ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD

DISCUSSION PAPER

Assessment of the risk of avian influenza viruses via the food chain

Issue

In 2003, the Committee carried out a risk assessment concluding that the risk of acquiring avian influenza through the food chain is low, and there is no direct evidence to support this route of infection. This view was retained by the Committee in 2006. Following the recent outbreaks of avian influenza on poultry farms in the UK and in other countries, the Agency has prepared a risk assessment taking into account some additional materials since the subject was last reviewed by the Committee. The Agency would like to ask the Committee to review this risk assessment and also indicate whether it is appropriate to classify the current health risk related to avian influenza viruses via the food chain as **very low**.

Background

1. In 2003, following an outbreak of avian influenza in poultry in the Netherlands, the Agency asked the Committee's advice on the risk to human health from exposure to avian influenza viruses through the food chain. While the Committee agreed in principle that the Agency's advice estimating that there is a low risk to human health via the food chain seemed accurate, the Committee agreed that a more formal assessment would be useful.

2. The Committee's virologist at the time, in collaboration with experts in the field, reviewed the subject and prepared a short report concluding that the risk of acquiring avian influenza through the food chain is low, and there is no direct evidence to support this route of infection. However, more studies of the factors affecting human infection, and studies of occupationally exposed groups, should be encouraged (ACM/663, **Annex B).** https://www.food.gov.uk/sites/default/files/mnt/drupal_data/sources/files/multimedia/pdfs/acm663.pdf.)

3. On 4 December 2003, the Committee endorsed this assessment http://acmsf.food.gov.uk/committee/acmsf/acmsfmeets/acmsfmeet2003/acmsf50thmeeting/acmsfminutes041203. In the following 2 years highly pathogenic avian influenza H5N1 circulated widely in poultry in S.E. Asia, Russia and Turkey. Over this period there were more than 100 cases of human infection with H5N1. On 16th November 2005, an ACMSF ad hoc group of influenza virologists and epidemiologists met to review new information on avian influenza and to discuss its implications for foodborne

transmission. Overall the group did not think that the new information required a significant change to the Committee's risk assessment.

4. In December 2005, the ACMSF agreed to establish a Working Group on avian influenza. In March 2006 the ACMSF Working Group met to review again the current ACMSF risk assessment of acquiring avian influenza through the food chain. The Group concluded that there was no new information to consider at this time, but a watching brief on new or emerging scientific evidence and publications needed to be maintained (ACM/783).

5. Following recent outbreaks of avian influenza on poultry farms in the UK, EU and globally, the Agency feels that it would be timely to revisit the question of the risk of acquiring avian influenza via the food chain to determine whether the Agency's existing advice on risk remains appropriate. The Secretariat has prepared a qualitative risk assessment (Annex A) which the Committee can use to help its evaluation.

6. The assessment considers some additional information available since the Committee last considered this issue such as up to date data on outbreaks and recent evidence and advice from organisations such as the World Health Organisation (WHO). The risk assessment uses the EFSA risk level classification as below in order to describe the output:

Risk Level Classification

Probability Category	**Interpretation**
Negligible	So rare that it does not merit to be considered
Very Low	Very rare but cannot be excluded
Low	Rare, but does occur
Medium	Occurs regularly
High	Occurs very often
Very High	Events occur almost certainly

Table from EFSA (2006) modified from OIE (2004)

7. Based on this approach, the Agency's estimate of the level of risk related to avian influenza viruses via the UK food chain is considered to be **very low.** A number of uncertainties are acknowledged but were not considered sufficient to alter the risk estimate. This estimation is based on thorough cooking and proper handling of food.

The Committee is asked:

- To review and comment on the attached risk assessment; and

- To advise whether it is in agreement with the Agency's advice that the overall health risk related to avian influenza viruses via the food chain is **very low.**

Secretariat September 2015

Annex A

Avian Influenza viruses - risk assessment related to exposure via the food chain

Statement of purpose

- To assess the risk to consumers from Avian Influenza viruses via the food chain.

Hazard Identification

1. Avian influenza or “bird flu” is a highly infectious viral disease of birds. Avian influenza viruses are negative single-stranded enveloped RNA viruses (Leong *et. al*., 2008). Multiple strains or types of avian influenza viruses are known, some are more severe in their clinical impact than others. Influenza viruses are divided into three types: A, B and C. All of these infect humans, but only influenza A viruses have been reported from birds and other animals (IFST, 2013).

2. Avian influenza viruses can be further divided into highly pathogenic (HPAI) and low pathogenicity (LPAI) strains based on their ability to cause disease in poultry. Highly pathogenic viruses result in high death rates (up to 100% mortality within 48 hours) in some poultry (galliforme) species (e.g. chickens and turkeys). Infection of poultry with LPAI viruses may cause no disease or only mild illness (such as ruffled feathers and a drop in egg production) and may not be detected. (The Centre for Disease Control and Prevention, 2015, WHO, 2014).

3. Avian influenza viruses may be further divided into subtypes on the basis of the antigenic properties of their haemagglutinin (H1-H16) and neuraminidase (N1-N9) surface glycoproteins (The Centre for Food Security and Public Health, 2014). All highly pathogenic avian influenza viruses that cause generalised rather than respiratory disease belong to either the H5 or H7 subtypes.

4. Human infections with avian influenza viruses are rare (WHO, 2014). Most avian influenza viruses do not infect humans; however some, such as H5N1 and H7N9, have caused serious infections in people. There are many subtypes of avian influenza viruses, but only some strains of five subtypes have been highly virulent in humans (H5N1, H7N3, H7N7, H7N9, and H9N2) (Leong *et al*., 2008). However, in December 2013, H10N8 virus infection in a person was reported in Nanchang, Jiangxi Province, China and two more human cases followed. The initial reported case was in a 73-year-old female who visited a local live poultry market four days before the onset of her illness (Zhang *et al*., 2014). AI viruses which can be regarded as low pathogenicity in birds appear to be capable of causing severe illness in humans. For example, infections with LPAI H7N9 viruses have caused more than 100 hospitalised human cases of severe influenza in China since February 2013 with a case fatality rate exceeding 25%

(Kreijtz et al., 2013). Most of these human infections presented with severe viral pneumonia.

Exposure assessment

5. **Transmission in poultry** - Avian influenza viruses are most often spread by contact between infected birds and healthy birds. The viruses may also be spread indirectly through contact with contaminated equipment and materials. The avian influenza viruses are found in secretions from the nares (nostrils), mouth, and eyes of infected birds and are also excreted in faeces. Contact with contaminated faeces is the most common means of bird-to-bird transmission, although aerosols are another important means of transmission, especially within poultry houses (FAO, 2015).

6. There is **uncertainty** about how HPAI viruses are initially introduced into poultry flocks. Wild waterfowl, e.g. ducks and geese, are considered to be a natural reservoir for all type A influenza viruses. There is some evidence to suggest that wild waterfowl can transmit avian influenza to domestic poultry (FAO, 2015). Low pathogenicity viruses circulate in wild waterfowl. It is likely that highly pathogenic avian influenza viruses arise through mutation after low pathogenicity viruses of H5 or H7 subtypes are introduced into poultry (APHA, personal communication).

7. The spreading, or wider distribution of the disease, takes place within flocks or sizeable numbers of poultry and is largely influenced by production and marketing practices. The spread of avian influenza between poultry facilities almost always results from the movement of infected birds or contaminated people, water and equipment (including clothing, boots, and vehicles)(FAO, 2015). Avian influenza viruses can also be found on the outer surfaces of egg shells (but rarely inside); therefore, egg transfer is a potential means of avian influenza transmission. Airborne transmission of avian influenza viruses from farm-to-farm is considered unlikely (FAO, 2015). Outbreaks of avian influenza continue to occur. Recent outbreaks of avian influenza at bird farms in the UK, involved LPAI H7N7 on 2 February 2015 in chickens at a farm in Hampshire, and HPAI H5N8 strain in ducks on premises in East Yorkshire on 16 November 2014; the strain was also found in birds in Germany, The Netherlands, Italy and Hungary. On 13 July 2015, there was an outbreak of highly pathogenic H7N7 at a large laying hen premises in Lancashire; the same strain was also found in Germany. Highly pathogenic H7N7 was also responsible for an outbreak in a commercial flock of chickens in 2008 in the UK, as well as several other outbreaks in Europe in the last five years. In March 2015, HPAI H5N1 strain (Asian lineage) was detected in poultry and wild birds in Bulgaria, while in Romania this virus was found in wild birds only. The last reported case of HPAI H5N1 in the UK was in early 2008 in wild birds and in poultry in 2007. The HPAI H5N1 strain has caused outbreaks in the UK in the past (January 2007 on a commercial turkey farm in Suffolk, November 2007 on turkey farms in Norfolk and Suffolk). Other outbreaks linked to LPAI H7N2 in a market and a poultry farm in N. Wales in March 2007 and a LPAI H7N3 strain on three poultry

farms in Norfolk were reported in 2006.When an outbreak of avian influenza is suspected in poultry in the UK, the Animal and Plant Health Agency puts in place controls aiming to eradicate infection and prevent the spread of disease. Samples are taken to confirm the presence of disease and to determine which AIV subtype is present. In the event that the virus is an notifiable avian disease (NAD) H5 or H7 subtypes irrespective of pathotype – LPAIV or HPAIV , the infected premises are depopulated and the carcases and eggs on the premises disposed of. An investigation is also carried out and contact premises are investigated to ensure infected birds and products do not enter the food chain. Where the subtype is found not to be NAD (H5 or H7 subtypes), movement restrictions are lifted and no culling takes place. Measures relating to culling, depopulation, establishing protection and surveillance zones around affected areas and conducting epidemiological investigations are carried out across the EU by all affected Member States (APHA personal communication).

8. A recent study (Bertran and Swayne, 2015) was carried out, where ferrets were exposed to different HPAI H5 and H7 subtypes of avian influenza viruses through consumption of infected chicken meat. The dose of virus needed to infect ferrets through consumption was much higher than via respiratory exposure and varied with the virus strain. Additionally, HPAI H5N1 produced higher titters in the meat of infected chickens and more easily infected ferrets than the HPAI H7N3 or H7N7 viruses.

9. **Transmission to humans** - Another **uncertainty** in this assessment relates to the exact route of transmission of avian influenza from birds to humans. Influenza A viruses have infected many different animals, including poultry, pigs, cats, whales, horses, and seals. However, certain subtypes of influenza A virus are specific to certain species, except for birds, which are hosts to all known subtypes of influenza A viruses (Centre for Disease Control and Prevention, 2015).

10. Avian influenza outbreaks in humans in recent years have shown that there is no absolute species barrier between humans and birds (ACMSF, 2003). Avian influenza viruses may be transmitted from animals to humans in two main ways; either directly from birds or contaminated environments or via an intermediate host, for example a pig.

11. Epidemiological evidence suggests that most human infections with avian influenza viruses have occurred following direct or close contact with infected (ill or dying) poultry (Hayden and Crossier, 2005).

12. While human infections are often limited to conjunctivitis or mild respiratory disease, some subtypes of avian influenza viruses can cause severe illness. In particular, Asian lineage HPAI H5N1 and LPAI H7N9 viruses have caused rare but life-threatening infections in humans (Brown, 2010).

13. Most avian influenza viruses are probably acquired via the respiratory tract, but the eye may also act as an entry point. Person-to-person transmission of H5N1 viruses seems to be rare, and is documented to

require close, unprotected contact. Likewise, a few family clusters suggest that the LPAI H7N9 virus might be transmitted between humans during close contact, but common source exposure is hard to rule out, and most infected people did not seem to transmit this virus to other individuals (The Centre for Food Security and Public Health, 2014). EFSA's BIOHAZ panel in 2006 reported that it is likely that a high dose of virus may be needed to initiate an infection and that a readily accessible entry route for the virus does not exist. The panel concluded that experimental studies would help to fill in the gaps related to route of virus entry into mammals (EFSA, 2006).

14. Human exposure is considered most likely during slaughter, plucking and butchering of birds, exposure via live bird markets (more common in the Far East) and backyard poultry husbandry practices in rural areas (The Centre for Food Security and Public Health, 2015).

15. However, a minority of cases of human infection in Vietnam could not be related to close/direct contact with infected birds and it has been speculated that it may be related to consumption of uncooked infected poultry or of water contaminated with infected bird or poultry faeces (IFST, 2013). In 2014 WHO reported that there have been a few cases of avian influenza H5N1 human infections possibly linked to the consumption of uncooked poultry products (raw blood dishes).

16. HPAIV can infect poultry (not just chickens, e.g. turkey and duck) in a systemic manner meaning that virus can be detected in muscle (e.g. thigh and breast) and other tissues, in addition to respiratory and gastrointestinal tracts (APHA personal communication). Nevertheless the risk of HPAI virus strains entering the UK food chain is likely to be contained, because clinically affected poultry will be excluded from slaughter as a result of pre-slaughter veterinary checks. Therefore, the only likely exposure in poultry meat could be to LPAI viruses (assumption). Low pathogenicity viruses are rarely systemic infections in poultry and generally limited to the respiratory and intestinal tract in poultry. Consequently, there is a low risk of contamination of chicken carcasses, although cross contamination during slaughter cannot be excluded (**uncertainty**). Sick birds are unlikely to produce eggs, although eggs laid in the early phase of the disease could contain the virus. Eggs can contain the virus both inside, in the egg membranes, the white and the yolk, and outside, on the shell. This is an **uncertainty** particularly as eggs are more likely consumed raw or uncooked than poultry.

17. There is no epidemiological evidence that avian influenza can be transmitted to humans through consumption of thoroughly cooked food, notably poultry and eggs (EFSA, 2006; ACMSF 2003 and 2007). EFSA and other organisations such as the WHO generally support longstanding food safety advice that chicken and eggs be thoroughly cooked in order to protect consumers from possible risks of food poisoning.

18. The H5N1 virus is reported to be able to survive sometimes for extended periods in the environment. Avian influenza viruses present in faeces or egg shells can survive for several weeks (European Parliament, 2015), although other data indicate this is likely to be days in faeces (APHA personal communication). Avian influenza viruses have been shown to survive in the environment for >3 months at 4°C, but much higher rates of inactivation occur at higher temperatures (>6 x 10^6 loss of infectivity within 2 weeks at 20°C (ACMSF, 2003). When protected from sunlight, virus persistence on various surfaces, or in soil, ranged from less than 2 days to more than 2 weeks (and possibly several months), at temperatures ranging from 4°C to 15-30°C (59-86°F). The extent of environmental persistence of these viruses seems to be variable and adds another **uncertainty** to the assessment.

19. If the virus is present in poultry meat, it can survive in this environment under chilling and freezing conditions with little effect on the viability of the virus; in general, low temperatures prolong the survival of the virus in poultry tissue. All avian influenza viruses are reported to be relatively susceptible to disinfectants including sodium hypochlorite, 60% to 95% ethanol, quaternary ammonium compounds, aldehydes (glutaraldehyde, formaldehyde), phenols, acids.

20. Influenza A viruses can be inactivated by temperatures of 56-60°C (133-140°F) for a minimum of 60 minutes (or higher temperatures for shorter periods), as well as ionising radiation or extremes of pH (pH 1-3 or pH 10-14); (The Centre for Food Security and Public Health, 2014). Avian influenza viruses are considered to be heat labile viruses (Swayne *et. al*., 2004) so cooking poultry and poultry products thoroughly will destroy them. There is a degree of **uncertainty** here as studies have not been conducted on all the known avian influenza viruses although no information has been found which would suggest that any particular subtype is likely to behave differently in terms of heat stability.

21. There is no evidence that properly handled and thoroughly cooked poultry or eggs can be a source of human avian influenza infection; the primary risk factor for human infection from all sources of literature appears to be direct or indirect exposure to infected live or dead poultry or contaminated environments, such as live bird markets.

Hazard Characterisation

22. Avian influenza results from infection by viruses belonging to the species influenza A virus, genus influenza virus A and family Orthomyxoviridae. Influenza A viruses are classified into subtypes based on two surface proteins, the hemagglutinin (HA) and neuraminidase (NA). At least 16 hemagglutinins (H1 to H16), and 9 neuraminidases (N1 to N9) have been found in viruses from birds The viral HA, and to a lesser extent the NA, are major targets for the immune response. There is ordinarily little or no cross-protection between different HA or NA types.

23. Avian influenza viruses are defined as highly pathogenic or low pathogenicity by their ability to cause severe disease in intravenously inoculated young chickens in the laboratory, or by possession of certain genetic features that have been associated with high virulence in HPAI viruses such the sequence at the HA cleavage site (World Organization for Animal Health, 2014). With rare exceptions, highly pathogenic avian influenza viruses found in nature have always contained the H5 or H7 hemagglutinin.

24. The two most commonly reported avian influenza viruses from human clinical cases have been the Asian lineage H5N1 viruses, and recently, H7N9 (low pathogenicity) viruses in China. Although there have been no reported cases of humans infected with either of these two strains of avian influenza in the UK, the picture is different globally. The WHO reported in July 2015 that between 2003 and 2015, a total of 844 human cases of H5N1 infections resulting in 449 deaths; Egypt was the country associated with the highest rates of infection and mortality (WHO, 2015). On 23 February 2015, the WHO reported a total of 571 laboratory-confirmed cases of human infection with H7N9 virus, including 212 deaths; 568 cases from China (WHO, 2015).

25. In 2013, a WHO risk assessment suggested that the H7N9 virus may have greater ability to infect mammalian species, including humans, than most other avian influenza viruses (WHO, 2013).

26. For both viruses, there have been some reports of limited human to human transmission, usually as a result of very close contact between family members. Current evidence suggests that avian H7N9 viruses do not transmit easily from poultry or environments to humans, although their transmissibility may be greater compared with avian H5N1 viruses (WHO, 2014).

27. Illnesses caused by other subtypes have also been reported sporadically, with documented clinical cases caused by H9N2, H6N1 and multiple H7 and H10 avian influenza viruses. Viruses that tend to cause milder illnesses (e.g., H9N2 viruses) are less likely to be identified than those causing severe disease.

28. Influenza A viruses are very diverse, and two viruses that share a subtype may be only distantly related. The high variability is the result of two processes, mutation and genetic re-assortment. Mutations cause gradual changes in the HA and NA proteins of the virus, a process called ‘antigenic drift” (Fenner *et. al*., 1987). Once the proteins have mutated sufficiently, immune responses against the former HA and NA may no longer be protective (The Centre for Food Security and Public Health, 2014).

29. The symptoms of avian influenza in humans vary considerably depending on the strain or subtype of the virus involved. The reported signs and symptoms of low pathogenic avian influenza virus infections in humans

have ranged from conjunctivitis to influenza-like illness (e.g., fever, cough, sore throat, muscle aches) to lower respiratory disease (pneumonia) requiring hospitalisation. Highly pathogenic avian influenza virus infections in humans have been associated with a wide range of illness from conjunctivitis only, to influenza-like illness, to severe respiratory illness (e.g. shortness of breath, difficulty breathing, pneumonia, acute respiratory distress, viral pneumonia, respiratory failure) with multi-organ disease, sometimes accompanied by nausea, abdominal pain, diarrhea, vomiting and sometimes neurologic changes such as altered mental status and seizures (Centre for Disease Control and Prevention, 2015).

30. In the unlikely event of the viruses being present after cooking, the ACMSF has in 2003 advised that human defence mechanisms such as saliva, gastric acid and a lack of appropriate receptors in the gut needed for the virus to enter the body would prevent or limit infection following ingestion. EFSA in 2006 concluded that there is as yet no evidence that these viruses replicate in the human intestine.

31. Shu *et. al*., (2010) stated that many humans infected with H5N1 present with gastrointestinal tract symptoms, suggesting that this may also be a target for the virus. These authors demonstrated that H5N1 viruses can directly infect and replicate in human gut tissues. Human-adapted influenza A viruses preferentially bind to “human like” sialic acid receptors (SA)—α2,6—galactose (Gal)-terminated saccharides (SA—α2,6-Gal), whereas avian influenza A viruses show preference to receptors with “avian like” α2,3 linkages (SA-α2,3-Gal). Shu *et. al.,* (2010) reported that the SAα2,6- Gal receptor was abundantly distributed on epithelial cells throughout the GI tract, but the distribution of the SA-α2,3-Gal receptor gradually increased from the ileum to the rectum. The authors reported that their results showed that the human gut can be readily infected *ex vivo* by the H5N1 virus, and produces infectious viral particles in organ culture. An autopsy colonic sample from an H5N1-infected patient showed evidence of viral antigen expression in the gut epithelium (Shu *et. al*., 2010).

32. There remains some **uncertainty** regarding the ability of avian influenza viruses to cause infection via the gastrointestinal tract. Whilst the studies by Shu et al., (2010) demonstrate a potential for infection with H5N1 virus via the gastrointestinal tract human defence mechanisms such as saliva and gastric acid are likely to pose significant barriers to this occurring.

Risk characterisation

33. Taking into account the above components of this assessment and considering the uncertainties that have been flagged, the risk from avian influenza viruses from consuming thoroughly cooked poultry and poultry products including eggs and egg products is considered to be **very low** (very rare but cannot be excluded). This estimation is considered to be the same for highly pathogenic and low pathogenicity avian influenza viruses as there is no information to suggest that subtypes should be

considered differently in terms of risk from human oral exposure (**uncertainty**). The risk estimate is based on hygienic handling and preparation of foods, ensuring appropriate storage and transport and thorough cooking. In the event of improper handling or cooking of poultry and poultry products, there will be more **uncertainty** relating to the overall risk estimate, largely due to lack of information on whether such foods might in reality be contaminated with the virus.

Uncertainties

34. Key uncertainties associated with this assessment are outlined in Appendix 1.

Overall risk

35. For thoroughly cooked and hygienically handled and stored food the risk of infection with avian influenza viruses via (handling and) consumption is considered to be **very low**. Uncertainties associated with this assessment have been highlighted but are not currently considered to make a significant impact on the risk estimate.

Appendix 1: Key uncertainties

1. Exposure assessment: There is **uncertainty** about how highly pathogenic avian influenza viruses are initially introduced into poultry flocks and how they are transmitted between poultry.

2. Exposure assessment: There is **uncertainty** relating to the exact route of transmission of avian influenza from birds to humans.

3. Exposure assessment: The extent of environmental persistence of these viruses seems to be variable and adds another **uncertainty** to the assessment.

4. Exposure assessment: Studies tend to be undertaken with a limited number of strains. There may be **uncertainty** concerning the response to heat and other factors for the complete range of avian influenza viruses although no information has been found to suggest that any particular subtype should be treated differently.

5. Risk characterisation: In a scenario where food is not thoroughly cooked or properly handled, it is likely that there is a low risk of contamination of chicken meat with avian influenza virus, although cross contamination during slaughter cannot be excluded (**uncertainty**).

6. Risk characterisation: Sick birds are unlikely to produce eggs, although eggs laid in the early phase of the disease could contain the virus, this is likely to be the greatest **uncertainty** associated with a scenario relating to undercooking and improper handling and storage of food, particularly as eggs are more likely consumed raw or uncooked than poultry meat.

7. Risk characterisation: There is no information to suggest that high and low pathogenic subtypes should be considered differently in terms of risk from human oral exposure. This is an **uncertainty**.

References

1. ACMSF risk assessments

   https://www.food.gov.uk/sites/default/files/mnt/drupal_data/sources/files/multimedia/pdfs/acm663.pdf

   http://acmsf.food.gov.uk/sites/default/files/mnt/drupal_data/sources/files/multimedia/pdfs/acm768v2.pdf

   http://acmsf.food.gov.uk/sites/default/files/mnt/drupal_data/sources/files/multimedia/pdfs/850aiupdate.pdf

2. Bertran K. and Swayne D. (2014). High doses of highly pathogenic avian influenza virus in chicken meat are required to infect ferrets. *Veterinary Research*. 45 (60).

3. Brown I.H. Summary of avian influenza activity in Europe, Asia, and Africa, 2006-2009. (2010). Avian Disease 54 (1 Suppl):187-93.

4. The Centre for Food Security and Public Health, Iowa State University (last updated 2015). Avian Influenza.

   http://www.cfsph.iastate.edu/Factsheets/pdfs/highly_pathogenic_avian_influenza-citations.pdf

5. Centre for disease control and prevention factsheets on avian influenza; updated February 2014.

   http://www.cdc.gov/flu/avianflu/avian-in-humans.htm

   http://www.cdc.gov/flu/avianflu/virus-transmission.htm

6. European Food Safety Authority: Scientific report of the Scientific Panel on Biological Hazards on “Food as a possible source of infection with highly pathogenic avian influenza viruses for humans and other mammals”, *The EFSA Journal* 2006, 74, 1-29.

   http://www.efsa.europa.eu/en/efsajournal/pub/74r

7. European Food Safety Authority: Highly pathogenic avian influenza A subtype H5N8. The EFSA Journal 2014; 12(12):3941 [32 pp.].

   http://www.efsa.europa.eu/en/press/news/141215

8. European Parliament briefing on Avian Influenza, 2015.

   http://www.europarl.europa.eu/RegData/etudes/BRIE/2015/564358/EPRS_BRI(2015)564358_EN.pdf

9. FAO, 2015. Avian Influenza.

http://www.fao.org/avianflu/en/qanda.html

10. Fenner F., Bachmann P.A, Gibbs E.P.J., Murphy F.A, Studdert M.J, White, D.O. (1987). Orthomyxoviridae. In: *Veterinary Virology*. San Diego, CA: Academic Press Inc.; 1987. p.473-484.

11. Hayden, F. and Croisier, A. (2005). Transmission of Avian Influenza Viruses to and between Humans. *The Journal of Infectious Diseases* 192 (8): 1311-1314.

12. Institute of Food Science and Technology (IFST); 2013. Avian Influenza and Food.

http://www.ifst.org/knowledge-centre/information-statements/avian-influenza-and-food

13. Kreijtz, J.H.C.M., Veldhuis Kroeze, E.J.B., Stittelaar, K.J. de Waal, L., van Amerongen, G., van Trierum, S., van Run, P., Bestebroer, T., Kuiken, T., Fouchier, R.A.M. (2013). Low pathogenic avian influenza A(H7N9) virus causes high mortality in ferrets upon intratracheal challenge: A model to study intervention strategies. *Vaccine*, 31 (43): 4995-4999.

14. Leong H.K., Goh C.S., Chew S.T., Lim, C.W., Lin, Y.N., Chang, S.F., Yap, H.H.,Chua, S.B. (2008). Prevention and control of avian influenza in Singapore" (PDF). *Ann. Acad. Med. Singap.* 37 (6): 504–9. PMID 18618063. Retrieved 2009-04-15.

15. NHS choices advice on avian influenza

http://www.nhs.uk/conditions/avian-flu/pages/introduction.aspx

16. Swayne, D.E., and Joan R. (2004). Heat inactivation of avian influenza and Newcastle disease viruses in egg products. *Avian Pathology* 33(5): 512-518.

http://www.tandfonline.com/doi/pdf/10.1080/03079450400003692

17. WHO fact sheet on Avian Influenza, March 2014.

http://www.who.int/mediacentre/factsheets/avian_influenza/en/

18. Cumulative number of confirmed human cases for avian influenza A (H5N1) reported to WHO, 2003 2015.

http://www.who.int/influenza/human_animal_interface/EN_GIP_20150717cumulativeNumberH5N1cases.pdf?ua=1

19. WHO risk assessment of human infections with avian influenza A (H7N9) virus, February 2015.

http://www.who.int/influenza/human_animal_interface/influenza_h7n9/RiskAssessment_H7N9_23Feb20115.pdf

20. Shu, Y., Li, C.K.F., Gao, R., Liang, Q., Zhang, Y., Dong, L., Zhou, J., Dong, J., Wang, D., Wen, L., Wang, M., Bai, T., Li, D., Dong, X., Yu, H., Feng, Z., McMichael, A.J., Xu, X.N. (2010). Avian Influenza A(H5N1) Viruses Can Directly Infect and Replicate in Human Gut Tissues. *Journal of Infectious Diseases* 201 (8):1173-1177.

http://jid.oxfordjournals.org/content/201/8/1173.full

21. Zhang, T., Bi, Yuhai., Tian, H., Li, X., Liu, D., Wu. Y., Jin, W., Wang, Y., Chen, Q., Chen, Z., Chang, J., Gao, G.F., Xu, B. (2014). Human Infection with Influenza Virus A (H10N8) from Live Poultry Markets, China, 2014. *Emerging Infectious Disease* 20 (12).