



OFFLU technical meeting: Developing guidance on vaccines and vaccination against HPAI from lessons learned

4 to 6 December 2013 in Beijing, China

OFFLU, the joint network of expertise on animal influenza between the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE), organized a technical meeting on vaccination against Highly Pathogenic Avian Influenza (HPAI) from 4 to 6 December 2013 in Beijing, China. A similar meeting took place in Verona, Italy in 2007, the recommendations from which are still mostly valid today. However, many of the countries participating in the Beijing meeting, in particular China, Egypt, Viet Nam, Indonesia and Mexico, have since gained large amounts of experience in the field of vaccination against HPAI. Government representatives from those countries and participants from FAO and OIE as well as the International Egg Commission (IEC), the International Federation for Animal Health (IFAH) and the World Health Organization (WHO) came together to share and discuss the experience and progress made at national and regional levels in vaccination against HPAI. The members of the OFFLU Technical Activity on vaccination acted as the scientific and organizing committee for this meeting.

Given that most statements and recommendations of the Verona meeting are still valid, or only required minor updates, this document was built from the sets of statements and recommendations of the Verona meeting. Only a few new statements or recommendations have been added and others have been updated.

Agenda and presentations are available at <http://www.offlu.net/index.php?id=303>

Considering the following:

On the role of vaccination in control and prevention of highly pathogenic avian influenza

1. Highly pathogenic avian influenza (HPAI) remains a serious disease of poultry with some viral strains causing severe zoonotic disease and having pandemic potential.

2. There is a need to manage, and ideally stop the spread of HPAI at its animal source to decrease the risk of human infections and potential emergence of a human pandemic strain.
3. The occurrence and dynamics of the circulating strains of virus has led to the use of vaccination in countries where enzootic infection with H5N1 HPAI developed.
4. The experimental and field evidence that vaccination with high quality, registered vaccines that comply with OIE standards and that have sufficient quantities of antigens reasonably well matched antigens to circulating strains of AI virus:
 - increases the resistance to infection,
 - decreases the shedding of the virus and
 - decreases the probability of infection of poultry, and other animals including humans, which makes vaccination a supplemental tool for control and prevention of AI.
5. The use of low quality or poorly matched vaccines and/or inappropriate vaccination schedules and strategies will have limited effects in preventing disease and on viral shedding if vaccinated poultry are subsequently infected, but often give producers a false sense of security.
6. Vaccination alone cannot eliminate the virus and is meant to be part of an integrated control program appropriate to the local situation combined with other elements such as:
 - humane culling of (potentially) infected animals and safe disposal of carcasses;
 - increase of biosecurity at farm, household and market level;
 - movement controls;
 - communication and general awareness for poultry producers and the public;
 - changes to the way poultry are reared, transported and marketed as to minimise the risk of infection;
 - regular surveillance throughout the poultry sector, including live bird markets.
7. There is no evidence of negative human health implications, directly related to the vaccination of poultry and the subsequent consumption of their products; and vaccination can have positive public health impacts from reduced virus circulation.
8. Use of vaccination has not had significant negative effects on consumer demand for poultry or poultry products in places where it has been used.
9. Antigenic drift occurs in all influenza viruses that can reduce the effectiveness of vaccines over time unless isolates are characterized and vaccine seed strains timely updated.
10. The OIE standards, guidelines and recommendations, the FAO guidelines and recommendations, the FAO/OIE Global Strategy on HPAI (2008), the FAO/OIE recommendations from the scientific meeting on vaccination (Verona 2007) and the information document from the OIE *ad-hoc* group on AI vaccination guidelines, and peer-

reviewed research, scientific papers and reviews provide appropriate guidance on avian influenza vaccination.

On implementation of vaccination

11. The experiences with AI control programmes in countries or regions where vaccines have been used, including experiences with blanket vaccination programs of small poultry flocks.
12. Vaccination can be a logistically demanding and a costly method with inherent uncertainties under field conditions regarding the level and duration of protection.
13. AI vaccination can be integrated into routine poultry vaccination schedules in the commercial sector in places where the virus is enzootic especially for layers and yellow feathered meat birds.
14. Maintaining high level flock immunity is difficult in some poultry populations, especially at household and small commercial level, including small scale duck production.
15. There is a low probability of successful implementation of vaccination programmes that are not compatible with short production cycles (especially industrial broiler and meat duck production).
16. There is a transition from mass vaccination to targeted vaccination for H5N1 HPAI in Viet Nam, Egypt, and Indonesia.
17. Limiting market availability to only well-matched potent vaccines correlated with the reduction of H5N1 HPAI contamination in markets and outbreaks in Indonesia.
18. The importance of appropriate resources for a vaccination campaign includes biosecurity, hygiene of personnel, cold chain assurance, trained vaccinators, equipment and appropriate payment for vaccinators, etc.
19. Vaccination effectiveness is limited in the presence of immune suppressive factors, regardless of the vaccine used and its application. Interference with maternally derived antibodies may also reduce vaccine effectiveness.
20. There is a need to preserve and protect valuable birds such as specific poultry breeds (conservation of genetic resources), zoo birds, pet birds, ornamental birds and (great grand and grand) parent flocks.
21. All previous recommendations on vaccination suggest that an exit strategy be developed but that this term has created some confusion, especially in places where the virus is enzootic. A decision tree of when to halt vaccination needs to be developed.

21. Previous recommendations on vaccination suggest that an exit strategy be developed. This term has however created some confusion, especially in places where elimination of the virus cannot be expected in the current situation and because the impact of the cessation of vaccination is not easily predictable.

22. The experiences in countries with endemic virus circulation or with regular recurrent viral incursions where vaccination has not been used or is being implemented on a trial basis, including illegal importation and use of unregistered vaccines of unknown origin and efficacy.

On vaccines

23. Vaccines demand lengthy registration procedures. In addition, influenza vaccines would require a process to quickly update vaccine seed strains, which is not covered in the actual regulatory process.

24. Illegal imports of unregistered vaccines have been identified in some countries once antigenic drift of field viruses rendered existing, poorly matched vaccines less effective. Illegal vaccination has also been described in areas where use of avian influenza vaccines is prohibited.

25. New vaccines and vaccine technologies, including vectored vaccines that can be delivered *in ovo* or to day old chicks in hatcheries have been developed and field trials/experiences with these products suggest they may have a role to play in vaccination of poultry against influenza.

26. Vector vaccines applied at hatchery level are already broadly used in many countries to prevent other poultry diseases (e.g. infectious laryngotracheitis, infectious bursal disease).

On research needs

27. Many gaps remain in knowledge on vaccination applied in HPAI disease prevention and control including the constraints encountered using most of the existing vaccines (such as the need for injection of individual birds, the need for repeated doses of vaccine to sustain immunity) and the new technology vaccines (interference of maternally derived antibodies, duration of immunity, vaccine efficacy in ducks, etc).

On veterinary services

28. The role of Veterinary Services (VS) is indispensable for the implementation of prevention and control programmes against HPAI.

29. There is a need for VS to be in compliance with the OIE standards as described in the OIE Terrestrial Code.

30. There is a chronic under-resourcing of VS in many countries.

31. There is a necessity for good veterinary governance, strong political commitment and appropriate legislation.

32. Unjustified trade barriers related to vaccination against HPAI need to be prevented.

On surveillance, monitoring and evaluation

33. Serosurveillance and case definitions are impacted by vaccination.

34. The importance of disease awareness and effective surveillance systems, combining active surveillance and enhanced passive surveillance, for the early detection and characterisation of influenza viruses, even in vaccinated populations.

35. The importance of official reporting and the need for real time information sharing at all levels for early detection and warning on new HPAI events, understanding the trends in epidemiological changes and emergence of new/variant HPAI virus strains as well as for effective prevention and control of this transboundary disease.

36. The need for overall transparency by all stakeholders on the production, sales and national use of vaccination, and the need to share knowledge and field data on the effectiveness of vaccination campaigns and virus circulation post-vaccination to improve vaccination approaches.

37. The detection of antigenic variants of H5N1 HPAI viruses in Indonesia, China, Viet Nam and Egypt has triggered the need for vaccine seed strain updates.

38. Lack of capacity in some developing countries for vaccine seed strain selection and vaccine production.

39. Positive experiences from China and Indonesia in updating vaccine seed strains in the face of emergence and establishment of antigenic variants of H5N1 HPAI field virus.

On public private partnerships and communications

40. Involvement of public and private sectors together is crucial for successful prevention and control of HPAI with sustainability and success of vaccination strategies requires strong private / public commitment at all levels including cost sharing.

41. Gaps in public-private partnerships, especially on regulation of vaccination in the commercial sector, sharing of outbreak information and strains, and information on vaccine failure still exist in many countries.

The meeting participants recommend the following:

On the role of vaccination in control and prevention of highly pathogenic avian influenza

1. Appropriate measures for the control and prevention of HPAI must be in place, with strategic use of the suite of measures available.

2. A comprehensive approach utilising the combined tools and measures for HPAI prevention, containment and elimination should be adopted in countries and sub regions.
3. If vaccination is used, the overall aim should be to use vaccination to assist in control and prevention of the disease until the virus can be eliminated using other methods.
4. To continue implementing the OIE standards, guidelines and recommendations, the FAO guidelines and recommendations, and the FAO/OIE Global Strategy on HPAI.
5. Vaccination should be considered on the basis of a comprehensive analysis including risk assessment of the country situation and context covering:
 - The disease situation in the country (e.g. endemic/enzootic, number and location of outbreaks, human cases, rates of virus isolation from markets, frequency of recurrence)
 - The structure of the poultry production systems, market chains and poultry density
 - The risk of introduction and subsequent secondary spread
 - The expected costs and benefits of vaccination to different stakeholders and the commitment of the stakeholders to fund the program
 - The feasibility, constraints and costs of applying vaccination compared to or in combination with other methods
 - The availability and quality of veterinary diagnostic laboratory services
 - The quality of the Veterinary Services and the institutional environment
 - The capability of the Animal Health Systems and producers to implement the various prevention and control measures including vaccination
 - The availability of quality controlled, matched vaccines authorised according to national regulatory standards, recognising that vaccines may require incorporation of more than one antigen or seed strain
 - The possible impact of HPAI in poultry on consumer behaviour (product avoidance) and subsequent market price development
 - Acceptance of policies by stakeholders, including poultry owners.
6. Planning support tools for vaccination, in development since the 2007 Verona meeting, should continue to be enhanced and vaccination handbooks providing practical guidance on vaccination programs should be developed.
7. The development of a comprehensive progressive control pathway as used for foot-and-mouth disease is not recommended at this stage for H5N1 HPAI prevention and control, given the current stage of endemic/enzootic countries.
8. All countries considering use of vaccines against HPAI should develop strategies for emergency use; and if vaccination is implemented, contingencies must be developed to include surveillance for antigenic variant field viruses. Such information should be used to evaluate the need to update vaccine seed strains.

On implementation of vaccination

9. Trigger points for consideration of vaccination (including emergency vaccination) should be included in country contingency plans for HPAI.
10. The objectives of any vaccination strategy/program should be defined before implementation in a country or region.
11. The objectives and the vaccination policy should be regularly reviewed and modified if required based on the assessment of the disease situation and the vaccination program. The objectives drive the vaccination strategy.
12. All vaccination programs should aim at obtaining highest possible level of immunity in the populations targeted for vaccination at the individual farm and population level, at least prior to high risk periods for infection.
13. An iterative approach should be adopted based on the continuous assessment of the HPAI disease situation and of the positive and negative aspects of the implemented prevention and control strategies so as to be able to adjust them as needed.
14. That any vaccination policy/program should include regular reviews during which the program is assessed as to whether vaccination is still required (exit from vaccination) and any changes to the scope of the program are determined.
15. Any country considering vaccination of household poultry should take into account the difficulties that have been encountered in implementing and sustaining these programs in some countries. Intensive programs have been implemented successfully for limited time period in some countries where public health was a priority.
16. The lessons learned from vaccination of smallholder and household poultry against H5N1 HPAI in Asia and Egypt should be examined if a routine or longer term vaccination program includes these production types.
17. Experiences on vaccination (field and laboratory) should be shared globally, including between developing countries.
18. The scope of vaccination programs depends on the local situation. Vaccination of household poultry should only be considered if there is a documented HPAI reservoir in this specific population, in case of increased human cases associated with this production sector, in cases of emergency ring vaccination, as a preventive measure immediately preceding and during high risk periods of virus incursion, or as part of a vaccinated buffer zone along borders that include all market places.
19. Alternative approaches to long-term vaccination should be considered for household poultry if it is apparent that it will be difficult to obtain or sustain appropriate levels of immunity in the target population.

20. Countries should consider vaccination to protect valuable birds such as specific poultry breeds (conservation of germplasm or maintain genetic biodiversity), zoo birds, pet birds, ornamental birds, (great grand and grand) parent flocks and fighting cocks when there is an increased risk of infection.

21. Biosecurity measures and other vaccinations to prevent immunosuppressive diseases should be applied.

22. It should be recognized that a ban on vaccination and its enforcement will not prevent illegal entry and use of vaccines. It should therefore be examined whether legal but tightly controlled trade in quality controlled vaccines is better than blanket bans.

On vaccines

23. Countries should ensure the availability of sufficient amount of quality controlled vaccines to support contingency plans, through the establishment of vaccine banks and/or strategic stockpiling of vaccines and/or specific arrangements with vaccine producers.

24. Systems for fast-track registration of vaccines containing updated seed strains should be introduced.

25. Investments into quality vaccine production should be increased through private led initiatives with local partnerships and these vaccines should be made available particularly in developing countries.

26. Poorly matched vaccines should be timely withdrawn from the market when they no longer provide appropriate protection against circulating strains of virus.

27. Vaccination using vaccines with inactivated avian influenza antigens should not be used before 7 days of age in poultry.

On surveillance, monitoring and evaluation

28. OIE member countries should comply with their obligations regarding the immediate and transparent reporting of any new HPAI outbreak through the World Animal Health Information System (WAHIS) and epidemiology capacity should continuously be strengthened in all countries.

29. Depending on the resources available and the sector(s) targeted, monitoring should be performed jointly by government veterinary services and the private sector through public-private partnerships comprising the following elements:

- Evaluation of post-vaccination immunity and monitoring of overall poultry population immunity level, including assessment against records of vaccines used,
- Monitoring of field virus circulation in vaccinated flocks,

- Maintaining records to know baseline mortality and routine testing of dead birds on farms,
- Clinical inspections and monitoring for AI viruses in live bird markets, and
- Monitoring of the genetic and antigenic characteristics of the circulating field viruses

30. These programs should be coordinated at national level and stakeholders should identify the most appropriate coordination mechanisms (e.g. the establishment of a technical committee with participation of main players).

31. The monitoring system should be audited regularly (including laboratory quality management).

32. Data from monitoring programs need to be generated and collected in a consistent manner with timely and transparent sharing of results between stakeholders.

33. The post-vaccination monitoring should be complemented by a parallel robust surveillance program in order to facilitate data interpretation by taking into account the actual field situation.

34. Case definitions should be modified to take into account the use of vaccination.

35. Epidemiologically sound surveillance for vaccination programmes should be used by strategists and policy-makers to target vaccine resources in the most effective way.

36. OFFLU, in collaboration with countries, will create a working group to collate and analyse genetic and antigenic data for AI vaccine seed strains and the circulating field viruses, and make recommendation as to which seed strains to include in poultry vaccines in order to maximize protection against HPAI. This depends on sharing of sequence data internationally and countries are encouraged to share such information.

37. The scientific and regulatory lessons from China and Indonesia on updating vaccine seed strains should be considered by countries that have had difficulty updating vaccines.

On research needs:

38. Research programmes in the following fields need to be developed and funded:

- New or improved vaccines for easier and broader application in the field, with induction of protective immunity earlier and lasting longer, and being DIVA compatible

- Protocol development for use of single or combinations of existing vaccine technologies (inactivated whole influenza virus oil emulsion vaccines, subunit protein vaccines, rNDV, rFPV and rHVT, rDVE¹) to improve protective immunity by eliciting broader and longer lasting protection
- Applied research to better correlate serological response data with expected protection in the field in different species (e.g. chickens, ducks) and ways to evaluate and understand effects of cell mediated immunity in vaccinated poultry
- On-going studies on the epidemiology (including molecular epidemiology) and ecology of AI viruses, the role of live poultry markets and market chains, AI viruses in wild birds and other animal species, possible social and economic impacts of vaccination, and collection and analysis of data generated during vaccination campaigns
- The combination of the AI vaccination with the control of other poultry diseases
- Operational research on field application of vaccination including the effects of seasonal vaccination campaigns.

39. OFFLU should assist in coordinating and compiling influenza research needs.

40. Further vaccination trials should be developed or supported in countries to evaluate the effectiveness of hatchery vaccination under field conditions.

41. FAO should continue efforts compiling information on trials with existing vector vaccines.

On veterinary services

42. Continued support should be provided to strengthen Veterinary Services and to improve their governance when appropriate to assist them in complying with the relevant OIE international standards notably through the use of the OIE Performance of Veterinary Services Pathway (PVS) tools

43. Countries should continue developing appropriate capacity building programmes including training in epidemiology, disease/virus surveillance and reporting, field and laboratory diagnosis, vaccination skills, campaign implementation, understanding and improving farming system, socio-economic analysis, programme evaluation, decision making and policy development.

44. Countries should provide the appropriate legislation and governance to implement HPAI control/preventive measures including vaccination and the means to enforce it and to

¹ Respectively: Newcastle disease virus, fowlpox, herpesvirus and duck virus enteritis vectored vaccines

streamline the regulatory process of vaccine authorization.

45. Importing countries should apply the OIE standards to avoid unjustified trade barriers related to vaccination against avian influenza.

On public private partnerships and communications

46. Vaccine distributors should provide improved support to smallholders including advice and availability of appropriate pack size of vaccine doses to facilitate vaccination of small poultry flocks at an acceptable price.

47. To overcome the cost of vaccination, targeted vaccination with epidemiological surveillance, cost sharing (public-private partnership) and increased biosecurity should be considered.

48. Public-private partnerships should be strengthened including links with poultry farmer groups, organisations or cooperatives.

49. The commercial poultry industry should reinforce its engagement in the control and prevention of HPAI with national/local authorities and a dialogue between the two stakeholders should be regularly established.

50. The international community should continue to support the control and prevention of HPAI including the application of vaccination, as a substantial Global Public Good component, particularly in developing countries.

51. Appropriate communication strategies should be used to enhance vaccination coverage and application by ensuring the commitment of producers, to allay concerns of farming communities and to assess the effectiveness of these campaigns.