OIE information document on avian influenza vaccination

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The report of the first meeting of the ad hoc group will be submitted, in accordance with OIE procedures, for endorsement by the SCAD and the International Committee.

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Introduction

The OIE recommends eradication of highly pathogenic avian influenza (HPAI) at its poultry source to decrease the virus load in susceptible avian species and environment and therewith to decrease the risk of human infection with those avian influenza viruses that have zoonotic potential, to secure the production sector and trade, as well as to safeguard food security and the livelihoods of farmers in developing countries.

The control of HPAI has become a more complex issue than in the past. The unprecedented and almost worldwide spread of HPAI infections, and the related serious animal and human health implications have increased the need to develop control strategies complementary to a stamping out policy, which has traditionally been used to eradicate this disease.

The first line of defence is early detection of disease outbreaks followed by a rapid response. This is strongly linked to a high level of awareness among veterinarians and animal owners, and high quality veterinary services. Veterinary services should comply with the OIE standards on the Quality of Veterinary Services. Compensation remains a strong point of discussion in infected and at risk countries, and having a compensation mechanism in place will encourage reporting and notification of AI by bird owners. Control strategies based on a combination of stamping out, movement restrictions and emergency vaccination could maximize eradication efforts in certain situations.

Controlled elimination of infected poultry, movement restrictions, improved hygiene and biosecurity, and appropriate surveillance should result in a significant decrease of viral contamination of the environment. These measures should be taken whether or not vaccination is part of the overall strategy. Vaccination is an additional measure aimed primarily at a reduction of viral replication and viral shedding. The availability of strategic stocks of vaccines in all at risk countries will contribute to the possibility of a rapid response, using all eradication measures, including vaccination if needed.

The scientific basis for the use of a vaccination strategy is the induction of a protective immunity in the target population. A good vaccination program would raise the levels of protective flock immunity and increase the resistance to infection. An exposure to AI virus may not lead to infection in the vaccinated birds or, if infection were to occur, the clinical presentation should be less severe and viral shedding reduced in terms of amount and duration. In combination with the implementation of effective biosecurity measures, vaccination could prevent the introduction of the AI virus, or alternatively in reducing its spread, minimizing the negative impact on poultry production and decreasing potential economic losses. Moreover, the risk of human exposure to AI viruses with zoonotic potential and the consequent human cases, may be reduced by vaccinating poultry.

It is essential that the consumption of meat from vaccinated poultry does not present a human health risk. Some vaccine manufacturers advise a withdrawal period after vaccination related to the use of certain adjuvants, during which period the poultry meat should not be consumed. This is always stated in the accompanying information and should be taken into account.

Scope of the document

The present document is aimed at providing information regarding to the use of vaccination against avian influenza viruses in poultry.

Analysis of the current situation

Before a vaccination program can be designed and implemented, it is necessary to analyse the current situation in the country and in the global context, and to analyse the logistical requirements for conducting an effective campaign.

Knowledge of the prevailing epidemiological situation is of critical importance. Ideally, an updated epidemiological assessment should be available, including the results of any surveillance, the status of neighbouring countries and trade partners, and of the risks. The human health implications may also be part of this analysis.

The poultry production system in place influences the risk of HPAI introduction and spread. The structure of the poultry industry, farming practices (free range, industrial, rural), the poultry species reared, farm density, biosecurity levels and the trading patterns are data that should be collected.

Logistical factors can influence the outcome of any vaccination campaign. The logistical constraints should be identified as a first step in the adequate planning of any field interventions. Logistical information should address the contingency planning and readiness of the country, structure and capacity of the veterinary services, the availability of human resources, the culling capacity, and the ability to introduce movement restrictions and controls.

The diagnostic capacity should be determined, since this greatly affects the possibility of implementing surveillance programs and using the DIVA[1] strategy. Whether there is a compensation mechanism in place or not may have a large effect on the willingness of farmers or bird owners to report disease. An effective and transparent disease reporting system assists implementation of the regular control methods.

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[1] A strategy in which vaccinated animals can be differentiated from infected animals (see www.oie.int).

Preventive vaccination in an area that is not yet contaminated should be based on risk analysis, using information from existing surveillance programs. When contemplating vaccination in a contaminated area, additional information is required: the virus type, bird species and the type of husbandry in the area (production sectors 1, 2, 3 and 4 as described in the "FAO recommendations on the prevention, control and eradication of Highly Pathogenic Avian Influenza in Asia" September 2004) should be taken into account.

Implementation of vaccination

In making a decision on which vaccine to use, the factors listed above should be taken into account. The vaccine should be produced according to the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* and evidence should be provided that the vaccine significantly reduces virus excretion from vaccinated birds if they are subsequently infected. Vaccines should be selected on the basis of evidence that the product is able to prevent virus circulation in the target species. It is desirable that the quality control tests associated with this degree of efficacy are reflected in individual batch documentation.

The following vaccine types are currently available

- Inactivated vaccines
  - Monovalent including either H5 or H7strains
  - Bivalent including H5 and H7 strains
  - Both monovalent and bivalent vaccines can contain homologous or heterologous neuraminidase subtype; this depends on the neuraminidase of the circulating virus and on the neuraminidase present in the vaccine.
  - Combination vaccines (other antigens): if it is foreseen that a prolonged vaccination program may be required, the use of combination vaccines should be considered.
- Live recombinant vaccines (fowlpox H5): these are efficacious only in chicken species, and then only in day-old chicks as exposure in later life to wild-type fowl pox virus would preclude the use of the vectored vaccine.

It is essential to use a vaccine against the virus hemagglutinin type that is currently circulating in the country or against the virus that is expected to be introduced into a country that is still free. The currently available vaccines and their usage are also described in the "FAO recommendations on the prevention, control and eradication of Highly Pathogenic Avian Influenza in Asia" September 2004. A list of vaccine producers which produce vaccines according to the OIE *Manual*, can be found On the OIE website (www.oie.int).

Decision on vaccination strategy

In general terms, for the use of vaccination against AI infections in target species, consideration should be given to the objective of the campaign:

- Emergency vaccination in the face of an epidemic,
- Preventive vaccination (i.e. prophylactic) carried out if a high risk of virus incursion is identified and early detection/ rapid response measures may not be sufficient
- Routine vaccination performed in endemic areas.

Emergency vaccination is an option when there is evidence of AI introduction, or whenever the epidemiological situation indicates that there could be massive and rapid spread of infection. In general terms, emergency vaccination might be implemented in a protective (vaccination-to-live) or a suppressive (vaccination-to-kill) way.

Protective vaccination (vaccination-to-live) means that vaccinated animals are allowed to live out their normal economic lives. If protective vaccination is to be used during an HPAI epidemic, it is essential to implement measures to determine virus circulation in the flock (implement a DIVA vaccination strategy) for the early detection of any newly HPAI

affected flock. The discrimination between infected and vaccinated birds and flocks is fundamental for progressive disease control and eventual eradication.

It is suggested that veterinary authorities consider this strategy in cases of:

- the detection of AI infection in an area with a high poultry density. In this event, protective vaccination could be envisaged as a tool along with the implementation of complementary eradication measures (including movement restrictions, culling, controlled marketing, zoning and compartmentalisation);
- evidence that an outbreak cannot be contained by the culling of infected, suspected, or dangerous contact poultry holdings alone.

With regard to trade implications, the new OIE *Terrestrial Code* chapter on AI recommends the continuation of trade in the presence of vaccination, provided that the exporting country is able to produce surveillance and other data that confirm that AI is not present in the flock or establishment from which the exports originate.

Preventive (prophylactic) vaccination for H5 and H7 subtypes of AI viruses is a long term measure that may be applied when there is evidence that a country/region/compartment faces significant risk of AI and when other prevention tools are considered to be insufficient. Vaccination should then be applied within the framework of a DIVA strategy.

At least 2 categories of risk may be identified:

- High risk of infection with either H5 or H7 subtype (e.g. from exposure to potentially infected wild/migratory birds);
- High risk of infection with a known subtype (e.g. live bird markets or from outbreaks in neighbouring countries or trading partners).

In the first case, a bivalent (H5 and H7) vaccine should be applied, whilst in the second case, a monovalent (either H5 or H7) vaccine could be a better choice.

A surveillance program in accordance with the *Terrestrial Code* should be ongoing for the early detection of, and rapid response to, HPAI virus incursions. This program could be extended through the application of a DIVA strategy, provided that the virus subtype at risk of introduction has been identified, or through the monitoring of unvaccinated sentinel birds, which must be present in each vaccinated flock.

Prophylactic vaccination should be carried out as long as the risk of infection exists, and can also be used in a targeted manner for limited periods of time. Based on the identified risk factors for AI introduction, a clearly defined exit strategy should be formulated before preventative vaccination is undertaken.

The implementation of an AI surveillance program in accordance with the *Terrestrial Code* is a pre-requisite for avoiding the application of unjustified trade restrictions on poultry commodities originating from the country/zone/compartment where preventive vaccination has been carried out.

Routine vaccination can be an appropriate method where the disease is endemic and due to local conditions:

- containment and eradication of infection can not be enforced;
- movement control cannot be instituted;
- widespread occurrence is documented;
- a DIVA strategy cannot be effectively implemented.

From a financial/livelihood standpoint, the cost of maintenance of an effective vaccination program is a significant factor.

Used properly, routine vaccination can be valuable in reducing mortality and production losses. In the longer term, it could also decrease the prevalence of infection to a level where stamping out and surveillance could also be applied. It is possible, then, to make the continued use of routine vaccination unnecessary as long as there are effective contingency plans in place to deal with the possible re-emergence of the disease.

Various vaccination strategies can be applied:

- Mass vaccination: vaccination is applied to all susceptible birds.
- Targeted vaccination: vaccination is applied to defined categories of birds.
- Ring vaccination: vaccination is applied in a defined area around an outbreak.

Mass vaccination can be used as an emergency, preventive or routine vaccination. Vaccination is applied to all susceptible birds in a country or part of a country. All poultry are to be vaccinated. The choice for this option can be made when it is unlikely that an outbreak (present or at risk) can be controlled in any other way.

Targeted vaccination is one in which vaccination is only applied to defined categories of birds. A risk analysis should be carried out and should address the bio-security levels of the holdings, the value of the flocks and the extent of the threat of the infection. The compensation mechanism in the case of an outbreak will influence willingness to notify disease outbreaks and therefore also the decision whether to practice targeted vaccination or not. It may be decided to vaccinate only certain species, certain compartments or only one or more of the sectors 1-4 (the "FAO recommendations on the prevention, control and eradication of Highly Pathogenic Avian Influenza in Asia" September 2004). When sufficient vaccine quantities are unlikely to be available, it may be decided to vaccinate only valuable parent flocks. When mass vaccination is preferred but there is insufficient vaccine available immediately, a choice of categories can be made based on the risk analysis.

Ring vaccination is vaccination in a defined area around an outbreak, and is therefore only relevant to an emergency vaccination, and may be used to bring the outbreak under control as quickly as possible. The vaccination should be used additional to the culling of the infected flocks and other measures and should be used in the framework of a DIVA strategy.

Vaccine availability and vaccination procedure

There is sufficient capacity in the international animal health industry for emergency and large scale vaccination programs. The supply time depends on the availability of product at the time of ordering. If stock is not available, the supply time can be 4 to 8 months from the start of the production process. Potential supply problems can be caused by a sudden unexpected and substantial rise in demand. Availability of vaccines when needed can be safeguarded by a vaccine bank which has to be instituted well in advance (see appendix I).

Only high quality vaccines produced according to OIE standards should be used in vaccination programs. Governments should ensure that vaccine producers comply with OIE standards continuously, with special emphasis on bio-containment standards. In the absence of independent quality certification, batch testing by an organisation independent from the manufacturer is useful. This independent service could be commissioned from an OIE / FAO Reference Laboratory with proven experience in vaccine testing and appropriate biosecurity facilities.

Evidence should be provided that all vaccine batches produced by the same means (i.e. not an individual batch requirement) in the same manufacturing plant fulfil the requirements. Storage and transportation conditions of the vaccines, and the vaccination schedule and application should be in strict adherence to manufacturers' recommendations. Vaccines should be applied by trained personnel. Special attention should be given to biosecurity measures. Appropriate protective gear and equipment for personnel should be provided.

Vaccination records should be kept by the *Competent Authority*, and the holdings. The records should include:

- Holdings, locations and categories of animals
- Vaccine used: brand, batch numbers, number of doses

- Date of vaccination
- The total number of susceptible animals in the holding
- Operators who applied vaccination

Monitoring

Monitoring of the efficacy of vaccination can be done in 2 ways: (1) vaccination compliance and (2) level of protection in the population.

Monitoring of vaccination compliance can be done on all species (e.g. antibodies and rings applied at the same time as vaccination). Monitoring of the level of protection can only be done in species where there is an established or at least likely relation between antibodies and protection. To demonstrate this, a large part of the population should show sero-conversion with a satisfactory mean titre, and titres should be consistently above the threshold values for protection. Other than chickens and turkeys, little is known of protective titres post vaccination, though it has been repeatedly documented that immunity in ducks and domestic geese wanes quicker than in chickens and these species would therefore require more frequent vaccinations. Inaccurate vaccination may lead to insufficient immunity and the development of apparently healthy virus carriers.

A vaccination campaign which is not managed appropriately is likely to result in the virus becoming endemic. Therefore, a monitoring program should be implemented in vaccinated populations to determine whether virus is still circulating in these populations; this can be based on either the DIVA principle or the use of sentinel birds. In addition, serological analysis can be used to monitor efficacy and coverage of the vaccination.

Several methods for the detection of field virus in vaccinated flocks should be considered, depending on the kind of vaccine used (homologous, heterologous or recombinant), the vaccination strategy implemented and the availability of proper diagnostic facilities and tools.

One method is to use unvaccinated seronegative sentinel birds housed with the vaccinated population. This is the only possible method when homologous vaccines have been used. All birds, except the sentinel birds, of the targeted population should be vaccinated and the non-vaccinated sentinels should be properly identified in order to avoid confusion or substitution. Daily clinical investigations should be undertaken and, ideally, periodic serological investigation. Clinical disease or mortality amongst these sentinels should be properly investigated to exclude avian influenza infection. Should the sentinel birds show clinical signs and AI virus confirmed, or specific sero-conversion documented, virus circulation within the flock (or virus re-introduction) is confirmed. This could be an appropriate method for commercial poultry.

A second method to monitor virus circulation in a vaccinated population is to determine the serological response of vaccinated birds against the neuraminidase glycoprotein of the field virus. This is only possible when heterologous vaccines have been used and the details of other circulating AI viruses are known. Exposure of the vaccinated population to field virus leads to the development of antibodies to the different neuraminidase antigen of the field virus not present in the vaccine.

When there is a suspicion of AI in a vaccinated flock, based on clinical signs, virus isolation, RT-PCR or validated antigen detection tests should be used for diagnosis.

After vaccination, all flocks should be checked for freedom from infection before the birds are transported. The diagnostic tests and procedures described in the *OIE Manual* can be used. The methodology of the classic diagnostic procedures is described in the *Manual*. Many novel rapid commercial tests have appeared on the market in recent times and it is essential that, for all diagnostic tests, fitness for purpose has been demonstrated.

The diagnostic test procedures in an outbreak situation must be under responsibility of the *Competent Authority*.

Other issues to be considered

Sero-response has been demonstrated in bird species other than those for which the products were registered, but efficacy may be unknown. Therefore, serology to monitor the efficacy of vaccination can only be applied in chickens, and possibly ducks.

An issue for vaccination is that the vaccine has to be applied to each bird individually by injection.

The vaccine storage conditions are pivotal for a successful vaccination program.

In addition to the technical aspects of vaccination, an awareness program and communication strategy should be implemented. Adequate communication to the broad society on all aspects of AI vaccination is essential for a successful vaccination campaign. Specific points that should be addressed are the public health aspects of AI, the beneficial effects of vaccination, food safety issues, the risk of carrier birds, the trade impact and the appropriate technical and scientific basis for vaccination.

The OIE and AU/IBAR[2] have signed an agreement for the management of a virtual bank of vaccines for Africa

- AU/IBAR/PACE[3] assess the national needs and transmit an order to the OIE
- The OIE manages a vaccine fund currently financed by the EC.
- The OIE consults providers and selects one or several that will be committed to send selected vaccines (produced in compliance with the OIE international standards) to countries.
- The IBAR/ PACE attest receipt of the vaccines.
- The OIE pays the providers.

Appendix 1

Vaccine bank for Avian Influenza vaccines

The contingency plan for a potential outbreak of Avian Influenza might provide for a vaccination campaign. The vaccine industry cannot guarantee continuous availability of sufficient quantities at all times. A vaccine bank will safeguard availability of the required vaccine within days after the decision to start vaccination.

There are different ways in which a vaccine bank can be arranged. In all options the vaccine is fully tested and released in line with the OIE Manual and the specifications of the manufacturer.

1. **Purchase by the ordering country, storage in the country of destination**: In this option the Government purchases the vaccine, the vaccine is imported in the country and locally stored at a central point. In this option the time between decision to vaccinate and the first vaccination is the local distribution time. This option is the fastest and most secure option.

2. **Purchase by the ordering country, storage at the manufacturer**: In this option the Government purchases the vaccine and the vaccine is stored at the manufacturer in the country of origin. The advantage is secure storage in cooled facilities. The time between decision to vaccinate and the first vaccination is the transport time between country of origin and country of destination plus local distribution time.

3. **Tailor-made solutions**: Other solutions, such as emergency stocks based upon a rolling system, could be negotiated the ordering party and the supplier.

[2] AU: African Union, IBAR: Inter African Bureau for Animal resources

[3] Pan-African Control of Epizootics

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