**OFFLU Statement on high pathogenicity avian influenza caused by viruses of the H5N1 subtype**

OFFLU has been closely monitoring the global high pathogenicity avian influenza (HPAI) situation since its inception in 2005. OFFLU has worked with multiple countries affected by H5N1 HPAI. OFFLU collates and publishes the results of studies on antigenic and molecular characteristics of avian influenza viruses every 6 months. This information is critical to assist decisions made by WHO on selection of candidate human pre-pandemic vaccine strains and to provide up-to-date information on the viruses circulating globally that pose a zoonotic and potential pandemic threat. OFFLU scientists in influenza reference laboratories and collaborating centres play a key role in characterising novel avian influenza viruses, including those that spillover to mammals.

Since October 2021, Members of the OFFLU Steering Committee and Executive Committee as well as members of OFFLU Technical Activities have been active in responding to media requests for accurate information on issues such as the significance of mammalian spillover cases and possible transmission between mammals, the pandemic threat posed by currently circulating viruses, and the role that vaccination can play in preventing HPAI in poultry. OFFLU scientists are concerned that there has been considerable misinformation and unwarranted speculation surrounding the current unprecedented epidemic of HPAI that has now affected countries across Eurasia, the Americas and Africa. Reports of spillover of the HPAI virus to scavenging and predatory mammals is expected when there is widespread infection in both wild birds and poultry. Evidence of contact transmission in mammalian species that are known to be susceptible to these viruses (especially mustelids) is also expected. These events warrant close monitoring and careful assessment of the characteristics of viruses given the potential for genetic changes of viruses in mammals through point mutations or reassortment. Although some adaptive genetic changes have occurred, none of the viruses from mammals characterised so far, including those detected in human cases, have evidence of changes to receptor binding specificity in the hemagglutinin glycoprotein typical of those seen in human pandemic Influenza A viruses. OFFLU scientists stress the importance of rapid sharing of the information on genetic characteristics of influenza A viruses when detected to inform animal and human risk assessment.

There are still gaps in knowledge that remain unresolved regarding the current epidemic including, but not limited to:

- What are the roles of different species of wild bird in long distance spread, and local transmission and maintenance of the current H5N1 virus?
- What are the underlying factors associated with an increased range of wild bird species affected and their relevance for future disease epidemiology?
- What specific viral factors allow the expanded geographical spread and continued circulation and causing outbreaks in the northern hemisphere summer (unlike 2014-15 strains)?
- What is the extent of existing surveillance programs in wild birds and poultry, especially in newly affected countries and continents and how can we improve these?
• Will the H5N1 HPAI viruses circulating in wild birds remain enzootic or will they self-extinguish as has been the case with HPAI viruses that have crossed over and spread in wild birds in the past (e.g. virus in wild birds in North America in 2014-2015 and in Europe from 2005 to 2008)?

• What is the cause of the comparatively high incidence of sporadic infections of wild terrestrial and marine mammals. Will these hosts serve as a pre-adaptation medium for further spread to humans?

Therefore, OFFLU urges the scientific community to:

1. Monitor AI events in animals and report to WOAH
2. Timely deposit and share genetic sequence data in publicly available databases
3. Coordinate studies to better understand pathogenesis, transmission and adaptation of virus lineages and share the results with OFFLU
4. Provide support to national risk managers

OFFLU (www.offlu.org) will continue to support the activities of its parent organisations (FAO and WOAH) and partners (WHO) in ensuring that scientifically sound information is available on strains of virus that are detected in poultry and in aberrant hosts.