OFFLU Strategy document for surveillance and monitoring of influenzas in animals

Background

General

Animal influenza threatens animal health and welfare, agricultural productivity, food security, and the livelihoods of farming communities in some of the world's poorest countries. The emergence of H5N1 highly pathogenic avian influenza (HPAI), the 1918 pandemic influenza, and pandemic H1N1 2009 (pH1N1) highlight the potential for animal influenza viruses to evolve into global public health threats. To ensure that the impact and risks for animals and humans are kept to a minimum it is vital that the animal health sector take the lead in monitoring influenza viruses in animals, in analysing the data, and in sharing this information with the international community particularly with public health partners.

There is a spectrum of influenza viruses circulating in animals that ranges in its ability to affect animal and human health: HPAIs have a severe impact on animal health, and human infections with H5N1 HPAI have severe consequences; other Notifiable Avian Influenzas are a threat to poultry health; equine influenza has a significant impact on equine health and performance; and swine influenza is often a mild disease in pigs.

The objectives and nature of animal influenza surveillance, and the response to positive findings depend on many factors including the significance of the influenza virus for animal and public health; the characteristics of the virus (which may evolve over time); the demographics of the host population; the epidemiology of the infection; geographical factors; involvement of wildlife; the type of control strategy being implemented; whether the disease is OIE listed (notifiable to the international community); and the capacity of the Veterinary Services to undertake surveillance and control. The response to disease detection must be proportionate to the risk and the exit strategy should always be considered when introducing any surveillance or control policy.

Timely sharing of virological and epidemiological information between the animal and the human health sectors and other key partners is crucial in developing a better understanding of influenza viruses and their risks, and for providing an early warning to emerging threats. On a global level this is underpinned by the level of reporting of important virological and epidemiological data to the relevant international organisations.

There are horizontal objectives that should apply for all animal influenza surveillance, these include:

- Early detection of mutations or reassortments that may alter risks for animal or public health, and inform preparedness and control strategies e.g. for influenza viruses circulating simultaneously in human and animal populations
- To gather information to develop a better understanding of influenza viral characteristics, epidemiology, and risk factors, including in virus reservoirs
- To assess the genetic basis of important viral characteristics such as antiviral resistance, transmissibility, and pathogenicity in different species
- To monitor the performance of diagnostic tools that aim to detect new influenza viruses

Owing to the wide range of characteristics and impacts of different influenza viruses in different animal species, the objectives of surveillance for influenza viruses in these species – and the response to positive findings – will vary accordingly.

Some more specific examples of objectives include:

- Early detection of animal disease, allowing rapid containment and/or control in affected populations
- To gather antigenic information and biological material for early preparation of animal vaccines e.g. for equine, avian, and swine influenzas; to detect antigenic drift or shift; to match vaccine strains with field virus; and to contribute to preparing vaccines against potential emerging human pandemic viruses
- To assess animal population immune response when vaccination is being implemented for prevention or control in animals
- To detect infected vaccinated animals in vaccinated populations

Each module in this document will describe the main objectives of surveillance for influenza in different animal species.

Pandemic H1N1 2009

Currently, pandemic H1N1 2009 (pH1N1) viruses are having a substantial impact on public health globally. Although pH1N1 infections in animals appear to cause varying clinical signs in different species, at this stage evidence does not suggest that infections in animals have a significant impact on public or animal health.

Occurrences of pH1N1 in several species of animals are not surprising given the high prevalence of the virus in human populations, the known susceptibility of some animal species to influenza virus infection, and level of contact between humans and animals. Currently pH1N1 has no significant adverse impact on animal health, it is therefore considered to be primarily a human disease with animals not playing a significant role in the occurrence of human infections. The response to the detection of infections in animals must be proportionate to the risk posed to humans and animals; it is recommended that control measures such as culling are not implemented when the virus is detected in animals. It is also recommended that restrictive trade measures are not taken against countries experiencing outbreaks of pH1N1 in animals.

Surveillance for pH1N1 should be a component of an overall strategy for surveillance of influenza viruses in animals. Surveillance for pH1N1 in susceptible animal species, in particular pigs and turkeys, has been recommended so that any changes in epidemiology or viral characteristics that might alter the risks to animal or human health are detected early.

Main objectives for surveillance of pandemic H1N1 2009 in animals

- Public health – Timely identification of mutations in pH1N1 viruses, or reassortments of pH1N1 with other influenza viruses in pigs and other animals that might be of public health concern. Monitoring of important molecular markers such as for resistance to antiviral drugs or for increased pathogenicity. This knowledge is used to inform preparedness, response, and communication plans.

- Animal health – Detect infections with pH1N1 in animal populations and identify changes in the epidemiology and virulence for pigs and other animals infected with pH1N1 which might have a negative impact on animal health and welfare, productivity, and economics.

Current evidence suggests that the majority of animal infections with pH1N1 are occurring in pigs, and that this species should be the priority when it comes to surveillance for pH1N1 in animals. Depending on the epidemiological situation and current scientific evidence, countries wishing to establish a surveillance system for pH1N1 may also consider including other species at risk and/or that have been demonstrated to be susceptible.

There is a need to balance the short term and long term objectives of surveillance for influenza viruses in animals. Surveillance systems for pH1N1 should, where possible, be adaptable to broader influenza surveillance in animal species.

Structure of the document

This document is a dynamic modular document that aims to provide an overview of the objectives and options for surveillance for animal influenza viruses in several different animal species. Contributions for each module are provided generously by experts who contribute to OFFLU, the OIE-FAO joint network of expertise on animal influenza.

The materials in this document are relevant to the disease situation and scientific evidence available at the time of writing. Each module is dated according to the time that it was written. If the disease situation or characteristics of an influenza virus change the approach to surveillance and recommended response may be modified accordingly.

Modules

1. Surveillance for influenza in pigs
   a. Swine influenza viruses – *under development*
   b. Pandemic H1N1 2009 (pH1N1) in pigs
   c. Other influenza viruses affecting pigs – *under development*

2. Surveillance for influenza in birds
   a. Notifiable avian influenza in domestic poultry – *under development*
   b. Pandemic H1N1 2009 (pH1N1) in poultry
   c. Avian influenza in wild birds
   d. Other influenza viruses affecting birds – *under development*

3. Surveillance for influenza in horses – *under development*

4. Surveillance for influenza in companion animals – *under development*

5. Surveillance for influenza in other animal species – *under development*

Surveillance for pandemic H1N1 2009 in pigs

Pandemic H1N1 2009 (pH1N1) is spreading globally from human to human. Sporadic occurrences of pH1N1 infections in pigs have been reported to the OIE. Experimental studies have also demonstrated that pigs are susceptible to pH1N1 virus isolated from humans and that the virus can be transmitted between pigs. Animal infections most likely result from contact with infective humans.

Main objectives for surveillance of pandemic H1N1 2009 in pigs

- Public health – Timely identification of mutations in pH1N1 viruses, or reassortments of pH1N1 with other influenza viruses in pigs and other animals that might be of public health concern. Monitoring of important molecular markers such as for resistance to antiviral drugs or for increased pathogenicity. This knowledge is used to inform preparedness, response, and communication plans.

- Animal health – Detect infections with pH1N1 in pig populations and identify changes in the epidemiology and virulence for pigs and other animals infected with pH1N1 which might have a negative impact on animal health and welfare, productivity, and economics.

Surveillance approaches

Detection of pH1N1 can be achieved using the following components of general and targeted surveillance. The degree to which each component is implemented is dependent upon the disease and the country situation. However, the combination of some or all of these methods will improve the sensitivity of surveillance.

Note: PH1N1 infections in pigs may lead to inapparent infections or may cause clinical signs that are indistinguishable from other influenza infections known to commonly circulate in pigs.

General surveillance:

- Disease detection – Clinical disease – *suspicious of ILI* – detected by animal owners, producers, veterinarians or other animal health workers; as part of the investigation consideration should be given to diagnostic testing for pH1N1. In cases where suspicion of pH1N1 is high, including when there is an epidemiological link with ILI in humans or animals the veterinary authorities should be informed.

Targeted surveillance:

Targeted or risk-based surveillance is the preferred approach over statistically based surveys for early detection of pH1N1. By targeting surveillance to high risk groups in the population greater efficiency and cost effectiveness will be achieved.

Sample targets can include but are not restricted to:

- Laboratory detection – Supplementary testing of samples submitted to laboratories for respiratory syndromes. Laboratory surveillance should focus on virological and molecular detection of pH1N1. All laboratory confirmed pH1N1 infections should be communicated to animal health authorities for further investigation.
- Slaughterhouse or market place surveillance – Testing of animals with signs of respiratory disease consistent with ILI (including at post mortem in slaughterhouses).
- Animals showing ILI at points of concentrated gathering such as markets, auctions or fairs
- Farms epidemiologically linked to known infected farms
- ILI in animals linked to known human cases
- Pigs in close contact with humans showing ILI

Categories of data needs

- Basics epidemiological information
    - Location and date
    - Farm type and demographics
    - Date when signs first started and when samples were taken
    - Morbidity, mortality, clinical signs
    - Link to suspected human cases

- Molecular genome sequencing. Full genome sequencing provides important information about the origins, evolution, and characteristics of the virus including genetic reassortment. Full genome sequencing is preferred, and is important in assessing the genetic basis of antiviral resistance and pathogenicity in different species. If full genome sequencing is not possible partial genome sequencing can provide some information.

- Antigenic data. Antigenic data will provide important information to ensure that diagnostic reagents are compatible with circulating field viruses and that diagnostic tests are therefore fit for purpose. It is also important to ensure that vaccine efficacy is optimal in terms of matching vaccine antigen to field viruses.

Reporting and response

All relevant findings from pH1N1 surveillance in animals including positive results from laboratory testing should be reported to animal health and public health authorities at the appropriate level. It is recommended that countries share information with other relevant stakeholders including local public health authorities.

Occurrences of pH1N1 and any other influenza viruses not previously reported in animals should be immediately notified by national veterinary authorities to OIE as an emerging disease.

Information about the epidemiological and viral characteristics of pH1N1 in pigs should be shared with the wider scientific community. This includes depositing genetic sequence data from pH1N1 isolated in animals into publicly available databases.

Under the current epidemiological situation, the response to pH1N1 infection in pigs should be proportionate. In particular:

- Culling of infected pigs is not recommended.
- Clinically ill pigs should not be shipped or sent to slaughter.
- Temporary movement restrictions of pigs between enterprises may be implemented.
- Movements of live pigs between holdings of the same enterprise may be allowed under licensing by the veterinary authorities to alleviate animal welfare concerns.
- Healthy pigs from infected farms can be sent directly to slaughter.
- Vaccination for pH1N1 in pigs is not currently available or recommended.

Risk communication

It is important that veterinary and public health authorities develop a coordinated risk communication strategy following positive surveillance findings. The risk communication strategy should strive to maintain an appropriate level of awareness amongst key stakeholders and the general public whilst not creating undue concern.

Outbreak investigation

Further to a positive surveillance finding, an outbreak investigation should aim to gather all relevant and useful epidemiological and virological information, and should be conducted without undue delay.

Role of epidemiological studies and research

It is recognised that valuable information can be gathered through epidemiologic studies and other research to inform the main objectives of surveillance for animal influenza. It is beyond the scope of this strategic document, however, to include all of the options under these categories. A recommendation would be that countries maximise the use of such studies and research to inform their surveillance programs, for example through building inter-sectoral partnerships with academic and other partners conducting such research.

Surveillance for pandemic H1N1 2009 in poultry

Occasional cases of natural pandemic H1N1 2009 (pH1N1) infection have been reported in turkeys. Animal infections most likely result from contact with infective humans. To date, attempts to experimentally infect poultry including turkeys, through the respiratory route, with pH1N1 virus isolated from people have not been successful, except in the case of quail that were infected but no onwards transmission was demonstrated.

Highly pathogenic avian influenza (HPAI) viruses and low pathogenic avian influenza (LPAI) viruses of subtypes H5 and H7 in poultry are OIE listed diseases because they are a serious threat to poultry health; pH1N1 in poultry is not an OIE listed disease and is not, at this time, a significant threat to poultry health. However occurrences of pH1N1 in avian species should be reported to OIE as an emerging disease.

Main objectives for surveillance of pandemic H1N1 2009 in poultry

- Public health – Timely identification of mutations in pH1N1 viruses, or reassortments of pH1N1 with other influenza viruses in poultry and other animals that might be of public health concern. Monitoring of important molecular markers such as for resistance to antiviral drugs or for increased pathogenicity. This knowledge is used to inform preparedness, response, and communications plans.

- Animal health – Detect infections with pH1N1 in poultry populations and identify changes in the epidemiology and virulence for poultry and other animals infected with pH1N1 which might impact on animal health and welfare, productivity, and economics.

Surveillance approaches

An increase in the proportion of influenza like illness (ILI) in animals should be investigated. Clinical suspicion of avian influenza should be investigated by competent Veterinary Services since Notifiable Avian Influenza is an OIE listed disease.

Note: ILI in birds may vary considerably in clinical presentation; there is limited information available about signs of disease associated with pH1N1 in poultry. In turkey breeders, a drop in egg production has been reported to be a sign consistent with pH1N1 infection.

Detection of pH1N1 can be achieved using the following components. The degree to which each component is implemented in a country is dependent upon the country situation. However, the combination of some or all of these methods will improve the sensitivity of the surveillance system.

General surveillance:

- Disease detection – Clinical disease – *suspicious of ILI* – detected by animal owners, producers, veterinarians or other animal health workers should be further investigated; consideration should be given to diagnostic testing for pH1N1. In cases where suspicion of pH1N1 is high including when there is an epidemiological link with ILI in humans or animals the veterinary authorities should be informed. Poultry keepers should monitor production parameters in order to detect the presence of influenza viruses (e.g. through egg drop).

- Testing of a subset of positive influenza A samples from routine avian influenza surveillance programmes for pH1N1 when samples are negative for H5 and H7

Targeted surveillance:

Targeted or risk-based surveillance is the preferred approach over statistically based surveys for early detection of pH1N1. By targeting surveillance to high risk groups in the population greater detection efficiency and cost effectiveness will be achieved. Sample targets can include but are not restricted to:

- Laboratory detection – Investigation of positive detections of influenza A virus for the presence of HPAI and subtypes H5, H7 – in addition samples can be tested for pH1N1 (in particular turkeys) when positive for influenza A and negative for H5 and H7. All laboratory confirmed pH1N1 infections should be communicated to animal health authorities for further investigation.
- Slaughterhouse/processing plant surveillance – Testing of animals with signs of disease consistent with ILI (including at post mortem in slaughterhouses).
- Poultry species on farms where pH1N1 has been detected in humans or other animals, particularly pigs.
- Animals showing ILI at points of concentrated gathering such as markets, auctions or fairs
- Farms epidemiologically linked to known infected farms.
- Supplementary testing of samples submitted to laboratories for avian influenza investigation or any other signs that may be consistent with pH1N1 infection in poultry.
- A subset of samples taken from routine statistical surveys can be tested for pH1N1 – these may be targeted to higher risk birds based on the current scientific evidence (e.g. turkeys).

Categories of data needs

- Basic epidemiological information includes
    - Location and date
    - Farm type and demographics
    - Date when signs first started and when samples were taken
    - Morbidity, mortality, clinical signs
    - Link to suspected human cases

- Molecular genome sequencing. Full genome sequencing provides important information about the origins, evolution, and characteristics of the virus including genetic reassortment. Full genome sequencing is preferred, and is important in assessing the genetic basis of antiviral resistance and pathogenicity in different species. If full genome sequencing is not possible partial genome sequencing can provide some information.

- Antigenic data. Antigenic data will provide important information to ensure that diagnostic reagents are compatible with circulating field viruses and that diagnostic tests are therefore fit for purpose. It is also important to ensure that vaccine efficacy is optimal in terms of matching vaccine antigen to field viruses.

Reporting and response

All relevant findings from pH1N1 surveillance in animals including positive results from laboratory testing should be reported to animal health and public health authorities at the appropriate level. It is recommended that countries share information with other relevant stake holders including local public health authorities.

Occurrences of pH1N1 and any other influenza viruses not previously reported in animals should be immediately notified by national veterinary authorities to OIE as an emerging disease.

Information about the epidemiological and viral characteristics of pH1N1 in poultry should be shared with the wider scientific community in a timely manner. This includes depositing genetic sequence data from pH1N1 isolated in animals into publicly available databases.

Under the current epidemiological situation, the response to pH1N1 infection in poultry should be similar to non notifiable avian influenza virus infection. In particular:

- Culling of infected poultry is not necessarily recommended.
- Clinically ill poultry should not be shipped or sent to slaughter.
- Temporary movement restrictions of poultry between enterprises may be implemented.
- Healthy poultry from uninfected units on infected farms can be sent to directly to slaughter.
- Vaccination for pH1N1 in poultry is not currently available or recommended.

Risk communication

It is important that veterinary and public health authorities develop a coordinated risk communication strategy following positive surveillance findings. The risk communication strategy should strive to maintain an appropriate level of awareness amongst key stakeholders and the general public whilst not creating undue concern.

Outbreak investigation

Further to a positive surveillance finding an outbreak investigation should aim to gather all relevant epidemiological and virological information, and should be conducted without undue delay.

Role of epidemiological studies and research

It is recognised that valuable information can be gathered through epidemiologic studies and other research to inform the main objectives of surveillance for animal influenza. It is beyond the scope of this strategic document, however, to include all of the options under these categories. A recommendation would be that countries maximise the use of such studies and research to inform their surveillance programs, for example through building inter-sectoral partnerships with academic and other partners conducting such research.

Surveillance[1] for avian influenza in wild birds

Wild birds play important roles in the global circulation of avian influenza viruses and are reservoirs particularly of subtypes of low pathogenicity. Avian influenza viruses in wild birds can be transmitted to and from poultry, and potentially to and from other domestic animals and people. In order to reduce health risks to wildlife, domestic animals and people, it is important to understand all aspects of the circulation of avian influenza viruses among susceptible populations: wild animals, domestic animals and humans. Thus, surveillance for avian influenza viruses in wild birds can supply critically important information.

Main objectives for surveillance of avian influenza viruses in wild birds

- To detect virus strains highly pathogenic to wild and domestic animals, and to people.
- To detect virus strains of low pathogenicity of any subtype that may pose risks to human and animal health.
- To detect infection of wild birds with virus subtypes derived from poultry.
- To gain a more comprehensive understanding of the epidemiology and ecology of avian influenza viruses.

Surveillance approaches

- General Surveillance (passive surveillance):

Avian influenza virus can be detected, through appropriate laboratory tests, in samples of wild birds received in diagnostic laboratories as part of programs of general disease surveillance in which all causes of morbidity and mortality are under investigation. Most often, general surveillance is carried out on wild birds found dead. General surveillance based on wild birds found dead has proved to be the most effective form of surveillance to detect highly pathogenic virus strains in wild birds.

- Targeted Surveillance (active or risk-based surveillance):

Targeted surveillance focuses on sampling according to specified criteria such as species, sex, and age of bird, geographic location, and time of year. Targeted surveillance is a more efficient way to meet the objectives of surveillance and can result in collection of influenza viruses for characterisation in terms of genetic and pathogenic properties. In addition it may contribute to the assessment of the infection status of specific wild bird populations. It may be most efficient to focus surveillance on bird species which use aquatic habitats since influenza viruses have been found most often in aquatic birds species, particularly ducks, geese, and swans. Birds included in targeted surveys are most commonly apparently healthy live wild birds, but survey design may include sick birds, dead birds, and freshly-expelled bird faeces.

[1] In this document, the word “surveillance” is used to include the activities sometimes separated under strict definitions of surveillance, monitoring and disease investigation.”

- Sampling:

The main samples to be taken from each bird, whether alive or dead, are a sample of oro-pharyngeal fluid and a sample of cloacal content. These two sample types from each bird are better analysed separately but may be combined. These samples are best taken with swabs (with tips and handles composed of synthetic materials) which then are placed in an appropriate virus transport medium. It is essential that samples be refrigerated or placed on ice as soon as they are collected, and either analysed immediately or frozen immediately for future analysis. Additional issues associated with sample procurement include possession of the necessary legal permits, training and competence to catch, handle, mark and release wild birds in keeping with international standards of animal welfare, and competence to identify correctly the species, and also often the sex and age, of each bird sampled. If serum samples are required, competence to obtain, handle and preserve blood samples, and separate and freeze the serum will be required.

- Laboratory testing:

Only validated laboratory tests should be used to test samples for the presence of virus or to test sera for antibodies to avian influenza viruses. To test for virus, PCR procedures using internationally accepted primers for the matrix protein gene, or virus isolation carried out by techniques compatible with the *OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*, are the methods of choice. Tests for antibodies in sera must be valid for the species of bird being tested. In general, standard ELISA procedures are not acceptable because these require species-specific reagents. Blocking ELISA tests and virus neutralisation procedures, as outlined in the OIE Manual, are recommended. It is useful to attempt to define the targeted haemagglutinin of the antibody response by performing HI tests on B ELISA reactors. Currently, serological tests have very limited capacity to distinguish among strains of influenza viruses to which the bird may have been exposed, and a positive test may indicate only that the bird was exposed at some time in the past to some strain of influenza A virus.

Categories of data needs

- Basic epidemiological information includes:
    - Location (Latitude and Longitude, or UTM coordinates)
    - Date of sample collection
    - Species (*Latin* name), and sex and age where possible
    - Morbidity, mortality and clinical signs, where relevant
    - Co-occurrence of disease in other species, including domestic animals and humans

- Virus Characterisation
    - Whether an influenza A virus isolate was recovered or whether information is on the basis of sequence analysis
    - HA subtype
    - N subtype

- Molecular genome sequencing:

Full genome sequencing provides important information about the origins, evolution, and characteristics of the virus, including genetic reassortment. Full genome sequencing is preferred, and is important in assessing the genetic basis of antiviral resistance and pathogenicity in different species. If full genome sequencing is not possible, partial genome sequencing can provide some important information.

  - all sequence data must be clearly linked to the date, location and species from which the sample was taken, particularly when deposited in public-access data banks.
  - sequencing should involve determining the inferred pathotype.
  - molecular sequencing studies are frequently initiated on the basis of HA and N gene analysis.

- Antigen data:

Antigenic data can provide important information to ensure that diagnostic reagents are compatible with circulating field viruses and that diagnostic tests are therefore fit for purpose. It is also important to ensure that vaccine efficacy is optimal in terms of matching vaccine antigen to field viruses.

Reporting and response

- The OIE should be notified of any infection of wild and domestic birds with highly pathogenic avian influenza H5 or H7 virus subtypes. This is a reporting requirement of OIE Members as laid out in the *OIE Terrestrial Animal Health Code*.
- All additional relevant findings from surveillance for avian influenza viruses in wild birds should be reported to wildlife, domestic animal and public health authorities at the appropriate level. It is recommended that countries share information with other interested parties.
- Results of surveillance for low pathogenic avian influenza viruses in wild birds should be included in the annual report on occurrence of non-listed infections in wildlife through the WAHIS-wild reporting system of the OIE.
- The occurrence of avian influenza viruses in wild birds, including H5 and H7 subtypes, does not justify the imposition of trade restrictions.
- In the event of wild bird mortality caused by avian influenza, local poultry farms should be advised to verify or implement appropriate biosecurity measures.

Risk communication

It is important that wildlife, veterinary and public health authorities develop a coordinated risk communication strategy following positive surveillance findings. The risk communication strategy should strive to maintain an appropriate level of awareness among key stakeholders and the general public while not creating undue concern.

Since avian influenza viruses occur regularly in wild birds, it is expected that wild bird surveillance efforts will detect these viruses irrespective of any role wild birds may play in local epidemiological events involving poultry. It is not justified to attribute the source of avian

influenza virus infection in poultry to wild birds unless complete investigations have been carried out and the results fully support such attribution. Response actions such as killing wild birds or destroying their habitat are not appropriate.

Outbreak investigation

Under some circumstances, it may be appropriate to remove and properly dispose of the carcasses of wild birds which have died from avian influenza, to prevent or reduce the spread of infection.

In the event of an outbreak of avian influenza in poultry, there may be some value in undertaking surveillance for the causal virus in live and dead wild birds in the vicinity of the affected farm to determine whether or not the causal virus is present in local wild birds. Interpretation of results will not permit determination regarding the direction of transmission of the virus between poultry and wild birds, but may inform biosecurity measures on other premises.

Role of epidemiological studies and research

It is recognised that valuable information can be gathered through ecological and epidemiologic studies and other research to improve our understanding of the movement, maintenance, transmission and persistence of influenza viruses across the wildlife–domestic animal–human interface. Countries should maximise the use of such studies and research, and share data and results with the wider scientific community to improve local, regional and global understanding.