



# OFFLU AVIAN INFLUENZA POST VCM REPORT

Avian Influenza Events for the period  
September 2017 to February 2018

## Scope

In this document we present a summary of H5, H7, and H9 avian influenza events that occurred between September 2017 and February 2018.

# Contents

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<b>Introduction</b> .....	3
Data Sources.....	3
Phylogenetic Analysis.....	3
Antigenic Analysis.....	3
<b>Global H5, H7, and H9 Events in Animals</b> .....	4
Vaccination .....	4
Table 1. H5, H7 and H9 activity reported to international agencies .....	5
<b>H5 Highly Pathogenic Avian Influenza</b> .....	6
Map 1. H5 HPAI reports (and presumed clades) in birds .....	6
Clade 2.2.1.2 .....	7
Clade 2.3.2.1 .....	7
Clade 2.3.4.4 .....	7
Figure 1. Genome constellation of recent H5N6 2.3.4.4 reassortant viruses. ....	8
<b>H7 Avian Influenza</b> .....	9
Asian H7N9.....	9
Other H7 .....	9
Map 2. Map of H7 reports in birds .....	9
<b>H9 Avian Influenza viruses</b> .....	10
H9N2 .....	10
<b>Major zoonotic concerns</b> .....	10
Annex 1. Sequence data submitted to OFFLU.....	12

## Introduction

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The WHO Consultation on the Composition of Influenza Virus Vaccines for the Northern Hemisphere 2017-2018 took place in Geneva, Switzerland on the 19-21 February 2018. The meeting gathered participants from the WHO Collaborating Centres for influenza (CCs), WHO Essential Regulatory Laboratories (ERLs), National Influenza Centres and WHO H5 Reference Laboratories, WHO Collaborating Centre for Modelling, Evolution, and Control of Emerging Infectious Diseases and from OFFLU. The OFFLU contribution on zoonotic influenza viruses was presented by Lidewij Wiersma from the Food and Agricultural Organisation and Mia Kim Torchetti from the United States Department of Agriculture National Veterinary Services Laboratory. The OFFLU team would like to thank Mary Lea Killian, Joanne Taylor, Tod Stuber, Yunho Jang, Nicola Lewis, Francesco Bonfante and Frank Wong for their valuable assistance in data collation towards this VCM contribution. The final zoonotic report is available [here](#).

### Data Sources

The epidemiological, molecular and antigenic data on zoonotic influenza viruses for the period 21st September 2017 to 12th February 2018 that were submitted by the OFFLU network laboratories were presented at the meeting. OFFLU thank all of the reference laboratories and influenza experts that had contributed virus data and analysis used in the consultation, including: Animal and Plant Health Agency (APHA), United Kingdom; Australian Animal Health Laboratory (AAHL), Australia; Avian Influenza Research & Diagnostic Division, Animal and Plant Quarantine Agency (APQA), Korea; China Animal Health and Epidemiology Centre (CAHEC), China; Federal Centre for Animal Health (FBGI ARRIAH), Russian Federation; Friedrich-Loeffler Institut (FLI), Germany; Hokkaido University, Japan; Istituto Zooprofilattico Sperimentale delle Venezie (IZSve), Italy; National Centre for Foreign Animal Disease (NCFAD), Canada; National Institute of High Security Animal Diseases (ICAR-NIHSAD), India; Poultry Disease Diagnosis Laboratory, Animal Health Research Institute, Taiwan; State Research Center of Virology and Biotechnology Vector, Russian Federation; and Wageningen Bioveterinary Research, Netherlands.

### Phylogenetic Analysis

Sequence data for 168 **H5**, **H7**, and **H9** were contributed to OFFLU by animal health laboratories representing 25 countries in Europe, Asia, Africa, and the Americas (**Table 1**, **Annex 1**). Of these, 114 from 19 countries were collected during the current period. Sequences from Genbank and GISAID generated by OFFLU reference laboratories were also obtained. In particular, it was possible to inform the meeting of detections of H9N2 in multiple countries that were not publically reported. Given that detections of H9 viruses are not officially reportable to the OIE these represent a significant gap in the knowledge of zoonotic H9 avian influenza, which we hope to continue to improve with the contribution from OFFLU laboratories.

### Antigenic Analysis

Three laboratories (AAHL, APHA and IZSve) submitted antigenic data for the meeting. OFFLU were able to report the antigenic relationships of recent, novel reassortant clade 2.3.4.4 H5N6 viruses from Asia and Europe against candidate vaccine strains, as well as an assessment of other recent clade 2.3.4.4 viruses (H5N8 and H5N2) and clade 2.3.2.1c H5N1 viruses.

## Global H5, H7, and H9 Events in Animals

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H5, H7 and H9 events for the current reporting period, **21<sup>st</sup> September 2017- 12th February 2018**, can be visualized dynamically using this link: <https://microreact.org/project/HJMHDk0Bf> (please note it may not be accessible with Internet Explorer).

For the current period, reports were available from 25 countries/territories representing a total of 319 H5, H7 or H9 avian influenza (AI) events (**Maps 1 and 2**). Of these, 220 reports were H5 or H7 detections in poultry. The majority of reports were due to goose/Guangdong lineage (Gs/GD) H5 clade 2.3.4.4 highly pathogenic avian influenza (HPAI). This period was marked by expansion of the 2.3.4.4 H5N8 virus to the Middle East as well as the emergence of new reassortant 2.3.4.4 H5N6 viruses in Asia, Europe and the Middle East.

H5 low pathogenic avian influenza (LPAI) events were also reported in poultry during this period from the Dominican Republic (H5N2, n=4), France (H5N3, n=9; H5N2, n=1), Republic of Korea (H5N2, n=15; H5N3 n=10), Taiwan (H5N6, n=2), and Japan (H5N3, n=1).

Reports of the highly poultry-adapted Asian H7N9 lineage were dramatically decreased during this period, with 12 reports of LPAI and only one report of HPAI during live bird market surveillance. This is compared to the 257 events in poultry reported during the 5<sup>th</sup> wave.

While it is not officially reportable, H9 viruses can significantly impact poultry. A highly poultry-adapted Asian lineage H9N2 continues to cause production losses in many countries in Asia and the Middle East. Other H9 lineages are sporadically detected. All reports of H9N2 for this period were submitted directly from partner laboratories rather than through official channels.

### Vaccination

In some countries, including Viet Nam, Indonesia, Bangladesh, and Egypt, H5 and other vaccination is employed as part of overall control efforts to endemic viruses.

Currently in China vaccination of poultry is mandatory in all provinces (including chickens, ducks, geese, quails, pigeons and other rare birds in captivity). From September 2017, a government sponsored campaign using a bivalent H5/H7 vaccine (H5 2.3.4.4 Re-8 based on A/chicken/Guizhou/4/13(H5N1); H7N9 Re-1) has been implemented. Although the backbone HA sequence for the H7 component of the bivalent vaccine is based on A/pigeon/Shanghai/S1069/2013(H7N9), the HA sequence was modified to reflect changes in more contemporary viruses in order to improve the antigenicity and titre of the vaccine strain. Institutions in China also produce various other H5 and H9 vaccines.

Despite the risk of potential incursion of Asian lineage H7N9, H7 vaccination is currently banned in Viet Nam, Lao PDR, Myanmar or Cambodia. Active surveillance for reportable H5 and H7 viruses occurs in poultry along the border in these countries.

**Table 1. H5, H7 and H9 activity reported to international agencies 21 September- 12 February 2017\***

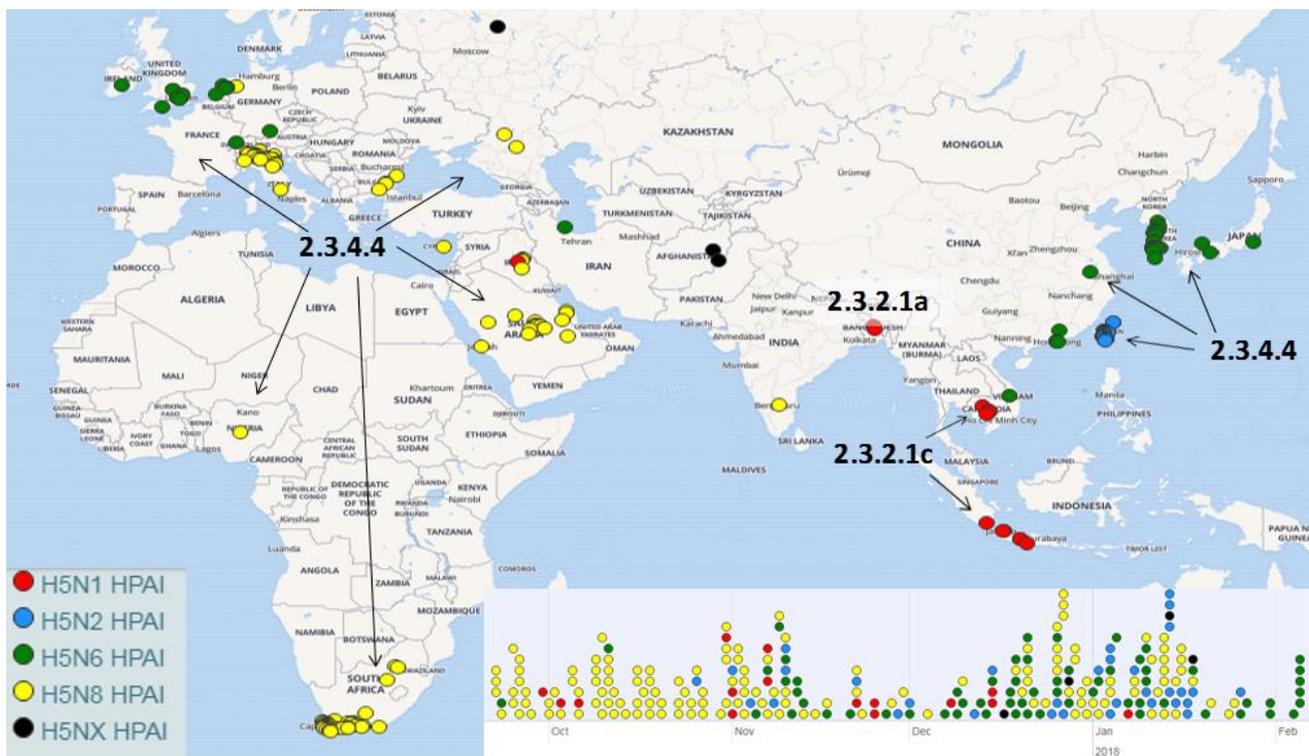
Country, area or territory	Host	Genetic clade
Afghanistan	Wild bird	Unknown (presumed H5N6)
Bangladesh	Wild birds	2.3.2.1a (H5N1)
	Poultry	2.3.2.1a (H5N1), 2.3.4.4 (H5N6)
Bulgaria	Poultry	2.3.4.4 (H5N8)
Cambodia	Poultry	2.3.2.1c (H5N1)
Canada	Environment	H5N2 LPAI
China	Poultry	2.3.4.4 (H5N6), H7N9 LPAI/HPAI, Y280 (H9N2)
	Human (5)#	2.3.4.4 (H5N6) (2), H7N9 LPAI (2), H9N2
Cyprus	Wild birds	2.3.4.4 (H5N8)
Dominican Republic	Poultry	H5N2 LPAI
France	Poultry	H5N2 LPAI, H5N3 LPAI
Germany	Wild birds	2.3.4.4 (H5N6), 2.3.4.4 (H5N8)
	Poultry	H5N2 LPAI, Y439 (H9N2)
Hong Kong SAR	Wild birds	2.3.4.4 (H5N6)
India	Poultry	2.3.4.4 (H5N8), G1 (H9N2)
Indonesia	Poultry	2.3.2.1c (H5N1)
Iran	Wild birds	2.3.4.4 (H5N6)
Iraq	Poultry	2.3.4.4 (H5N8), 2.3.2.1c (H5N1)
Ireland	Wild birds	2.3.4.4 (H5N6)
Italy	Wild birds	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Japan	Environment	H5N3 LPAI
	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
Netherlands	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6), H5N2 LPAI
Nigeria	Poultry	2.3.4.4 (H5N8)
Republic of Korea	Environment	H5N1, H5N2, H5N3, H7N7 LPAI; 2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
Russian Federation	Poultry	2.3.4.4 (H5N8), 2.3.4.4 (H5N2)
Saudi Arabia	Poultry	2.3.4.4 (H5N8)
South Africa	Wild birds	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
	Ostrich (domestic)	2.3.4.4 (H5N8)
Switzerland	Wild birds	2.3.4.4 (H5N6)
Taiwan	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N2), H5N6 LPAI
United Kingdom	Wild bird	2.3.4.4 (H5N6)
Vietnam	Poultry	2.3.4.4 H5N6

\*Red font indicates genetic data has been received from the OFFLU network.

## H5 Highly Pathogenic Avian Influenza

The majority of events were due to goose/Guangdong lineage H5 clade highly pathogenic avian influenza (HPAI) (n=246, 77%: H5N8 n=139, H5N6 n=61, H5N2 n=32, H5N1 n=14) which circulate in poultry and wild birds (**Map 1**). Widespread circulation of Goose/Guangdong 1996–lineage viruses continues in Asia, the Middle East and West Africa, with introduction of new strains of virus via wild birds (long distance) and/or trade (usually local and transboundary) to both unaffected and “endemic” countries.

Endemic strains vary by location, with some strains having remained endemic since the first incursion (for example, viruses derived from the early Clade 2.2 anecdotally continue to circulate in Egypt).



**Map 1.** H5 HPAI reports (and presumed clades) in birds between 21 September 2017 and 12 February 2018\*

- H5N2 2.3.4.4A continues to only be reported in Taiwan (n=32).
- H5N8 2.3.4.4B was reported in Italy (n=49), South Africa (n=53), **Saudi Arabia (n=23)**, Bulgaria (n=4), Cyprus (n=1), Russia (n=2), Germany (n=1), **Iraq (n=4)**, **Israel (n=1)**, **Iran (n=1)**, India (n=1) and Nigeria (n=1).
- H5N6 2.3.4.4B was reported in **South Korea (n=23)**, **Taiwan (n=1)**, **Netherlands (n=8)**, **Japan (n=9)**, **United Kingdom (n=9)**, **Switzerland (n=1)**, **Germany (n=1)**, **Ireland (n=1)**, **Iran (n=1)** and (presumed) **Afghanistan (n=1)**.
- H5N6 (2.3.4.4C) was reported in China (n=2), Vietnam (n=1) and Hong Kong (n=3).
- H5N1 2.3.2.1a continues to be reported in Bangladesh (n=3).
- H5N1 (2.3.2.1c) continues to be reported in Cambodia (n=4), Indonesia (n=6) and Iraq (n=1).

\*Red font indicates new emergence since last period

### *Clade 2.2.1.2*

Though no official reports have been submitted, sources have indicated that H5N1 viruses of this clade continue to circulate in Egypt and have caused frequent outbreaks in poultry during the current period. These viruses are also known to be in co-circulation with 2.3.4.4 (B) H5N8 as well as endemic H9N2 viruses, indicating that there is potential for reassortment between these various strains. No data was submitted for this period.

### *Clade 2.3.2.1*

H5N1 viruses of Clade 2.3.2.1a remain endemic to Bangladesh. Clade 2.3.2.1c H5N1 viruses presumably remain endemic in Viet Nam, Cambodia, Nigeria, Iraq and Indonesia. There have been no recent reports from China, where it was previously one of two dominant strains, but may still be circulating in the north of the country.

There have been no reports of Gs/GD/96-lineage viruses in North America in the past 12 months.

### *Clade 2.3.4.4*

H5 HPAI viruses within clade 2.3.4.4 have predominated across mainland Eurasia since 2015 and continue to reassort with native wild bird viruses encountered in wild migratory birds. Four phylogenetically distinct sub-lineages currently exist within this clade, informally referred to as A through D, though the nomenclature has not been finalised by the WHO/OIE/FAO H5 Evolution Working Group.

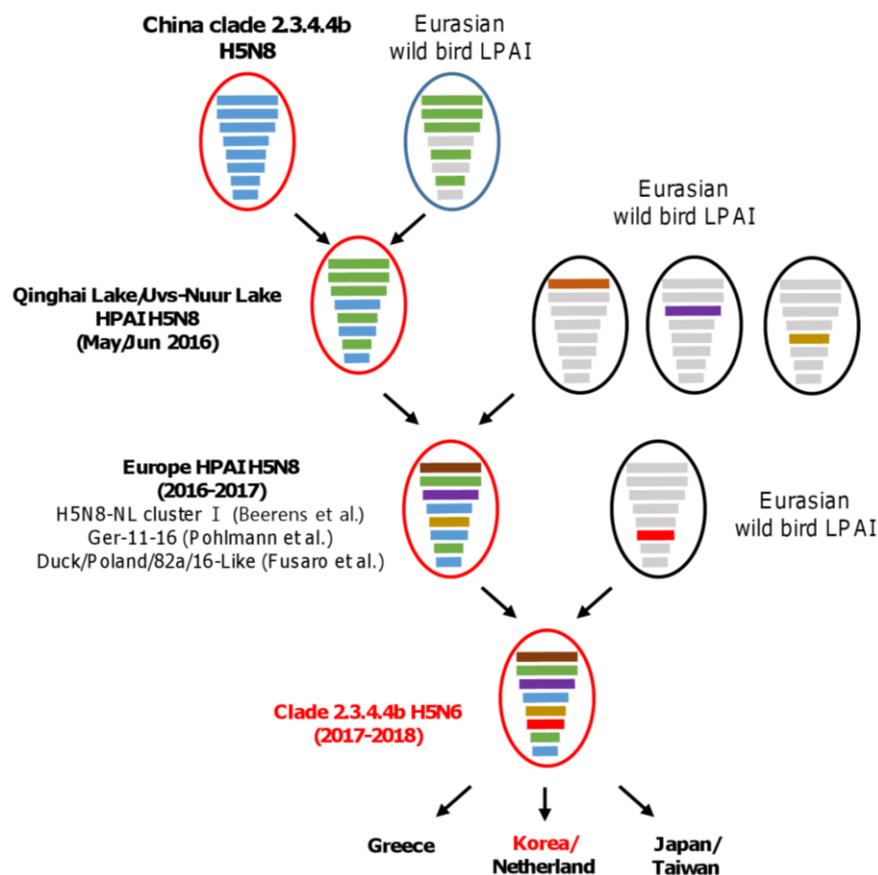
In 2014-2015, the Buan-like (2.3.4.4 lineage A) H5N8 viruses were spread by wild birds from China to Korea, Japan, Taiwan, Canada, the United States, and European countries, with subsequent reassortments of this lineage reported in the U.S. and in Taiwan. Since December 2016, Buan-like (A) H5N2 viruses have only been detected in poultry in Taiwan.

Gochang-like viruses (2.3.4.4 lineage B) have had the greatest global reach outside of Asia since 2016. This lineage B HA gene segment has reassorted with genes of native LPAI strains in Asia and Europe to produce different subtypes, including H5N8, H5N6, H5N3, H5N2 and H5N1. In 2016-2017, 2.3.4.4 (B) H5N8 viruses containing 5 Eurasian LPAI segments (PB2, PB1, PA, NP, and M) spread from China across to Europe, Africa and Asia in an intercontinental transmission event carried by wild birds.

Again, in the current period, the viruses introduced by long distance wild bird mediated transmission fall within clade 2.3.4.4 (B) but have continued to evolve through point mutations and reassortment. H5N8 viruses of this clade have continued to cause outbreaks in poultry and wild birds with reports from 12 countries, including Italy, South Africa, Saudi Arabia, Bulgaria, Russia, Cyprus, Germany, Iraq, Iran, Nigeria and India. Since the last reporting period, this virus has newly emerged in Saudi Arabia, Israel, Iran and Iraq. Though not officially reported, outbreaks have also occurred in poultry in Egypt during the current period, with opportunities for reassortment with earlier, endemic strains (for example clade 2.2.1.2 H5N1).

Since mid-November 2017, reassortant 2.3.4.4 (B) H5N6 viruses with an assortment of genes from the widespread H5N8 virus and Eurasian LPAI viruses (**Figure 1**) have been detected in South Korea, Taiwan, Japan, Netherlands, United Kingdom, Switzerland, Germany, Ireland and Iran. Although similar to an H5N6 reassortant reported February 2017 from Greece (the zoonotic report from last period indicated 2016 but has since been clarified), this sub-lineage apparently continues to evolve and mutate with ongoing opportunities to reassort with native strains. In this period, human morbidity associated with a reassortant 2.3.4.4 lineage B H5N6 virus was reported; while the HA gene was similar to other lineage B H5N6 viruses, the gene constellation was different.

Two older H5 clade 2.3.4.4 sub-lineages, CVV Hubei/Hyogo/VN15A59-like (C) and CVV Sichuan-like (D), have not yet been reported outside of Asia. Clade 2.3.4.4(C) H5N6 viruses, which have a demonstrated history of zoonotic infection, are still circulating in poultry in China and Vietnam and were detected in South Korea and Philippines up until August 2017.



**Figure 1.** Genome constellation of recent H5N6 2.3.4.4 reassortant viruses. Courtesy of LH Chen, DH Lee, DE Swayne et al.

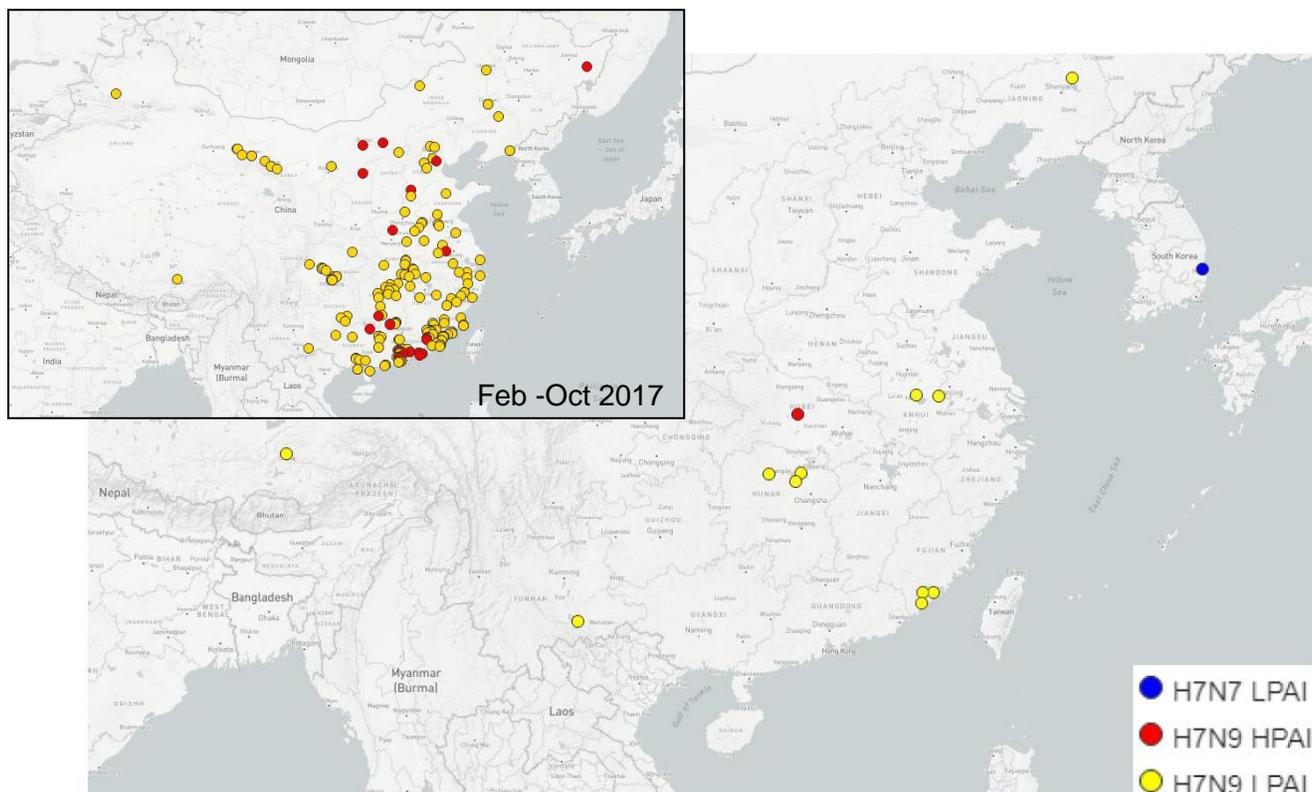
# H7 Avian Influenza

## Asian H7N9

H7N9 subtype viruses that have caused five waves of epidemics in people and birds continue to circulate in China, though a marked reduction in the number of H7N9 reports has been documented during the current period (**Map 2**). There was only one report of H7N9 HPAI in November 2017 from a live bird market in Hubei. H7N9 HPAI was also detected in a quarantine sample in Japan when a duck carcass originating from China was tested in November 2017, marking the second reported occasion since a similar event in June 2017. Twelve events of H7N9 LPAI were reported in China from sampling chickens and ducks in live poultry markets in mid-October and mid-December 2017.

## Other H7

H7N7 LPAI was reported in a wild bird faeces sample collected in South Korea in November 2017.



**Map 2.** Map of H7 reports in birds between 21 September 2017 and 12 February 2018 with insert map of reports from the fifth wave in the top left corner. The H7N9 LPAI reports continue to be widely distributed, affecting 12 regions: Pohang city, Zhangzhou, Yuanjiang city, Changde city, Xiamen city, Hefei city, Datun Town, He County, Yiyang City, Zhanpu County, Shenjiagou and Lhasa.

## H9 Avian Influenza viruses

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### *H9N2*

Though H9N2 viruses have purportedly been associated with significant production losses in poultry, there were no official reports of H9 viruses during the current period. Data submitted to OFFLU revealed numerous detections of H9N2 G1, Y439 and Y280 lineages in poultry. This data does not reflect the true distribution of H9N2 that has become endemic in many parts of Asia, Africa and the Middle East, often co-circulating and reassorting with other influenza subtypes. In particular the G57 internal gene cassette, donated from a dominant H9N2 that emerged during 2010 in China poultry, has provided a fit internal gene scaffold for the reassortment of up to 11 subtypes to date and was key in the emergence of H7N9. H9N2 viruses continue to reassort with H7N9 viruses in China, contributing to genotype diversity of H7N9 viruses.

### **Major zoonotic concerns**

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In contrast to the Asian H7N9 virus which remains highly poultry adapted, the Gs/GD lineage H5 HPAI viruses can be sustained in migratory waterfowl, which has contributed to intercontinental spread. Although the Gs/GD H5N1 lineage circulated for decades with rare reassortment, which was unusual, the H5 2.3.4.4 clade has already reassorted with native strains on different continents.

According to Influenza Risk Assessment Tools, the H7N9 virus remains the most likely avian influenza virus to cause a pandemic of significant impact in humans. In the current period, there have been two cases of H7N9 infection in people in China, both elderly males who succumbed to severe illness or death following exposure to poultry.

The FAO qualitative risk assessment for spread of H7N9 within and outside of China is available [here](#). While experimental evidence is lacking in wild birds other than ducks, surveillance data suggests that spread of H7N9 via wild birds continues to be of negligible risk, with low uncertainty, while potential for spread via fomites between China and Lao PDR, Cambodia, Viet Nam and Myanmar (as has occurred with H5 viruses) remains a moderate risk with medium uncertainty.

A spillover infection of H7N4 (LPAI) was reported in a 68 year-old woman in China in mid-December 2017. The patient, who reported owning backyard poultry, was hospitalised and recovered. Genetic sequencing has confirmed that the virus originated from native wild bird LPAI and is unrelated to the Asian H7N9 lineage that is circulating in poultry in China.

There have been two cases of H5N6 HPAI in people in China, one 33 year-old male in Guangxi who developed clinical disease and one three-year-old girl in Fujian who displayed mild symptoms. The virus isolated from the case detected in Guangxi province had an HA gene genetically related to previous H5N6 Clade 2.3.4.4 (lineage C) viruses detected in people in China. However, the virus from Fujian province had an HA gene genetically similar to 2.3.4.4 lineage B H5N8 viruses that are

now widely detected in birds across Asia, Europe, Africa and the Middle East, but was a different reassortment, more closely related to other viruses in China.

H9N2 caused one reported human infection, in a 20-month-old girl in China. She recovered from mild symptoms.

All reported cases of infection with avian influenza had contact with poultry before onset of disease, and there were no cases of onward human-to-human transmission.

The pandemic preparedness outcomes from the antigenic and genetic characterisation of zoonotic influenza viruses arising from the February 2018 WHO-VCM meeting are available in the [zoonotic report](#). A new candidate vaccine virus strain (CVV) was proposed from the human-origin virus H5N6 isolate from Fujian, given the poor protection provided by current CVVs against clade H5 HPAI 2.3.4.4 lineage B. That the promiscuous H5 2.3.4.4 (B) gene continues to emerge in new regions (latest Middle East) and continues to reassort in various regions (Asia, Europe) proves a major concern for poultry industries and for public health. While viruses of the H5N8 2.3.4.4 lineage B clade have so far only infected birds, the rapid global spread of this virus, as well as the varying pathogenicity in wild birds, may be indicative of the unpredictability of this H5 HPAI clade in combination with other gene donors. This is especially highlighted by the spillover zoonotic infection of H5N6 containing this H5 gene that occurred recently in China.

Reports of swine-origin influenza viruses detected in people were also reviewed and antigenic data for swine-variant strains that were detected in the United States was presented. It is well acknowledged that swine are also very present at the human-animal interface worldwide and maintain a reservoir for antigenically divergent HA and NA proteins that pose a risk for pandemic emergence. The global OFFLU network should thus maintain its vigilance and surveillance for emergent or novel swine-origin influenza A viruses with the aim to contribute this information from a global perspective at future WHO VCM meetings.

Also, in cooperation with the efforts of international organisations to further understand the risks and effective control measures of avian influenza worldwide, OFFLU will continue to collate information from regions regarding vaccination practices in poultry as well as to provide expert advice for vaccination strategies as needed, and encourages data sharing from laboratories in this regard.

**Annex 1.** Sequence data submitted to OFFLU during the current period by subtype, clade and country.

	H5	H5N1	H5N2	H5N6	H5N8	H7N9	H7N9 HP AI	H9N2	TOTAL
<b>2.3.2.1c</b>									
Cameroon		2							2
Iraq		2							2
Viet Nam		7							7
Indonesia		10							10
Cambodia		11							11
Myanmar (Burma)		4							4
<b>2.3.4.4</b>									
China				1					1
Greece				1					1
Italy					55				55
Russia					5				5
Taiwan			1	1	1				3
Republic of Korea				7					7
Cyprus					1				1
Germany					1				1
Switzerland					1				1
United Kingdom (UK)				1					1
Cameroon					4				4
Nepal					1				1
Philippines					2				2
Viet Nam					3				3
<b>2.3.4.4 (A)</b>									
Taiwan			1		1				2
<b>2.3.4.4 (B)</b>									
Italy					55				55
Russia					5				5
Taiwan				1					1
Republic of Korea				3					3
Cyprus					1				1
Germany					1				1
Switzerland					1				1
United Kingdom (UK)				1					1
Cameroon					4				4
Greece				1					1
Nepal					1				1
Philippines					2				2
<b>2.3.4.4 (C)</b>									
China				1					1
Republic of Korea				4					4
Viet Nam					3				3
Philippines				2					2
<b>H7N9</b>									
China							2		2
<b>H9N2 G1</b>									
Nepal								3	3
India								3	3
<b>H9N2 Y280</b>									
Viet Nam								3	3
China								5	5
Myanmar (Burma)								6	6
Indonesia								5	5
<b>H9N2 Y439</b>									
Australia								1	1
Germany								2	2
<b>H5 LP AI</b>									
Dominican Republic	6								6
Georgia	1								1
Canada	6								6
Netherlands	1								1
<b>TOTAL</b>	<b>14</b>	<b>36</b>	<b>1</b>	<b>14</b>	<b>73</b>	<b>2</b>	<b>2</b>	<b>25</b>	<b>168</b>