking steps to separate them from wild birds and ensuring that feed and water is not accessible to wild birds were also required. There was a special focus on backyards, due to lack of biosecurity measures.

Enhanced surveillance ativities

Due to the unfavourable epidemiological situation in the country since December 2016 and based on the risk factors and assessment, it has been considered to enhance the control and active surveillance beyond to the minimum reguirements for the routine surveillance programme, set up in Commission Decision 2010/367/EU. A number of restriction measures have been enforsed.

The measures are applied in all poultry holdings, aiming at early detection of infection and prompt eradication of AI in the country.

Strenthening biosecurity measures in farms and indoor keeping of poultry (including waterfowl) are part of the control measures verified by means of increased official veterinary inspections.

Laboratory serology surveillance in each domestic poultry farms (excluding the force feeding farms, where duck are kept for 12-13 days) has been enforced since June 2018, starting with sampling in interval 21 days fo three months and continued with sampling every 2 months (mulard and laying hens at 50-60 days old). The outcomes show 17% duck farms serology positive for A(H5N8) (135 out of 201 duck farms tested, 25 farms Ab positive for H5N8 and negative for HPAI Vi). Serology positive poultry, even if negative at virological testing, are sent for immediate slaughtering aiming at avoiding the presence of poultry population of HPAI Ab positive.

Six of these farms were confirmed as HPAI A(H5N8) outbreaks in 2017. Possible survival of HPAI virus in these farms should be excluded as since 2017 a repopulation in previous infected farms has been carried out using sentinels for 21 days and tested twice with negative results additional to the provisions of Article 49 of Directive 2005/94/EC.

In Novemebr 2018, the laboratory surveillance was further improved by introducing pre-movement sampling (virological sampling) between holdings (for all poultry species) and from holdings to slaughterhouses (for duck kept in force feeding holdings, located in the high risk area) as result of the increased outbreaks in the country. It ensures that only non infected poultry are reared in the holdings and moved between holdings/and to slaughterhouse.

No derogation for trade and poultry movement within the protection and surveillance zones is allowed, only those in line with the Directive 2005/94/EC.

Restriction from repopulation was six months enforced for holdings where HPAI virus or antibodies were confirmed more then twice within 12 months in order to restrict and rule out any possible reintroduction of infection because of break of biosecurity measures applied in the holdings.

Strengthening biosecurity measures (other than housing orders)

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 the poultry indoor if necessary, etc.)

Preventive culling

Not applied.

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

Not applied.

Derogations on restriction zone implementation after risk assessment

Derogation in line with the Directive 2005/94.

Hunting

Hunting was not forbidden.

A.2 Denmark

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Table A.2: Overview of main actions

Date	Event that triggered action	Type of action taken	Target audience (if applicable)
31/08/2018	Confirmation of HPAI A(H5N6) in wild birds (mallards, *Anas platyrhynchos* and common pheasants, *Phasianus colchicus*)	03/09/2018 - Meeting of the AI expert group. - Press release about the finding with information about biosecurity. - In addition poultry owners in the infected area were recommended to protect poultry against contact with wild birds with roofs, horizontal fabrics or nets. 07/09/2018 - Information to the municipalities in the infected area about safe disposal of dead wild birds not selected for testing.	Poultry industry and general public - especially owners of hobby poultry/backyard flocks.
10/09/2018	Confirmation of HPAI A(H5N6) in wild birds (mute swan, *Cygnus olor* and common eider, *Somateria mollissima)*	-	-
11/09/2018	Confirmation of HPAI A(H5N6) in a wild bird (greylag goose, *Anser anser*)	-	-
25/09/2018	Confirmation of HPAI A(H5N6) in wild birds (Common pheasants, *Phasianus colchicus*)	26/09/2018 Information to the Danish Hunters Association about precautions to be taking when handling dead wild birds in the nature.	Danish Hunters Association, hunters

Action taken

On 27 August, two mallards (*Anas platyrhynchos*) and two common pheasant (*Phasianus colchicus*) were found dead on Egholm on the island of Agersø in the municipality of Slagelse in the Southern part of Zealand. On 31 August, the National Veterinary Institute confirmed HPAI A(H5N6) in the samples from both the mallards and the common pheasants. The pheasants originated from a holding with game birds and were released in the nature for hunting purposes on 1 July. When released into the nature pheasants are no longer categorized as poultry.

The positive mallards and pheasants were found in the same part of the country as the other positive wild birds this summer leading to the conclusion, that a cluster of HPAI A(H5N6) virus had been established in the area around 'Smålandsfarvandet', i.e. the water between the southern Zealand and Lolland-Falster. The virus strain proved to be identical with the virus strain detected during the winter migration of birds in the beginning of 2018.

A meeting in the AI expert group was held on 3 September and subsequently a press release was issued with focus on protection of poultry against wild birds in the infected area. The Danish

Veterinary and Food Administration (DVFA) recommended to protect poultry against contact with wild birds with roofs, horizontal fabrics or nets.

Three other findings of positive wild birds were made during the period, all cases were found in the 'cluster area' described above. The latest detection of HPAI was made in three common pheasants on 25 September. They were all found on the same location on 19 September. The DVFA contacted the Danish Hunters Association and informed about the importance of biosecurity in connection with hunting and how to report finding of dead wild birds using the app 'Fugleinfluenza Tip'.

A.3 The Netherlands

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Table A.3: Overview of main actions

Date	Event that triggered action	Type of action taken	Target audience (if applicable)
31/08/2018	Confirmation of HPAI A(H5N6) in a wild bird (mallard, *Anas Platyrhynchos*)	1. Using a mandatory hygiene protocol for visiting commercial poultry holdings 2. Mandatory visitor registration 3. Informing for increasing awareness of the stakeholders and the general public.	poultry associations, general public, etc.

Action taken

On 31 August 31, a common mallard (*Anas platyrhynchos*) was found dead in a wetland area. On 31 August the National Reference Laboratory WVR Lelystad, the Netherlands, confirmed HPAI virus A(H5N6) in the sample from the common mallard.