Highly Pathogenic Avian Influenza and sustainability of the global poultry industry

The global poultry industry is the major supplier of animal protein for human consumption worldwide and this worldwide demand depends heavily on international trade of products and breeding stock. The high number of outbreaks of Highly Pathogenic Avian Influenza (HPAI) H5 significantly affects the sustainability of the poultry industry and the continuity of International trade particularly in valuable breeding stock. The Poultry Veterinary Study Group of the EU is in favour of an open-minded evaluation of the possibilities of using modern A/V vaccines in association with DIVA diagnostics and monitoring and surveillance so that essential trade in breeding stock and poultry products can proceed without disruption. An approved package by OIE can then allow countries to offer better protection to poultry against HPAI outbreaks in certain seasons or to achieve better protection in poultry at risk (e.g., free range and organic poultry) from HPAI outbreaks. The outcome of this policy will be benefits to national and international poultry farming, animal welfare and the continued supply of breeding stock globally.

Avian influenza viruses (AIV) are a group globally distributed viruses that know no geographic boundaries, have no political agenda, and can infect commercial and non-commercial poultry, indoor- and outdoor-reared poultry, pet birds, captive-bred and feral wild birds, birds in zoological collections and reserves, and a variety of other avian and non-avian species (Swayne, 2017). Avian influenza virus strains can be divided into highly pathogenic (HP) and low pathogenic (LP) strains based on the results of the intravenous pathogenicity index (IVPI) in 6-weeks-old chickens and presence of multiple basic amino acids at the cleavage site of the hemagglutinin molecule (HO) (Swayne et al., 2013; OIE, 2018). Natural infection by avian influenza viruses results in a wide range of clinical outcomes which are dependent on virus strain, host species, host age, host immunity, coinfections with other primary or secondary pathogens, and environmental factors. The virus is transmitted by direct contact between infected and susceptible birds or indirect contact through aerosol, droplets, or exposure to virus-contaminated fomites (Ssematimba et al., 2012; Bertran et al., 2017; Zhao et al., 2019; Swayne et al., 2020). Outbreaks of highly pathogenic avian influenza (HPAI) strains were all of the H5 and H7 subtype

and have been responsible for dramatic losses in the poultry industry, especially since 1996 (Sims & Brown, 2017; Brown et al., 2017). HPAI strains are highly virulent for chickens and closely related gallinaceous birds and cause a severe, fatal, per acute systemic disease with high mortality. The clinical signs in non-gallinaceous birds as waterfowl are usually less and can even be absent but may vary per bird species and HPAI virus strain. The economic damage is not only related to the loss of infected flocks. The indirect damage may exceed the direct costs multiple times due to culling of surrounding flocks, stand-stills, disruption of the structure of the industry and long-lasting trade implications for poultry (such as high value breeding stock) and poultry products. Other indirect costs which are hard to quantify in figures are animal welfare problems, the mental health damage to livestock keepers and long-lasting damage to the image of the industry with consumers, retailers, and politicians.

Until 1996, outbreaks with HPAI were scarce and local (Swayne et al., 2020), this changed with the appearance in 1996 of the Gs/GD-lineage H5 HPAIV in Guangdong Province, China (Sims & Brown, 2017). Until the early 2000, it was generally accepted that HPAI viruses emerged following the transmission of LPAI viruses of the H5 and H7 subtypes from wild birds to gallinaceous poultry, and through the host adaptation process acquire changes in the hemagglutinin gene that confer high pathogenicity (Brown et al., 2017). Prior 2002, there was only one reported isolation of an HPAIV strain from free-living birds that were not known to be associated with infected domestic poultry (Becker, 1966). Early detection and culling of a HPAI infected flock that resulted from a mutated LPAI virus resulted in eradication of that HPAI virus as it was only present in that area (Table 1) (Swayne et al., 2020). This situation changed dramatically with the appearance of the Gs/GD-lineage H5 HPAIV and its decedents in free-living birds since 2002 (Stallknecht & Brown, 2017). Since 2005, HPAIV H5 strains have been detected in migratory birds, especially in species of ducks and geese. Now, HPAIV H5 has been detected in more than 50 species of wild birds in Asia, Europe and Africa (Stallknecht & Brown, 2017). Figure 1 shows the detections of HPAI in European wildlife and poultry from 2016 early 2021. The presence of HPAIV H5 strains in wild birds including migratory birds has resulted in a major increase of the risk of H5 outbreaks in poultry. So recent incursions of HPAI in European commercial poultry are more readily associated with the direct introduction of the HPAIV through contact with infected wild birds or fomites contaminated with the HPAIV. This risk is further increased by the substantial number of free range and organic layer and broiler flocks that have a significantly higher risk of introduction of AI than indoor-housed flocks (Bouwstra et al., 2017). It is to be expected that the number of free range and organic flocks will further increase due to the consumers' demand. The endemic presence of HPAI H5 strains in Eurasian and African wild birds and the poultry industry of many countries in Asia and Africa means that mass culling of infected birds in an area does not necessarily eradicate the HPAI strain, it can reoccur in an area at any time by contact with infected wild birds. Due to the endemic state of a number of HPAI H5 subtypes in the Eurasian-African wild birds (H5N1, H5N2, H5N4, H5N5, H5N6, H5H8, H5N9), it has become very unlikely that HPAI H5 will disappear from the wild birds in the coming decades. This creates a continuous, seasonal threat of HPAI H5 outbreaks for the decades to come (Su et al., 2015; Lycett et al., 2016).

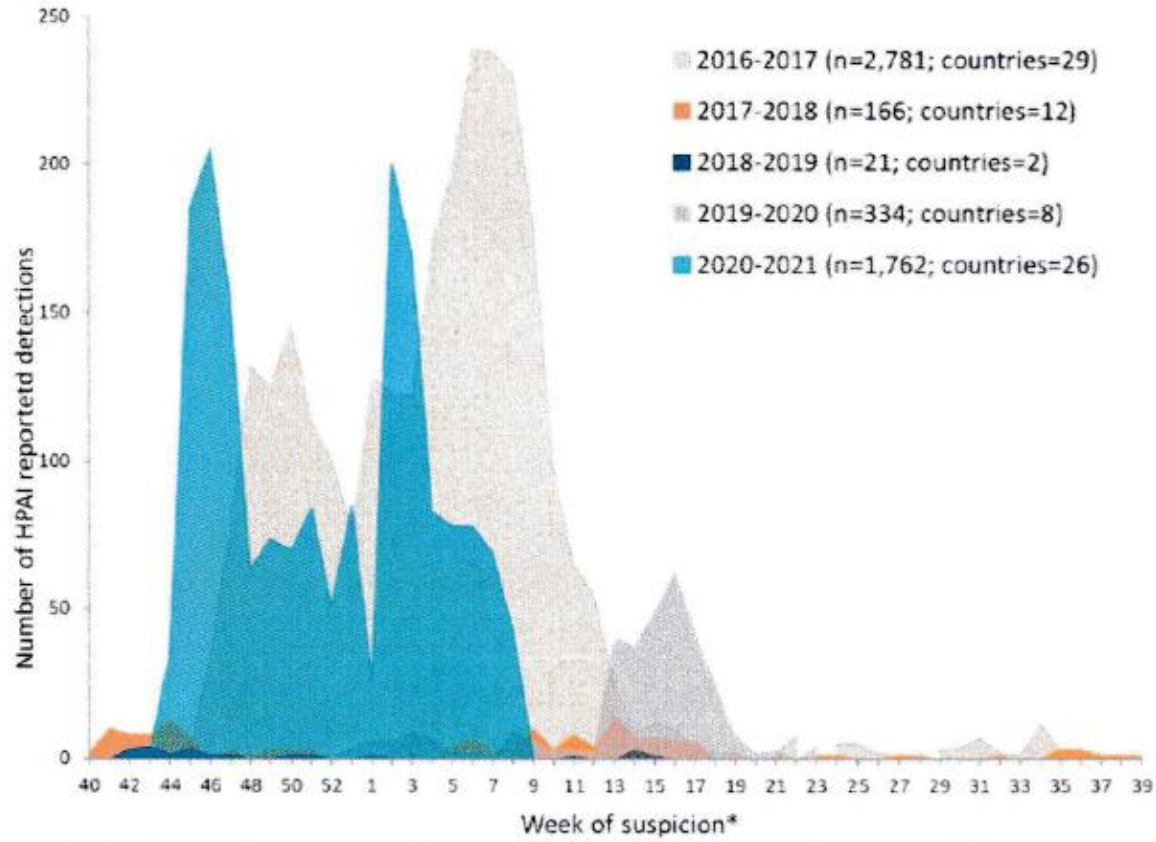

Figure 1: Distribution of total number of HPAI virus detections reported in Europe in the seasons 2016–2017 (green), 2017–2018 (orange), 2018–2019 (blue), 2019–2020 (grey), and 2020–2021 (turquoise) by week of suspicion, 28 September 2016 – 23 February 2021 (n=5,064)

A high number of outbreaks of HPAI H5 affects the sustainability of the global poultry industry that has become the major supplier of animal protein for human consumption worldwide and depends heavily on international trade of products and breeding stock. HPAI outbreaks cause a wide variety of damage: culling of flocks, animal welfare issues, trade barriers, disruption of the industry, damage to the consumer's image of the industry and its products, discussions about potential zoonotic risks, downgrading of eggs and meat due to long-lasting indoor housing of organic/free range flocks. For decades, the fight against HPAI has been based on (1) prevention of introduction of virus, (2) reduce likelihood of infection of virus once virus is introduced, (3) prevent movement of virus from a premise with infected birds to another premise and, if possible (4) eliminate/eradicate the virus (Swayne et al., 2020). For a number of reasons, vaccination against HPAI is not recommended for countries where the disease is not endemic and that can afford stamping-out policies. Until recently, vaccination against HPAI could only be performed by using inactivated vaccines using whole virus antigens which were able to induce high levels of protection against clinical disease strains that were antigenically close to the antigen, albeit they did not necessarily prevent infection. Use of these AI vaccines has been limited by the impossibility of differentiating vaccinated/infected from vaccinated/non-infected animals (DIVA approach). A major concern was that through trade or movement of apparently uninfected animals or products, the disease could spread further or might be exported to other countries. For this reason,

export bans have been imposed on countries enforcing a vaccination policy (Capua & Marangon, 2003). For many countries and companies, export bans are very damaging.

The set of rules for the battle against HPAI including the rules of trade was designed decades ago for the situation of before 1996 (Table 1). Since then, the global HPAI situation has changed dramatically for the worse. At the same time major progress has been made on vaccines and diagnostic tools for AIV. New generations of vaccines against H5 have been developed that allow DIVA monitoring as they only induce antibodies against the H5 antigen. Screening for antibodies against the conserved matrix or nucleoprotein allows detection of any field infection using routine commercially available ELISA tests. RT-PCR using primers for the conserved Matrix gene will not be able to detect a DIVA vaccine that only expresses the H5 hemagglutinin gene. RT-PCR and on-site tests have become both widely available and affordable. Several of the H5 vaccines (e.g., live-vector vaccines, RNA-vaccines) are not only inducing antibodies against H5 as the traditional inactivated vaccines do, but also T-cell immunity due to the transient of long-lasting replication. It has been shown that this broadens the induced protection against H5 strains (Rauw et al., 2011; Gardin et al., 2016).

The question is whether the traditional, internationally (OIE) prescribed content of the toolbox for the fight against HPAI is still suitable for the current HPAI situation. Is it responsible and sustainable to continue in the old way and consciously not make use of the technological progress while the risk of HPAI outbreaks is and will continue to be greatly increased? And that while the criticism from consumers, customers and politicians is increasing? Would it be possible to update the contents of the toolbox in order to reduce the risk of HPAI outbreaks and related damages and increase durability? Adjustment of the approved toolbox is not possible without simultaneous adjustment of the trade rules, because the trade in poultry products and breeding material is essential for the global poultry industry.

Table 1. Comparison of the global HPAI situation and tools before and after 1996

Parameter	Before 1996	From 1996, last years
Frequency HPAI outbreaks	Rare	Frequent
Size outbreak	Small area, short period	Countries/continents, endemic in big areas
Eradication HPAI strain post culling	Yes	No, only locally
HP in wild (migratory) birds (mammals)	No	Yes
Illness/mortality in humans	No	Yes (mainly in developing countries)
Housing chickens	Inside	Increasing free range/organic

Image/understanding of public, politicians, media	Understanding	Decreasing
Trade problems	Relatively limited (frequency, size)	More often, longer
Vaccines	Only inactivated vaccines, complete virus, drift, homology	Also new technology, genetically modified live vector vaccines, RNA vaccines (replication)
Mass application	No (2x injection in field)	Mostly no (hatchery injection)
DIVA monitoring possible	Hardly, very complicated, limited	Yes (new technology vaccines)

To summarize, the fight against HPAI has been based on (1) prevention of introduction of virus, (2) reduce likelihood of infection of virus once virus is introduced, (3) prevent movement of virus from a premise with infected birds to another premise and, if possible (4) eliminate/eradicate the virus (Swayne et al., 2020). Use of new generations of DIVA vaccines against HPAI for poultry or poultry types at risk might be a valuable additional tool to decrease the likelihood of infection of virus once the virus is introduced. The use of reliable and affordable DIVA monitoring and surveillance according to internationally approved standards will be required for vaccinated flocks to prevent transmission of HPAI with poultry from country to country.

PVSG is in favour of an open-minded evaluation of the possibilities of using modern AIV vaccines and associated DIVA diagnostics and the associated monitoring and surveillance, whereby the trade in poultry and poultry products may not be disrupted. An approved package can then allow countries to better protect poultry against HPAI outbreaks in certain seasons or to better protect poultry at risk (e.g., free range and organic poultry) from HPAI outbreaks, which benefits national and international poultry farming and animal welfare.

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