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ANIMAL HEALTH RISK ANALYSIS

ASSESSMENT No. 8

CHINESE-ORIGIN H7N9 AVIAN INFLUENZA SPREAD IN POULTRY AND HUMAN EXPOSURE

Qualitative risk assessment update

The current risk assessment covers the period February to May 2019 and concerns the H7N9 viruses that emerged in China as a cause of zoonotic disease in 2013. These are now referred to as A/Anhui/1/2013-1 lineage (AH/13-lineage) H7N9 avian influenza viruses (WHO, 2018a), including both low and highly pathogenic strains. The qualitative risk assessment presents new information available since the last risk assessment published in February 2018. It should be noted that due to limited information from recent on-going surveillance in China uncertainty in this assessment is generally high.

SUMMARY

- The likelihood of an increase in the prevalence of AH/13-lineage H7N9 virus infections or outbreaks in poultry in **previously affected areas of China**¹ during the period February to May 2019 is considered **low** for chickens, ducks and other poultry (such as geese, quail and turkeys) **with high uncertainty**.
- The likelihood of AH/13 lineage H7N9 viruses spreading from China to unaffected countries of **South and South-east Asia** during the period February to May 2019 through:
 - **Formal or informal trade or transportation of poultry** is considered:
 - **Low with high uncertainty** through informal trade for Viet Nam and Myanmar, but negligible through formal trade.
 - **Low with high uncertainty** for the Lao People's Democratic Republic through informal or formal trade.
 - **Low with low uncertainty** for other countries of South-east Asia (e.g. Thailand and Cambodia) through informal or formal trade, assuming official control policies are effectively implemented.
 - **Negligible with low uncertainty** for countries of South Asia (e.g. Nepal and India).
 - **Poultry product trade** is considered **low with medium uncertainty**, regardless of virus survival in those products.
 - **Fomites** are considered:
 - **Low with medium uncertainty** for Viet Nam, the Lao People's Democratic Republic and Myanmar for informal trade with China;
 - **Negligible with medium uncertainty** for other countries of South and South-east Asia (e.g. India, Cambodia and Indonesia).
- The likelihood of AH/13-lineage H7N9 viruses spreading from China to unaffected countries **beyond South and South-east Asia** during the period February

¹ Previously affected areas of China comprise those where detections of H7N9 viruses were reported during period 6 (1 October 2017 to 30 September 2018), namely: Anhui, Fujian, Guangdong, Hubei, Hunan, Jiangsu, Liaoning, Shanxi, Shaanxi, Yunnan Provinces and Ningxia, Tibet and Xinjiang Uyghur Autonomous Regions.

to May 2019 through **global trade** in poultry and related products **and the movement of travellers** remains **negligible with low uncertainty**, although the virus may occasionally be found in smuggled poultry meat.

- The likelihood of detecting **at least one avian influenza A(H7N9) human case in China** during the period February to May 2019 is considered **low with medium uncertainty**. Even though this assessment targets the high-risk period for influenza, where greater H7N9 virus activity is usually recorded, lower temperatures favour virus survival in the environment and the celebration of local festivals, in particular Lunar New Year, increase the opportunity for human exposure,

only very few (if any at all) human cases are expected owing to the reduction of virus circulation as a result of the nationwide poultry vaccination programme.

- The likelihood of AH/13-lineage H7N9 viruses spreading during the period February to May 2019 through **movements of migratory or nomadic wild birds** is considered:
 - **low with high uncertainty** for China;
 - **negligible with high uncertainty** for South and South-east Asia countries;
 - **low with high uncertainty** for the Russian Federation, Mongolia, Japan and the Republic of Korea;
 - **negligible with low uncertainty** for other countries.

BACKGROUND

Since their first reported occurrence in March 2013 in China, AH/13-lineage H7N9 avian influenza viruses have been associated with 1 567 reported human cases of which 615 were fatal (WHO, 2018b). Until 2017 all strains of virus within this lineage were H7N9 low pathogenicity avian influenza (LPAI) viruses that spread widely in China, affecting most administrative regions. The LPAI virus produced little or no disease in poultry but it posed a severe threat to public health. In 2016, a highly pathogenic (HP) H7N9 strain within the AH/13-lineage that was capable of producing disease in humans and poultry emerged and spread in mainland China, reaching provinces formerly unaffected by its LPAI precursor strains and leading to additional human cases as well as severe outbreaks in chicken farms. The majority of human cases in 2016-2017 were caused by LPAI viruses (only 31 cases were caused by HPAI viruses during the fifth wave – WHO, 2018c). This fifth wave (October 2016 to September 2017) of H7N9 virus was the largest in terms of geographical distribution, number of cases in humans and outbreaks in poultry. The majority of H7N9 viruses detected in 2018 for which gene sequences are available and all viruses from poultry outbreaks have been HP strains. Between October 2017 and January 2018, LPAI viruses were detected in Hunan and Liaoning Provinces, in a live bird market (LBM) and on a farm, respectively (Shi *et al.*, 2018).

In September 2017, prompted by the persistence and spread of both H7N9 HP and LP viruses and the ongoing circulation of H5 avian influenza virus with zoonotic potential (e.g. H5N6), the Chinese government modified its avian influenza vaccination programme, targeting all poultry on mainland China with the main focus on longer-lived chickens, adding H7 into the already existing H5 vaccine. More than a year has now passed since H7 vaccination started, and as a result, there was a significant drop in the number of H7N9 detections in avian hosts as well as reported poultry outbreaks in 2018 through national active surveillance. Likewise, only three A(H7N9) human cases were reported

during this sixth period (1 October 2017 to 30 September 2018), compared to 766 human cases in the same period during the previous year (WHO, 2018b). This was most likely as a result of reduced virus circulation in poultry due to the effectiveness of the vaccination programme in terms of vaccine efficacy and sufficient vaccination coverage.

Enforcement by China's Ministry of Agriculture and Rural Affairs (MARA) and the poultry industry of countrywide and rapid vaccination before the beginning of the avian influenza high activity season in 2017 (November-December) is regarded as the key factor in controlling the disease. However, even after vaccination the virus continued to circulate in poultry albeit at lower levels. Continuous surveillance and monitoring are essential to follow the evolution of H7N9 virus circulation dynamics closely in terms of geography, species and affected poultry value-chains, genetic changes and host adaptation. In this regard, the emergence of AH/13-lineage H7 subtypes other than H7N9 (e.g. H7N2, H7N3) in domestic duck populations in China warrants close attention. The extent of the spread of these viruses is currently unknown.

This is an update to the FAO risk assessment issued in February 2018 on the risk of the potential spread of H7N9, both low pathogenic and highly pathogenic strains, within China and to other countries in South-east Asia and beyond, as well as human exposure in China. The period covered in this assessment, February to May 2019, is characterized by increased avian and zoonotic influenza virus activity and the occurrence of major Asian festivals¹ which generate increased demand and movements of live poultry and poultry-related products in the region, potentially leading to increased transmission and circulation of H7N9 in poultry and greater opportunity for human exposure.

¹ Major festivals in Asia during the period January to May 2019 are: Lunar New Year, Têt festival, Qingming festival and Khmer New Year.

Additional data sources include GISAID (Global Initiative on Sharing All Influenza Data, 2019a, 2019b, 2019c) and Shi *et al.* (2018). The two H7N9 isolates from Jiangsu Province (green diamonds with yellow dots) have genetic markers of high pathogenicity in their HA sequence. H7N4 detections in poultry and a human case were reported in the same location. *Note that the precise location of the H7N3 HPAI isolate (GISAID, 2019c) origin is unknown, therefore this case is not shown on the map.* Inset map: H7N9 detections, both LP and HP, from the fifth wave (October 2016–September 2017), i.e. the year before period 6, for comparison.

ASSESSMENT

Main risk questions

The risk questions considered in this assessment are:

1. What is the likelihood of an increase in the prevalence of AH/13-lineage H7N9 virus infections or outbreaks in poultry in previously affected areas of China during the period February to May 2019?
2. What is the likelihood of AH/13 lineage H7N9 viruses spreading from China to unaffected countries of South and South-east Asia during the period February to May 2019 through formal or informal trade or transportation of poultry, poultry products or fomites?
3. What is the likelihood of AH/13-lineage H7N9 viruses spreading from China to unaffected countries beyond South and South-east Asia during the period February to May 2019 through global trade in poultry and related products and the movement of travellers?

4. What is the likelihood of detecting at least one avian influenza A(H7N9) human case in China during the period February to May 2019?
5. What is the likelihood of AH/13-lineage H7N9 viruses spreading through wild bird movements or migrations, within China, to South and South-east Asia and beyond during the period February to May 2019?

Methodology for qualitative risk assessment and uncertainties

Levels of likelihood for each of the risk questions were defined as follows (from highest to lowest levels): **high** (highly likely to occur), **moderate** (potentially occurring), **low** (unlikely to occur) and **negligible** (extremely unlikely to occur). Evidence used to answer each question of the risk assessment is in the Considerations section. Given the lack of data and studies on the current H7N9 epidemiological situation in China at the time of the assessment, some considerations are based on assumptions derived from previous work on other avian influenza (AI) viruses. Levels of uncertainty (low, medium and high) were added to reflect this.

- High uncertainty (H): lack of data, limited data, or lack of conclusive data; weak correlation or crude speculation;
- Medium uncertainty (M): small sample, fair correlation/good fit; reliable method;
- Low uncertainty (L): large sample set; known fact, event known to occur, or exact measure.

FIGURE 1. Human cases and positive findings in birds or the environment for H7 viruses* during period 6 (1 October 2017 to 30 September 2018)



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Assumptions

- From June 2018 to January 2019, vaccination has been performed with post-vaccination monitoring (PVM) results indicating vaccine coverage above 70 percent, similar to the period November 2017 (average 88.01 percent [73.13 – 96.02 percent]) to May 2018 (average 92.14 percent [71.13 – 98.87 percent]) (MARA, 2018a). Since then, no further PVM results have been published.
- H7N9 is still circulating in China, albeit at reduced levels. Before introduction of the bivalent H5+H7 vaccine (January 2013–August 2017), the median H7 positivity rate during surveillance in LBMs of Guangdong Province was at 0.8 percent, whereas after introduction of the vaccine (September 2017–June 2018) the rate was 0.1 percent (Wu *et al.*, 2018). Environmental samples from washing water and chopping boards tested positive in poultry markets in January and May 2018 in Jiangsu Province, China (GISAID, 2019a, 2019b).
- The last reported H7N9 HPAI outbreaks of 2018 occurred in northern China: Liaoning (22 May), Shanxi (23 March), and Shaanxi (17 February) Provinces and Ningxia Autonomous Region (3 and 25 April), demonstrating that the virus was still circulating (FAO, 2018b). Outbreaks of disease such as the one in a layer farm in Liaoning Province

would not occur in a well vaccinated flock indicating that not all flocks are fully protected.

- Vaccination against H5 has been implemented in China for over ten years as part of the regular poultry vaccination programme. In September 2017, the H7 subtype was added to the ongoing vaccination programme in the form of bi- or trivalent vaccines (together with H5). Given that farmers are well acquainted with AI vaccination schedules, appropriate vaccination implementation is generally expected. However, based on experiences with H5 vaccination, immunity can wane in older poultry (Tarigan *et al.*, 2018) and not all farmers will choose to vaccinate. Shi *et al.* (2018) indicated that few ducks were vaccinated. Under field conditions experiences with H5 vaccine in yellow feather chickens in Hong Kong was associated with a poorer response than two doses (Ellis *et al.*, 2005).
- Affected area: All provinces where H7N9 was detected during period 6 (Anhui, Fujian, Guangdong, Hubei, Hunan, Jiangsu, Liaoning, Shanxi, Shaanxi, Yunnan Provinces and Ningxia, Tibet Autonomous Region and Xinjiang Uyghur Autonomous Region). Data was collected from MARA bulletins, peer-reviewed articles, and GISAID platform.

CONSIDERATIONS

1. What is the likelihood of an increase in the prevalence of AH/13-lineage H7N9 virus infections or outbreaks in poultry in previously affected areas of China during the period February to May 2019?
 - Evidence presented in the February 2018 assessment (FAO, 2018a).
 - In September 2017, MARA China launched a massive vaccination campaign against H5 and H7 subtypes targeting all poultry on mainland China including chickens, ducks, geese, quail, pigeons and rare birds in captivity. The vaccine used is a H5+H7 bivalent inactivated vaccine produced using reverse genetics. The vaccination of poultry is mandatory in every administrative region unless the provincial veterinary authorities grant permission not to vaccinate, as can be the case in AI-free zones or for export purposes (FAO China [FAOCN], 2017 - personal communication; MARA, 2017a).
 - From October 2017 to May 2018, a total of 351 859 samples were collected from poultry and the environment in 29 administrative regions through national animal H7N9 surveillance performed by MARA, China. Twenty samples reported positive for LPAI H7N9 were from chickens, ducks, and from the environment (19 from LBMs and one from a farm) in seven different provinces/regions of China, namely: Anhui (three), Fujian (six), Hubei (one), Hunan (two) and Yunnan (two) Provinces and the Tibet Autonomous Region (six); (MARA, 2018a). A fall has been

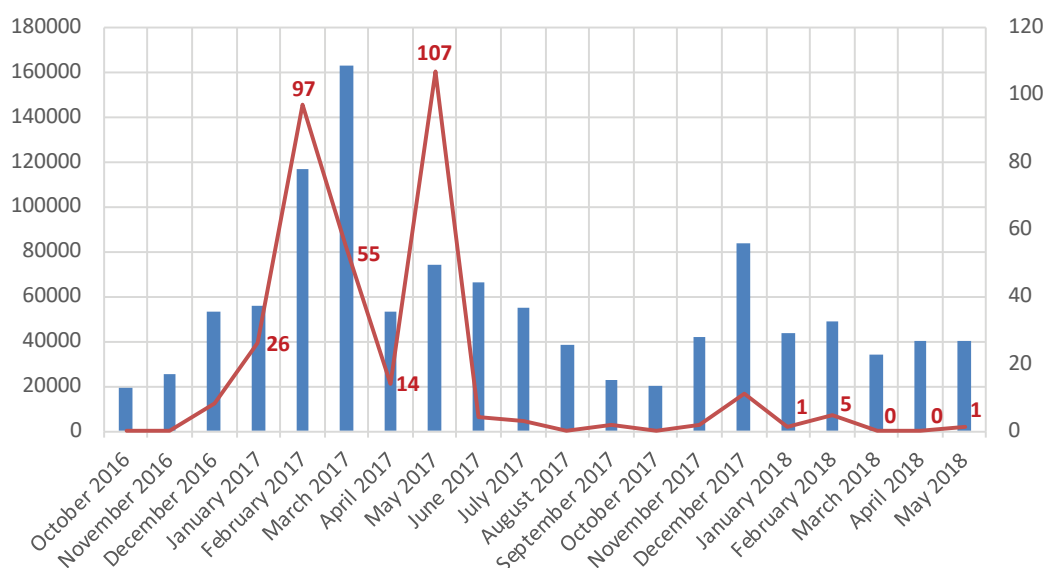
observed when comparing January and May 2018 results with those from January to May 2017 (Figure 2). The reader should be aware that sample collection during national surveillance may vary from one month to another in terms of provinces, sample size and sites, thus conclusions from results comparison are limited, but a trend can still be shown.

- MARA China has conducted active H7N9 surveillance and post-vaccination monitoring throughout 2018 (FAOCN, 2019 – personal communication). However, results from national animal H7N9 surveillance have not been made publicly available since June 2018, therefore the extent of H7N9 circulation in China is currently unknown. Other groups are also conducting surveillance but their results are likewise unavailable.
- Additional data provided by the study of Shi *et al.* (2018), showed reduced circulation of H7N9 LP and HP virus during the period October 2017-January 2018. Out of the 12 967 samples collected from 204 LBMs, only one H7N9 LPAI positive sample was detected in Hunan Province and 12 H7N9 HPAI positive samples in Anhui and Fujian Provinces and Tibet Autonomous Region. The study also investigated poultry farms but out of the 10 716 samples from 374 farms, detected only one H7N9 LPAI virus and one H7N9 HPAI virus, in Liaoning and Yunnan Provinces respectively (Shi *et al.*, 2018).
- A recent publication depicted the detection frequency of H7 positive samples from 2013 to 2018 in LBMs distributed in 21 cities in Guangdong Province. The bivalent H5+H7

vaccination programme that started in September 2017 was associated with a reduction of 92 percent in the H7 positivity rates at LPMs and 98 percent in the number of human H7N9 cases (Wu *et al.*, 2018). This study emphasizes the decrease of H7N9 virus circulating in LBMs of Guangdong. This is likely to have occurred in other provinces with high poultry density in eastern and southern China as reflected in the very low number of H7N9 detections in LBMs over the period October 2017 to May 2018.

- Since October 2017, five H7N9 HPAI outbreaks occurred, all in layer chicken farms, in four northern provinces: Liaoning (one), Shanxi (one), and Shaanxi (one) Provinces and Ningxia Autonomous Region (two). This is less than the number of HPAI H7N9 outbreaks reported over the eight month period February to September 2017, which totalled nine outbreaks in chicken layer farms. From June 2018 until January 2019, no H7N9 HPAI outbreaks were reported (FAO, 2018b).
- Provincial veterinary authorities carry out PVM. Results between October 2017 and May 2018 showed an overall flock immunization rate above the 70 percent protective threshold defined by MARA, China (MARA, 2017; see also Table 1). Only one or two provinces were under the immunization threshold in any given month.
- In laboratory settings, vaccinated chickens challenged with homologous LP or HP H7N9 strains survived inoculation and did not shed virus (CADC, 2017; Shi *et al.*, 2017). Two other recent laboratory studies showed that the H5+H7 bivalent inactivated vaccine provided complete protection in chickens against 2017 LP or HP H7N9 isolates, with no virus shedding

FIGURE 2. National animal H7N9 influenza surveillance results from October 2016 to May 2018 (FAO, 2018b)



Note: Horizontal axis: Reporting period; left vertical axis: Total number of virological samples collected (both animal and environmental) – blue histogram; right vertical axis: Number of virological samples positive for H7N9 – red line. The graph does not include additional H7N9 data from Shi *et al.* (2018) and GISAID platform, AH/13-lineage H7N2 HPAI virus detected in Fujian or H7N3-lineage H7N3 HPAI virus from Muscovy duck meat exported from China to Japan.

TABLE 1 Post-vaccination monitoring results for November and December 2017 (MARA, 2018a)*

Reporting period	Total number of samples collected from birds	Average PVM immunization rate (target 70%)	Range of post-vaccination immunization rate
November 2017	167 059	88.01	15.24% (Yunnan Province) to 96.02% (Shandong Province)
December 2017	216 186	86.34	55.17% Xinjiang to 94.77% Shandong
January 2018	117 284	87.30	58.19 (Xinjiang) to 100 (Inner Mongolia - only 20 samples same site)
February 2018	95 312	86.85	19.40 (Yunnan) to 100 (Qinghai - 10 sites 60 samples)
March 2018	101 175	90.00	67.35 (Xinjiang) to 97.32 (Jiangsu)
April 2018	106 148	91.26	53.33 (Qinghai) to 100 (Inner Mongolia - 1 site 20 samples only)

* Note that sample sizes and collection sites can vary significantly from one administrative region to another.

detected from any of the vaccinated birds (Hou *et al.*, 2018; Shi *et al.*, 2018). However, since vaccination under field conditions may not necessarily provide optimal immunity, some level of H7N9 virus shedding cannot be excluded.

- On 9 December 2018 MARA China issued an announcement listing six recently developed recombinant bivalent (H5+H7) inactivated vaccines, using a new H7 vaccine strain – H7-Re2 (MARA, 2018b). This will provide a better match with current H7N9 strains circulating in China and is likely to improve vaccine effectiveness.
- Since its emergence in early 2013, H7N9 LPAI virus has been detected in several domestic bird species including chickens, ducks, turkeys, quail and pigeons (FAO, 2018b). H7N9 LPAI isolates from 2013 are shown to be effectively shed and transmitted among chickens (Jiao *et al.*, 2018), quail, Muscovy ducks (Vidaña *et al.*, 2018) and turkeys, with an unexpected mortality for the latter (Slomka *et al.*, 2018).
- H7N9 HPAI viruses were detected in chicken samples collected in Guangdong Province in June 2016 and January 2017 and laboratory trials indicated that these double or triple reassortants were highly pathogenic for chickens (Qi *et al.*, 2018; Shi *et al.*, 2017). Experimental infections in chickens and ducks with two HPAI viruses collected in early 2017, A/Guangdong/17SF003/2016 – likely generated from the H7N9 LPAI viruses in Shanghai (Wang *et al.*, 2018) – and A/Taiwan/1/2017, indicated that ducks were less sensitive to these isolates, with less virus replication and shedding but no clinical signs displayed as compared to chickens where mortality was observed in all infected birds (Tanikawa *et al.*, 2018).
- H7N9 HPAI viruses that emerged in 2016, likely from reassortments of H7N9 LPAI viruses (Shi *et al.*, 2017; Wang *et al.*, 2017), were replicated in and were lethal for chickens, but showed very limited replication in domestic duck populations at that time. Since then, genetic evolution of H7N9 HPAI viruses, through mutations, or reassortments with co-circulating H7N9 or H9N2 strains or other H7 subtypes, have resulted in enhanced adaptation of certain H7N9 HPAI viruses to ducks (Ma *et al.*, 2018; Pu *et al.*, 2018;

- Shi *et al.*, 2018). Indeed, systemic replication and lethality were observed in ducks inoculated intra-nasally with one H7N9 HPAI isolate (A/Duck/Fujian/SD208/2017) collected in late 2017 in Fujian Province (Shi *et al.*, 2018). Two other HPAI isolates (A/chicken/Hubei/G1/2017 and A/duck/Xizang/2035/2017) inoculated in ducks showed systemic replication, but no mortality (Hou *et al.*, 2018). These studies did not assess shedding of virus from vaccinated ducks.
- Other H7 subtypes falling within the AH/13-lineage and with high pathogenicity have been detected recently in ducks. An H7N2 HPAI virus was isolated from a duck farm in Fujian Province during the period October 2017 to January 2018 and showed high pathogenicity with mortality in ducks infected experimentally (Shi *et al.*, 2018). The H7N2 HPAI isolate is likely to have originated from reassortments between an H7N9 HP virus and another duck virus (closely related to H3N2 A/duck/Guangxi/135D20/2013). Likewise, another H7N3 HPAI virus was isolated in March 2018 from raw Muscovy duck meat smuggled into Japan (GISAID, 2019c; WHO, 2018a). The current extent of spread of these viruses in domestic duck populations in China is unknown.
- Important Asian festivals take place between February and May 2019, such as Chinese New Year and the Têt festivals (both starting on 5 February 2019), Qingming festival (5 April 2019) and Khmer New Year (14-16 April 2019). Prior to and during these festivals, there is usually an increase in demand for live poultry and poultry products. This also results in an increase in poultry movements, either formal or informal, not only in China but also within neighbouring countries.
- With the current epidemic of African swine fever (ASF) striking China, pork value chains are heavily affected. Consequently, poultry demand may increase in the coming months at the expense of the pork market (FAO/CN, 2019 – personal communication).

Therefore the likelihood of an increase in the prevalence of AH/13-lineage H7N9 virus infections or outbreaks in poultry in previously affected areas of China during the period February to May 2019 is considered **low for chickens, ducks and other poultry** (such as geese, quail, and turkeys) **with high uncertainty**.



Poultry-related occupation and regular live bird market visits are important risk factors for human exposure to zoonotic avian influenza viruses, such as H7N9.

2. What is the likelihood of AH/13 lineage H7N9 viruses spreading from China to unaffected countries of South and South-east Asia during the period February to May 2019 through formal or informal trade or transportation of poultry, poultry products, or fomites?

2.1. Live bird trade

This section considers:

- Evidence presented under 1., and in the February 2018 assessment (FAO, 2018a).
- Vaccination of poultry against H7 avian influenza is still prohibited in Viet Nam, Myanmar and Cambodia (FAO Viet Nam [FAOVN], 2019; FAO Myanmar [FAOMM], 2019; FAO Cambodia [FAOKH], 2019 – personal communications; Cambodia national comprehensive avian and human influenza plan, last access January 2019). No policies on avian influenza vaccination currently exist in the Lao People's Democratic Republic (FAO Lao PDR [FAOLA], 2019 – personal communication).
- In Viet Nam and Myanmar, there is active surveillance in LBMs and townships in administrative regions bordering China (e.g. in Cao Bang or Lang Son Provinces of Viet Nam that border Guangxi Zhuang Autonomous Region or in Shan Burmese state bordering Yunnan Province); so far, no H7N9 viruses have been detected (FAOMM, 2019; FAOVN, 2019 – personal communication).
- Regulatory officials in countries of South-east Asia are aware of hazards from avian influenza and strict regulatory frameworks are in place at the borders, including banning imports of live poultry and/or strictly regulated movements (FAOCN, 2019; FAOKH, 2019; FAOLA, 2019; FAOMM, 2019; FAOVN, 2019 – personal communications; MAFF Cambodia, 2019).
- Since the detection of LP H7N9 virus and the HP H7N9 human case, both in Yunnan Province in November 2017, no other H7N9 virus was officially reported from provinces bordering Viet Nam, the Lao People's Democratic Republic or Myanmar (FAO, 2018b). However the virus is suspected to circulate at low levels in China and these countries continue to be at risk of cross-border H7N9 introduction, especially through informal trade or transportation of live poultry and related products.
- There are no official imports of live poultry from China to Viet Nam or Myanmar. However, a significant number of spent hens, day-old-chicks and young layer birds (five to 25 days), enter these countries daily via informal trade (FAOMM, 2019; FAOVN, 2019 – personal communication). The Lao People's Democratic Republic officially imports live poultry including adult chickens and ducks, and day-old chicks and ducks from China, however there is no systematic testing of live poultry imported from China due to the lack of a veterinary workforce at border checkpoints (FAOLA, 2019 – personal communication).

- With major festivals occurring from February to May in Asia, there is generally an increased demand for live poultry and poultry products, leading to more informal cross-border movements between China and other countries of South and South-east Asia. Increased poultry trade in southern China around the Lunar New Year has historically been associated with higher H5N1 HPAI virus infection risk in humans and poultry (Soares *et al.*, 2012).
- Young chickens (14-30 days old) are the main type of poultry officially exported to neighbouring countries and are likely to be vaccinated (FAOCN, 2019 – personal communication).
- Apart from Viet Nam, Myanmar and the Lao People's Democratic Republic, countries in South and South-east Asia have little or no live poultry trade with China, such as in Cambodia where poultry trade occurs mainly with Thailand and Viet Nam (MAFF Cambodia, 2019; FAOKH, 2018 – personal communication).
- A growing number of Chinese citizens travelling to South and South-east Asian countries for professional or tourism reasons may carry live poultry and poultry products from China (FAOVN, 2019; FAOKH, 2019 – personal communication). However, their purpose is own consumption, not trade.

Therefore the likelihood of AH/13 lineage H7N9 viruses spreading from China to unaffected countries of South and South-east Asia during the period February to May 2019 is considered:

- **Low with high uncertainty** through informal trade for Viet Nam and Myanmar, but negligible through formal trade.

- Low with high uncertainty for the Lao People's Democratic Republic through informal or formal trade.
- Low with low uncertainty for other countries of South-east Asia (e.g. Thailand and Cambodia) through informal or formal trade, assuming official control policies are effectively implemented.
- Negligible with low uncertainty for countries of South Asia (e.g. Nepal and India).

2.2. Poultry products

This section considers:

- Evidence presented under 1, 2.1, and in the February 2018 assessment (FAO, 2018a).
- AH/13-lineage H7N9 HPAI virus, similar to other HPAI subtypes, causes systemic infection and was detected in various internal organs, tissues and feathers of live birds and in the meat of carcasses. Although H7 LPAI viruses can replicate in poultry gastrointestinal or respiratory tracts, they are generally not found in meat, feathers or other internal organs (Shi *et al.*, 2017, 2018; Swayne, 2016).
- In layer chickens and breeders vaccinated against H7, a vertical transmission of H7N9 virus is unlikely to occur, due to the effective protection provided by compulsory vaccination.
- Chicken feathers are usually destroyed or destined for industrial processing. Duck feathers, considered a more valuable product, are usually cleaned, dried and may be sold to neighbouring countries (e.g. Viet Nam).
- H7N9 virus is able to survive in raw poultry meat, either frozen or chilled. In addition, raw poultry meat may be



Lack of biosecurity practices during transportation of poultry increases risk of avian influenza virus spread and its introduction into new geographic areas.

contaminated during slaughtering and dressing processes (Shibata *et al.*, 2018). However, influenza viruses do not survive in properly cooked meat or eggs.

- Poultry product imports from China (e.g. frozen chicken meat, eggs) are officially banned in Myanmar and Viet Nam (FAOMM, 2019; FAOVN, 2019 – personal communication) unlike the Lao People’s Democratic Republic which allows official importation of poultry products from China (FAOLA, 2019 – personal communication). However, for live poultry, informal trade or transportation of poultry products does occur on a daily basis, increasing during festival periods, i.e. mid-January to end of April.

Therefore the likelihood of AH/13 lineage H7N9 viruses spreading from China to unaffected countries of South and South-east Asia during the period February to May 2019 is considered **low with medium uncertainty**, regardless of virus survival in those products.

2.3. Fomites

This section considers:

- Evidence presented under 1, 2.1, 2.2., and in the February 2018 assessment (FAO, 2018a).
- In China, small-scale farms and live bird markets located in semi-urban or rural areas often have insufficient biosecurity practices regardless of the vaccination status of flocks. In addition, it is unlikely that vaccination will be administered efficiently in these small-scale poultry production units or households.
- H7N9 virus is able to survive up to several weeks in the environment if suitable conditions occur such as low humidity, cool temperatures, and the presence of organic matter (Swayne, 2016; Tamerius *et al.*, 2013). However, proper cleaning and disinfection can drastically reduce the viral load on any material, e.g. crates, chopping boards, etc. that come into contact with poultry.
- HPAI H7N9 virus may be present in poultry manure which is often sold as a valuable resource to other farms (e.g. fertilizer for crops). The poultry manure that originates from LBMs is at higher risk of containing avian influenza viruses due to the presence of bird faeces from various sources, including unvaccinated birds, and the bioaccumulation of the virus in such premises.
- Informal trade in live poultry and related products is common and biosecurity measures are likely to be inappropriate (e.g. absence of truck disinfection between farms) to mitigate the risks of H7N9 spread or any other avian influenza virus effectively.

Therefore the likelihood of AH/13 lineage H7N9 viruses spreading from China to unaffected countries of South and South-east Asia during the period February to May 2019 is considered **low for Viet Nam, the Lao People’s Democratic Republic and Myanmar** for

informal trade with China and **negligible for other countries of South and South-east Asia** (e.g. India, Cambodia and Indonesia), both with **medium uncertainty**.

3. What is the likelihood of AH/13-lineage H7N9 viruses spreading from China to unaffected countries beyond South and South-east Asia during the period February to May 2019 through global trade in poultry and related products and the movement of travellers?

This section considers:

- Evidence presented under 1., 2., and in the February 2018 assessment (FAO, 2018a).
- According to trade statistics, the greater part of Chinese poultry product exports go to Japan and Hong Kong SAR (GAIN, 2017; FAOSTAT, 2019), see Table 2. In Hong Kong SAR, farms provide live chickens for local consumption and for export and currently there are only imports of eggs, chilled or frozen poultry meat and carcasses from mainland China. Japan only authorizes processed poultry meat imports from designated facilities in mainland China and the Republic of Korea, (MAFF Japan, last access January 2019).
- For 2019, most of the forecast increased demand for Chinese processed chicken meat exports will be centred on Japan and the European Union (European Commission, 2018; GAIN, 2018; MAFF Japan, 2019).
- Outside South and South-east Asia, in countries with significant poultry imports from China, strict regulatory frameworks are generally enforced for poultry specific imports such as processed meat and when crossing national borders through mandatory certification, testing and quarantine of imports (EUR-Lex, 2001; FSIS, 2018). However, there may be infected or contaminated poultry product exports from China. In Japan, from 2016 to 2017, H7N9 virus (both LP and HP) was detected three times in seized and confiscated raw Muscovy duck meat brought informally from China by air passengers, but the contaminated products were confiscated at the airport before entering the country (FAO, 2018b; Shibata *et al.*, 2018).

TABLE 2 Major importing countries for chicken and duck meat from China in 2016 – data source: FAOSTAT. As per FAOSTAT indicators poultry meat includes: heat-processed, fresh, chilled or frozen chicken and duck meat.

Importing countries/regions	Import quantity of poultry meat (tonnes)
Japan*	170 641
Hong Kong SAR	169 606
Malaysia	14 483
Kyrgyzstan	14 309
Netherlands*	9 101

* Only heat-processed chicken meat is exported.

Therefore the likelihood of the AH/13-lineage H7N9 viruses spreading from China to unaffected countries beyond South and South-east Asia during the period February to May 2019 through global trade in poultry and related products and the movement of travellers remains **negligible with low uncertainty**, although the virus may occasionally be found in smuggled poultry meat.

4. What is the likelihood of detecting at least one avian influenza A(H7N9) human case in China during the period February to May 2019?

This section considers:

- Evidence presented under 1. and in the February 2018 assessment (FAO, 2018a).
- Only three human cases were officially reported during period 6 (October 2017 to September 2018) after the H7 vaccination programme started, compared to 766 human cases during wave 5 (October 2016 to September 2017) (WHO, 2018b). Since the last human case occurred in Guangdong Province in February 2018, no human cases were officially reported. These numbers may be underestimated since mild H7N9 infection can occur and therefore may not be reported.
- The main risk factors associated with human exposure to H7N9 viruses are direct exposure to live poultry (i.e. raising backyard poultry, buying live poultry in LBMs and sale or slaughter of live poultry) and indirect exposure by visiting LBMs (Yang *et al.*, 2017; Liu *et al.*, 2014). Touching sick or dead poultry is an important factor associated specifically with H7N9 HPAI human exposure, as shown in the case reported from Guangdong Province (Kang *et al.*, 2017).
- With a high density of birds from different species, live poultry markets provide an ideal environment for avian influenza viruses to spread among birds, reassort or mutate, and also spill over from birds to humans. As a mitigation measure for AI spread, market closures have been shown to reduce A(H7N9) human infections significantly due to less contact between live poultry and humans (Teng *et al.*, 2018; Yu *et al.*, 2013). However, closure of markets results in changes in poultry trade patterns which may lead to H7N9 virus introduction into areas that were previously unaffected (Li *et al.*, 2018). To date, no information is available on whether market closures are planned during the 2019 festivals to mitigate any potential spread of H7N9.
- After the vaccination started, detection rates of H7 AIV in Guangdong LBMs were significantly reduced (Wu *et al.*, 2018), which may be attributed to a drop in the level of H7N9 circulation as compared to previous years. These results, along with the small number of H7N9 detections in Chinese live bird markets in 2018 may also provide an indication of what happened in other areas of China since vaccination was conducted countrywide and that the average flock immunization rate in China was high (>85 percent) from

November 2017 to May 2018 (MARA China, 2018a).

- Both LP and HP H7N9 viruses have been shown to infect humans, the majority of the cases being attributed to the LP strain (FAO, 2018b). The HP strain is generally associated with clinical signs in poultry, from mild to severe, which are easier for people to identify, hence reducing human exposure to the virus.
- An experiment conducted by Prof. Kawaoka indicated that the H7N9 virus could be indirectly transmitted efficiently among ferrets via respiratory droplets (SCMP, 2018). H7N9 virus was found in respiratory droplets up to a distance of 80 centimetres from the cage of the infected ferret. Previous experimental infections showed that H7N9 LP or HP viruses were able to replicate efficiently in ferrets and mice, the HP isolates being more pathogenic than the LP isolates, and could also be transmitted through direct contact in these species (Imai *et al.*, 2017).

Therefore the likelihood of detecting at least one avian influenza A(H7N9) human case in China during the period February to May 2019 is considered **low with medium uncertainty**.

Even though this assessment targets the high-risk period for influenza, where greater H7N9 virus activity is usually recorded,



Live bird markets containing different species of poultry from different origins are at increased risk of avian influenza virus circulation and facilitate further spread.

lower temperatures favour virus survival in the environment. Local festivals, in particular the Lunar New Year, increase the opportunity for human exposure, but very few (if any) human cases are expected owing to the reduction of virus circulation as a result of the nationwide poultry vaccination programme. For more details on human exposure risk, please refer to WHO Risk Assessment on influenza at the human-animal interface.

5. What is the likelihood of AH/13-lineage H7N9 viruses spreading through wild bird movements or migrations, within China, to South and South-east Asia and beyond during the period February to May 2019?

- Evidence presented under 1., 2., and in the February 2018 assessment (FAO, 2018a).
- To date, H7N9 virus has only been detected twice in wild birds, in one tracheal sample from a healthy tree sparrow in Shanghai during spring 2013 (Zhao *et al.*, 2014) and in one faecal sample from a healthy oriental magpie-robin in Hubei Province in late 2015 (Yao *et al.*, 2018). There is no evidence of H7N9 HPAI virus circulating in local wild bird populations (FAOCN, 2019 – personal communication).
- The recent adaptation of some AH/13-lineage H7 (H7N9 and H7N2) isolates to domestic Pekin ducks with systemic replication, severe clinical signs and lethality (Shi *et al.*, 2018) is a cause for concern given the close genetic relationship between domestic ducks and other wild *Anatidae*. In the past, Gs/GD/96-lineage H5 viruses that were initially not adapted to domestic ducks rapidly evolved through reassortments and were then able to replicate efficiently in these populations (Sims *et al.*, 2005). Once adapted to domestic ducks, the transmission of these viruses to and among wild *Anatidae* populations occurred within a few years, followed by intercontinental spread.
- Results from a recent study indicate that H4N6 avian influenza virus can be transmitted among wild Mallards (*Anas platyrhynchos*) through dabbling, preening of infected feathers, and cloacal sipping (Wille *et al.*, 2018), and it would be reasonable to extrapolate those results to the context of H7N9 virus. Free-grazing domestic ducks often share habitats with other wild birds and waterborne transmission of H7N9 HPAI from any infected domestic duck to wild birds could occur in such settings.
- In the period covered by the risk assessment, February to May 2019, spring migration patterns occur, i.e. wild birds flying from middle or southern latitudes to breeding grounds under northern latitudes in temperate or arctic summer, following the west, Central and East Asia flyways (Olsen *et al.*, 2006). However, any spread will only occur if the virus is able to survive in one or more species during long-distance migration. So far, no AH/13-lineage H7 virus has been detected in wild anatids. This includes data from

the Republic of Korea where intensive surveillance of wild birds is regularly conducted and where other H7 viruses that are not part of this lineage have been detected (Lee *et al.*, 2018).

Therefore the likelihood of the AH/13-lineage H7N9 viruses spreading during the period February to May 2019 through movements of migratory or nomadic wild birds can be considered:

- **low with high uncertainty** for China
- **negligible with high uncertainty** for South and South-east Asia countries
- **low with high uncertainty for the Russian Federation, Mongolia, Japan and the Republic of Korea**
- **negligible with low uncertainty for other countries.**

DISCUSSION

The risk of the AH/13-lineage H7N9 viruses, both low and highly pathogenic strains, emerging or re-emerging in affected areas of China and leading to outbreaks or detections in poultry or even spreading beyond China to neighbouring countries through trade in poultry or poultry products and fomites is assessed as low for the period February to May 2019. However, the data available at the time of the assessment are scarce, with no information on the epidemiological situation in China since June 2018, hence an increased level of uncertainty should be noted when compared to previous assessments. The nationwide vaccination programme implemented in China since September 2017 appears to have substantially reduced the prevalence of H7N9 virus in poultry flocks in mainland China and, as a result, a drop in H7N9 virus circulation was observed in LBMs during the following year through studies and other targeted surveillance.

The absence of official reports from both animal and public health authorities since May 2018 may be an indication of the continuing effectiveness of the vaccination programme. However, the virus is still expected to circulate, albeit at lower levels, which may provide opportunity for virus spillover to naïve populations, especially in rural and semi-urban areas where flock vaccination may be less stringent or less thorough. Sporadic A(H7N9) human cases and outbreaks or detections in poultry in China cannot be excluded for the period February to May 2019, but the likelihood is low. If human cases or poultry outbreaks were to occur, the people most at risk remain those who are in direct or indirect contact with live poultry (farmers, slaughterers, traders) or consumers visiting live bird markets. However, recent findings in ferrets – that serve as the animal model for avian influenza in mammals, including humans – indicate that airborne transmission of some H7N9 virus strains can occur efficiently among ferrets in laboratory settings. These findings reinforce the need to investigate all human cases in order to detect any changes in transmission patterns rapidly.

The seed virus previously used for the H7 vaccine was based



H7N9 highly pathogenic avian influenza (HPAI) virus can replicate in domestic ducks, which may die from disease.

on a H7N9 LPAI virus isolated in 2013 (A/pigeon/Shanghai/S1069/2013). As highlighted in recent publications (Lu *et al.*, 2018; Ning *et al.*, 2018; Shi *et al.*, 2018), H7N9 viruses are evolving and adapting to hosts. Some antigenic change has been detected over time in H7N9 viruses but the marked reduction of avian and human cases post-vaccination strongly suggests that this has not been sufficient yet to result in reduced vaccine effectiveness. Also, there is an obvious co-circulation of high or low pathogenic subtypes, other than H7, in domestic poultry in China, with some having zoonotic potential (e.g. LP H9N2, HP H5N6, HP H5N1). Such interactions between subtypes during co-infection of poultry provide opportunities for H7N9 virus to undergo reassortment and to develop the potential to adapt to a broader spectrum of hosts including humans, other mammals and wild birds. Therefore, close monitoring is crucial to detect any change in the behaviour of H7N9 viruses and guarantee vaccine matching. In this regard, MARA China has recently updated the inactivated recombinant vaccines with a new H7 vaccine strain – H7-Re2 – which will likely provide a better match for circulating H7N9 strains. The need to introduce a new vaccine in December 2018 however raises questions as to the level of vaccine effectiveness and virus circulation during previous months, for which no data are available as post-vaccination monitoring or field surveillance results have not been published since June 2018.

Furthermore, the circulation of AH/13-lineage H7 subtypes other than H7N9 (e.g. H7N2 or H7N3) in domestic duck populations in China warrants close attention. In the study of Shi *et al.* (2018), the H7N2 HP virus isolated from a duck farm in Fujian Province during the period October 2017 to January 2018 is likely to have originated recently from

reassortments between a H7N9 HP virus and another duck virus (closely related to H3N2 A/duck/Guangxi/135D20/2013) and showed high pathogenicity with mortality in ducks infected experimentally. In March 2018 an H7N3 HPAI virus within the AH/13-lineage was detected in Muscovy duck meat smuggled from China into Japan (GISAID, 2019c; WHO, 2018a). The extent of the spread of these viruses remains unknown but if they persist in domestic ducks, transmission to wild *Anatidae* or back to chickens is possible.

Other H7 viruses that do not fall within the AH/13-lineage have also been detected. In January 2018, a novel H7N4 reassortant of wild bird origin (A/Jiangsu/1/2018), phylogenetically distinct from previously reported H7N4 and H7N9 viruses, was isolated in Jiangsu Province, China from a human patient with severe symptoms and from her backyard poultry (chickens and ducks) that did not show signs of illness (Huo *et al.*, 2018). With the better match provided by the new H7 vaccines, we cannot rule out the possibility that other H7 subtypes may fill the resulting space and eventually replace H7N9 AI in domestic poultry, given their phylogenetic distinction. These H7 viruses may pose a public health threat if they infect humans. Timely genetic and antigenic characterization of these viruses and other influenza viruses with human pandemic potential is crucial for risk assessment and to update pre-pandemic candidate vaccine viruses (CVVs) as part of global efforts for pandemic preparedness.

It should be further noted that at the time of assessment, African swine fever (ASF) is striking China and has spread countrywide. At the time of publication, 25 administrative regions (18 provinces, four municipalities and one autonomous region) have been affected (FAO, 2018c). In the period February

to May 2019 ASF prevention and control will be one of China's priority tasks. The limited availability of veterinary personnel at grassroots may dilute the prevention and control measures for H7N9 to a certain extent, especially the vaccination of free-range poultry.

Regarding the formal trade in live poultry and poultry products in China, the regulations detailed in the February 2018 assessment (FAO, 2018a) (testing, vaccination certificates and quarantine) are still enforced and as such are essential to mitigate the risk of H7N9 spread from one affected province to others. However, informal trade in live poultry takes place in China and with neighbouring countries, likely involving unvaccinated birds and inadequate biosecurity measures.

The low risk of introduction through informal trade or movement of live poultry and related products from China to countries bordering southern China, namely Viet Nam, the Lao People's Democratic Republic and Myanmar, assumes limited virus circulation in China. In the absence of surveillance data from China, the uncertainty for this assessment is high. Currently, countries in South and South-east Asia other than China (including Hong Kong SAR) are not vaccinating and therefore flocks are vulnerable to H7N9 virus introduction and spread. Continuous border disease control based on the detection and further culling and destruction of infected poultry and poultry products is essential for the prevention of H7N9 spread outside China. The FAO Regional Office in Asia and the Pacific has put in place arrangements for rapid supply of vaccine in the event of an outbreak in these countries. The spread of H7N9 beyond South and South-east Asia is assessed as negligible given that formal and informal trade in poultry from China to other countries is concentrated on neighbouring Asian countries and strict trade regulations are in place in most importing countries outside Asia.

Regarding the role of wild birds, evidence of H7N9 virus in these populations remains unchanged since February 2018. Nevertheless, the recent discovery of H7N9 reassortment with wild bird lineage viruses, demonstration of infected ducks with these reassortants, and host adaptation of H7N9 HP viruses pose new challenges. In China, when reared in open fields, domestic ducks, which are closely related to other wild *Anatidae*, have ample opportunity for interaction with wild birds. While it remains to be confirmed whether these reassortment viruses can be sustained in wild waterfowl, isolation from ducks and the environment elevate the concern of spread via wild birds. Consequently, the likelihood of H7N9 spread within China through wild birds was assessed as low and is currently considered negligible for Asia and beyond for February to May 2019. Should H7N9-like HP virus reassortants become capable of efficient transmission among duck species in China, regional and even intercontinental spread could occur as formerly seen with goose-Guangdong lineage H5 HPAI viruses (e.g. H5N1

or H5N8). For the period February to May 2019 and with the current knowledge this is a greater concern.

Given the observed ongoing genetic evolution of H7 viruses in the AH/13-lineage, FAO considers broadening future risk assessments to include H7 viruses other than H7N9 (e.g. H7N2, H7N3, H7N4).

CONSEQUENCE ASSESSMENT

Although H7N9 virus is suspected to circulate at low levels in China, the economic impact, following its introduction, spread and necessary actions to control the virus, could be high. However, assuming the continued and countrywide immunization of poultry flocks, any poultry outbreaks should be sporadic and limited to rural areas in isolation or just a few provinces in China, which means the severity of the consequences should be low to medium. China is to be congratulated on its nationwide H7 poultry vaccination efforts, which significantly reduced H7N9 risk for both human and poultry populations, but it is paramount that active surveillance and post-vaccination monitoring are continued and results made publicly available. If H7N9 crosses the Chinese border, the economic impact may be very serious due to the absence of H7N9 poultry vaccination in other countries, which could lead to extensive spread among naïve poultry populations as well as exposure for humans. Since the H7N9 emergence in 2013, countries bordering on China are aware of the hazard and have prepared for its potential introduction (e.g. Viet Nam, Republic of Korea, Japan), which will help in reducing such impact.

If a human is exposed to either the low or highly pathogenic strain from infected live poultry or poultry products, or to contaminated environments or fomites, it does not necessarily lead to human infection or disease. The latter depends on the virus strain, the amount of virus present and infectious dose required, the susceptibility of the individual, etc. However, where human infection does occur, it can result in severe respiratory disease and death. Small clusters of human infections with H7N9 have been reported, but thus far, there are no reports of sustained human-to-human transmission of this virus. If the H7N9 virus were to transmit efficiently from person to person, the consequences would be major.

As seen with the H5N1 HPAI epidemic in 2003-2006, H7N9 spread in the poultry value chain causing human cases may result in consumers avoiding consumption of fresh poultry meat and poultry products. Consequently, the national economy, the poultry industry as well as associated livelihoods could be severely affected. Nevertheless, the intended benefits of the measures currently implemented in China, including countrywide H7 vaccination of poultry, include a decreased risk of human infection, and thus protecting livelihoods and safeguarding the economy and viability of poultry production systems.

Gaps (sources of uncertainty)

The following information is lacking, therefore increasing the uncertainty associated with the likelihood estimates presented in the current assessment:

- MARA active surveillance and post-vaccination monitoring results since June 2018 and detailed information on vaccination campaign coverage rates;
- LBM surveillance results to assess current levels of AH/13-lineage H7 contamination in such markets, being the most common source of human infection and probably critical for spreading infection back to farms;
- Current infection status of the provinces, especially those bordering Viet Nam, the Lao People's Democratic Republic and Myanmar, or those previously affected and where H7N9 is known to be endemic, i.e. Guangdong and Yunnan Provinces and Guangxi Zhuang Autonomous Region;
- Cross-border value-chain studies addressing China and neighbouring countries to the south, namely Viet Nam, the Lao People's Democratic Republic and Myanmar;
- Information on biological characteristics of currently circulating isolates (host range, transmissibility, virulence);
- Information on efficacy and effectiveness of the recently updated H7 vaccine on chickens and ducks;
- Experimental infection in vaccinated ducks and other commonly commercialized poultry with recently circulating H7N9 isolates;
- Results from China's wild and migratory bird surveillance.

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NOTES



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RISK ANALYSIS IN ANIMAL HEALTH

Risk analysis is a procedure which we all do intuitively in our everyday life as we also do in our professional work to assess the risk of any hazard or threat. In animal health, risk analysis has been most widely used as a decision tool to help select the most appropriate health interventions to support disease control strategies, guide disease surveillance and support disease control or eradication strategies.

It should be remembered that risk is not equal to zero and never stays static. Risk changes as drivers or factors of disease emergence, spread or persistence change such as intensification of livestock production, climate change, civil unrest and changes in international trading patterns. Risk analysis should therefore not be seen as a “one off” but as good practice for animal health systems as part of their regular activities.

Therefore, risk analysis process should be repeated and updated regularly.

Risk analysis comprises the following components:



Hazard identification: the main threats are identified and described.



Risk assessment: risks of an event occurring and developing in particular ways are first identified and described. The likelihood of those risks occurring is then estimated. The potential consequences or impact of the risks if they occur are also evaluated and are used to complete the assessment of the risk.



Risk management: involves identifying and implementing measures to reduce identified risks and their consequences. Risk can never be completely eliminated but can be effectively mitigated. The aim is to adopt procedures that will reduce the level of risk to what is deemed to be an acceptable level.



Risk communication: an integrated process that involves and informs all stakeholders within the risk analysis process and allows for interactive exchange of information and opinions concerning risk. It assists in the development of transparent and credible decision-making processes and can instil confidence in risk management decisions.

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