Comments on Avian Influenza of Terrestrial Animal Health Code

In the first half of 2020, OIE proposed to revise chapters on avian influenza of Terrestrial Animal Health Code, aiming to distinguish requirements for the notification of high and low pathogenicity avian influenza. In the process of revision, the drafting experts agreed to remain the high pathogenicity avian influenza viruses as OIE-listed diseases, but it's controversial over whether or not to include H5/H7 low pathogenic avian influenza in the listed diseases. At last, the drafting experts recommended to delete low pathogenicity avian influenza from the list, except the low pathogenicity avian influenza that "causing a significant impact on animal or public health". Once the amendment is accepted, it means that low pathogenic avian influenza will not need to be notified to the OIE. Considering its wide distribution in the world, high tendency to mutate into high pathogenic avian influenza and the ability to infect people, if the disease is no longer included in the list, the real status of Avian Influenza in the world will hard to be fully and truly reflected. Therefore, it's recommended to retain the current avian influenza notification requirements. Meanwhile, after extensively soliciting opinions of domestic animal health experts, we are submitting the following comments.

CHAPTER 10.4.

Infection with High Pathogenicity Avian Influenza Viruses

GENERAL COMMENT 1: We agreed with the commission's view of "decisions regarding these specific LPAIV should be made based on the gathered data at an appropriate point in time", but we think "while that decision is pending, the members can respond to the event by considering it as 'emerging disease'" is not appropriate.
RATIONALE: According to the definition of "emerging disease", the disease that "causing a significant impact on animal or public health" can be notified to OIE. To satisfy requirements of the definition also need huge data on population level to prove which LPAIV strain has significant impact on public health. There are great difficulties to interpret and apply this criterion to the group of LPAIV. Therefore, it is not feasible to identify which LPAIV strains shall be notified to the OIE as "emerging disease".

GENERAL COMMENT 2: There is a contradiction between the commission's viewpoint in Sep. 2020 and the *ad hoc* Group's viewpoint in 2019 about "Assessment of 'H5 and H7

low pathogenicity avian influenza' against the criteria for the inclusion of diseases, infections and infestations in the OIE list in Chapter 1.2. of the Terrestrial Code".

RATIONALE: In 2019, *ad hoc* Group, without basing on the gathered data on population level, it reached the conclusion that H5 and H7 low pathogenicity avian influenza does not meet the criteria for the inclusion of diseases, infections and infestations in the OIE list disease described in Chapter 1.2. of the Terrestrial Code due to the assessment for 4(a) criterion was inconclusive. In 2020, the commission's report described "The public health impact of the LPAI should be taken into consideration at the population level, rather than individual level. So far, ther is no related data or evidence available to demonstrate which LPAIV strains satisfy requirements of infecting human and causing severe consequence. This means the 2020 commission report overturned the 2019 assessment.

GENERAL COMMENT 3: Considering the above 2 opinions, and the H5 and H7 LPAIV mutate easily and usually cause human infection. From the perspective of global public health security, it is recommended all H5 and H7 LPAI should be notified to the OIE.

RATIONALE: The mutation of LPAIV occurs quickly and may causes human infection. As we know, AIVs have a broad range of host and spread rapidly [1-3]. The LPAIV were usually confirmed to be the direct ancestors of the HPAI strains [4, 5]. The latest research confirmed that a minority population (0.06%) of viruses with an HP HA cleavage site sequence were mutated from a LP H7N3 virus and could be rapidly mutated in chickens to a HPAI[6]. This research indicates that LPAI can mutate into HPAI easily and rapidly. Currently, eleven different subtypes of AIVs have been confirmed as capable of infecting humans at least: H5N1, H5N6, H6N1, H7N2, H7N3, H7N4, H7N7, H7N9, H9N2, H10N7, and H10N8, nine of which were LPAI viruses. Therefore, the strict monitoring and notification procedures of LPAI are essential to strengthen the public health and enhance the international trade order.

References:

[1]Ping, J., et al., Low-pathogenic avian influenza virus A/turkey/Ontario/6213/1966 (H5N1) is the progenitor of highly pathogenic A/turkey/Ontario/7732/1966 (H5N9). The Journal of general virology, 2012. **93**(Pt 8): p. 1649.

[2]Yang, Y., et al., Comparison between human infections caused by highly and low pathogenic H7N9 avian influenza viruses in Wave Five: Clinical and virological findings. Journal of Infection, 2019. **78**(3): p. 241-248.

[3]Seekings, A., et al., Direct evidence of H7N7 avian influenza virus mutation from low to high virulence on a single poultry premises during an outbreak in free range chickens in the UK, 2008. Infection, genetics and evolution, 2018. **64**: p. 13-31.

[4]Shi, J., et al., Rapid evolution of H7N9 highly pathogenic viruses that emerged in China in 2017. Cell host & microbe, 2018. **24**(4): p. 558-568. e7.

[5]Monne, I., et al., Emergence of a highly pathogenic avian influenza virus from a

low-pathogenic progenitor. Journal of virology, 2014. **88**(8): p. 4375-4388.
[6]Beerens, N., et al., Emergence and selection of a highly pathogenic avian influenza H7N3 virus. Journal of Virology, 2020. **94**(8).

Article 10.4.20.

Text as presented:

~~Some~~ H5 and H7 low pathogenicity avian influenza viruses have the potential to mutate into high pathogenicity avian influenza viruses, but ~~and currently~~ it is not possible to predict ~~whether and~~ which viruses will mutate or when ~~this~~ these mutations will occur.

Proposed alternative text:

It is not possibe to predict which H5 and H7 low pathogenicity avian influenza viruses will mutate into high pathogenicity and when these mutations will occur, but they have the potential to mutate into high pathogenicity avian influenza viruses.

RATIONALE: It is well known that H5 and H7 low pathogenicity avian influenza viruses have the potential to mutate into high pathogenicity avian influenza viruses, and whether it is possible to predict "which viruses will mutate or when this these mutations will occur" will not affect this fact. It's recommended focusing on the key point of "H5 and H7 low pathogenicity avian influenza viruses have the potential to mutate into high pathogenicity avian influenza viruses" to alert members to enhance risk assessment and monitoring.

CHAPTER 3.3.4.

Avian Influenza

Line 2-4

Text as presented:

AVIAN INFLUENZA
(INCLUDING INFECTION WITH HIGH PATHOGENICITY AVIAN INFLUENZA VIRUSES)

Proposed alternative text:

AVIAN INFLUENZA
~~(INCLUDING INFECTION WITH HIGH PATHOGENICITY AVIAN INFLUENZA VIRUSES)~~

RATIONALE: The Avian influenza chapter in Terrestrial Manual is the laboratory diagnostic standard for avian influenza virus and should not deliberately emphasize the detection method of HPAI baseon controversy in the corresponding chapter of Terrestrial Code. Furthermore, the chapter 10.4. requires the monitoring of both HPAI and LPAI, and corresponding diagnostic methods should be given in the current chapter of the Terrestrial Manual.

Line 65-69(track change edition)

Text as presented:

~~Agar gel immunodiffusion tests can be used to detect antibodies to these antigens. Concentrated virus preparations containing either or both type of antigens are used in such tests. Not all species of birds develop demonstrable precipitating antibodies. Enzyme-linked immunosorbent assays have been used to detect antibodies to influenza A type-specific antigens in either.~~

Proposed alternative text:

Agar gel immunodiffusion tests can be used to detect antibodies to these antigens. Concentrated virus preparations containing either or both type of antigens are used in such tests. Not all species of birds develop demonstrable precipitating antibodies. Enzyme-linked immunosorbent assays have been used to detect antibodies to influenza A type-specific antigens in either

RATIONALE: The AGID method has been mentioned many times in the article and it is recommended to keep AGID method in the summary section.

Line 135

Text as presented:

Virus isolation is the ~~"gold standard"~~reference method but is laborious and time insensitive

Proposed alternative text:

Virus isolation is the “gold standard” as reference method but is laborious and time insensitive

RATIONALE: Virus isolation is the “gold standard” of most viruse diagnosis, not just a reference method.

Line 139-143

Text as presented:

When pooling samples the brain should be collected and processed first (to avoid cross contamination with other tissue types) and kept separate as presence of virus in the brain may be an indicator of HPAI. Further pools should be made consistent with known virus tropisms between HPAI and LPAI, i.e. grouped at the level of respiratory, systemic and gastrointestinal.

Proposed alternative text:

When pooling samples the brain should be collected and processed first (to avoid cross contamination with other tissue types) and kept separate as presence of virus in the brain may be an indicator of HPAI(add reference). Further pools should be made consistent with known virus tropisms between HPAI and LPAI, i.e. grouped at the level of respiratory, systemic and gastrointestinal.

RATIONALE: It is better to add one reference after the description, because some LPAIVs such as H9N2 are proven to be isolated in brain[1].

Reference:

[1]Soda K, Asakura S, Okamatsu M, et al. H9N2 influenza virus acquires intravenous pathogenicity on the introduction of a pair of di-basic amino acid residues at the cleavage site of the hemagglutinin and consecutive passages in chickens[J]. Virology journal, 2011, 8(1): 64.

Line 681-682

Text as presented:

viruses under emergency vaccination programs, but since the 2000s, most vaccines have been against H1 and H3 swine influenza A viruses.

Proposed alternative text:

~~viruses under emergency vaccination programs, but since the 2000s, most vaccines have been against H1 and H3 swine influenza A viruses.~~

RATIONALE: The description of SIV vaccine here is unnecessary. It is recommended to delete it.