Vaccination and Surveillance for HPAI in Poultry:

Current Situation and Perspectives

Venue: World Organisation for Animal Health, Paris - France

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Conclusions:

- Since the last International Alliance for Biological Standardization (IABS) workshop on high pathogenicity avian influenza (HPAI) vaccination (22-23 October 2022), the H5Nx goose/Guangdong (Gs/GD) lineage of HPAI has seen substantive changes in ecology and epidemiology including extending across South America and into the Antarctic to now affect six continents; negatively impacting a diverse and large number of wild birds and mammal species including mainly carnivores but also dairy cattle; mammal-to-mammal transmission in dairy cattle, sea lions and elephant seals; and some genetic changes indicating increased risk to mammals, including humans.
- Biosecurity and stamping-out have not been fully effective at preventing and controlling the H5N1 Gs/GD HPAI panzootic and infection is persisting in and being spread by wild birds.
- The World Organisation for Animal Health (WOAH) Terrestrial Animal Health Code (Terrestrial Code) supports use of vaccination as a complementary tool in prevention and control of HPAI in poultry, and such use should not impact HPAI freedom of a country/zone/compartment when supported by appropriate surveillance.
- Vaccination should facilitate safe trade by decreasing the risk of HPAI in poultry and poultry products.
- Vaccination shall not be the sole measure for prevention and control of HPAI, which should also be accompanied by biosecurity measures, movement controls and stamping-out of infected flocks.
- The primary barriers to increasing uptake of vaccines for HPAI in poultry include:
    - Non-tariff trade barriers on poultry and poultry products from vaccinating countries,

    - the undefined recommendations in the WOAH Terrestrial Code for appropriate surveillance to demonstrate HPAI freedom in vaccinated populations,
    - the limited global availability of vaccines against H5Nx Gs/GD HPAI,
    - Perceived high cost of vaccination and accompanying surveillance, and
    - Concerns that vaccinated farms will still have all birds destroyed even if only a single bird is found to be infected with HPAI virus.

- HPAI vaccination with fit-for-purpose vaccines and appropriate surveillance can be an effective and successful tool in controlling HPAI outbreaks and stopping sustained HPAI transmission and spread based on the experience of several countries or regions.
- Laboratory contact transmission studies and field experience with adequate surveillance in well-vaccinated flocks exposed to virus indicate “silent infection” (i.e. sustained transmission without birds getting sick or dying) occurs rarely in chickens.
- If transmission does occur, a minority of birds with low or no protection will develop disease thus allowing detection of virus in a naturally susceptible subpopulation, i.e. daily mortality or morbidity surveillance samples. In domestic ducks, silent infection already occurs in non-vaccinated flocks.
- Sustained transmission with elevated mortality can occur in well-vaccinated chicken flocks if the vaccine antigen does not adequately match the field challenge virus, or if the flock is poorly or sub-optimally immunized.
- Vaccinated flocks are a much lower threat of having sustained infection than non-vaccinated flocks, and of transmitting the infection to other hosts because of reduced shedding and environmental contamination.
- If infection does occur in a vaccinated flock, it will lead to much lower mortality than a non-vaccinated flock.
- Additional doses of vaccines (i.e. booster vaccinations) may be required for protection over the long production cycle of some poultry species and production systems.

- Serological monitoring, by HI test using homologous antigen to circulating strains, can inform the success of the vaccination process by determining if the vaccinated birds have a uniform, protective immune response.
- The use of expensive and unnecessary surveillance testing methods inhibits uptake of vaccination.
- An appropriate surveillance system will draw on multiple sources of information.
- Risk-based virological surveillance (e.g. targeting dead or secondarily, clinically affected birds) is a more sensitive, cost-effective and efficient approach, especially for chickens and other species that are likely to die from HPAI, than random sampling of healthy birds.
- Routine testing of vaccinated chicken flocks by random sampling of healthy birds is inefficient and unnecessary as other signals will be present if HPAI virus is circulating.
- Non-vaccinated sentinels are no longer a useful surveillance tool in vaccinated poultry populations because of potential drawbacks and practical concerns with managing sentinel poultry based on countries' experiences.
- Surveillance must consider the requirements of health certificates necessary for trading of day-old chicks, hatching eggs and meat.
- Based on countries' experience, constant review on the vaccine protectiveness against the circulating field strains with a view to update the HPAI vaccine strains in a timely manner is necessary to assure vaccine efficacy against circulating strains HPAIV infection.
- Virological surveillance in wild birds and poultry (vaccinated and non-vaccinated) will provide isolates that can be used in determining HPAI status and assessing the national HPAI prevention and control programs and antigenic match of vaccines to circulating strains. Field viruses and their genomic information should be shared with national and WOAH avian influenza reference laboratories, and the WOAH and Food and Agriculture Organization Animal Influenza Expert Network (OFFLU) Avian Influenza Matching (AIM) program for genomic and antigenic analysis to assess protection of available inactivated vaccines, and for recommendations for timely updates to vaccines as needed.
- Serological surveillance to detect infected among vaccinated animals ('DIVA') has limited use in vaccinated populations and is not an essential component of

surveillance systems. It can provide evidence of freedom from infection in a retrospective manner; however, its technical limitations and interpretation need to be recognized.

- Serological surveillance for demonstration of HPAI virus freedom may not be useful under certain situations, e.g. in the presence of circulating LPAI viruses in the field (especially H5, H7, and H9), with the concurrent use of LPAI vaccines, or with the use of inactivated whole virus vaccines. In addition, even with a highly specific DIVA serological test, positive results due to infection with influenza A viruses other than the target strain will regularly appear leading to unnecessary suspicion of infection which would need further testing by other serological tests or collection of additional samples for qRT-PCR testing for active virus infection.
- There is a worldwide shortage of government personnel to collect surveillance samples and in government laboratory capacity to test such samples in a national or regional surveillance program.
- The Terrestrial Code is well-developed and utilized in developing HPAI-free compartments, especially for poultry genetics, but importing country acceptance needs additional transparency and communication on the validity of the process.
- It is evident that HPAIV vaccination can be beneficial not only for large commercial poultry producers, but also for smaller production systems and hobby flocks. In low- and middle-income countries, these flocks play a significant role in family income generation and contribute substantially to the basic supply of animal protein. In high-income countries such as in Europe and North America, the small hobby poultry flocks are a growing phenomenon.
- The primary objective of vaccinating small and hobby poultry flocks is to safeguard against clinical manifestations of HPAI and to minimize the risk of infections during frequent and intensive contacts between poultry and human caretakers, especially children. This sector plays no role in transboundary trade and has negligible risk of HPAI virus transmission to commercial poultry in high-income countries.

Recommendations:

- Trade policy should be based on science and not politics or protectionism.
- Molecular diagnostics, primarily quantitative real-time polymerase chain reaction (qRT-PCR), should continue to be the primary test for sensitive, specific detection of

HPAIV infections during the period of active infection in both vaccinated and non-vaccinated poultry.

- WOAH international standards with the inputs of scientists will establish mechanisms and relationships that provide assurance for best vaccination practices. Because of shortage of government personnel, surveillance samples collected by private field veterinarians or trained people should be accepted under a government accreditation program. In addition, private laboratories should be approved by the competent authorities in the member state through an auditable certification program to perform tests, allowing the results to be utilized in the official prevention and control program.
- Virological surveillance should be conducted in wild birds and poultry (vaccinated and non-vaccinated), to support identification of HPAI virus infections for assessing successfulness of control programs and any detected viruses should undergo further evaluation.
- Strengthening international collaboration, as well as data, virus isolate and genomic sequence sharing, should facilitate development and deployment of efficacious vaccines and timely updates to vaccine formulations, and support implementation and updates to vaccination programs.
- Appropriate surveillance of vaccinated poultry, to find active infections, should be risk-based, multi-layered and primarily virological surveillance using highly specific and sensitive qRT-PCR assays.:
    - The approaches that are suitable for a particular context vary but should provide equivalent outcomes in terms of surveillance sensitivity and time to detection.
    - According to a recent EFSA (European Food Safety Authority) opinion, primary samples should focus on dead birds up to 15 per flock (i.e. “bucket surveillance” with birds collected over 24-hour period and maximum of 48 hours), but if insufficient numbers of dead birds are available, clinically ill birds with specific HPAI signs (e.g. neurologic signs, blue [necrotic] combs, etc.) are viable supplemental samples, and if insufficient, clinically ill birds with non-specific signs (e.g. listlessness, hunched posture, etc.) are suitable.
    - Bucket surveillance is an established, sensitive surveillance system for detecting early infection and confirming HPAI freedom in vaccinated and non-vaccinated poultry, especially in chickens, and utilize pooling of samples to reduce cost without loss of sensitivity.

    - Because of low mortality in ducks from HPAI virus infection, bucket surveillance alone may provide insufficient number of specimens and should be supplemented with birds having clinical signs and environmental samples.
    - Bucket surveillance should be used to detect sustained transmission. If a single positive dead bird is found, retesting should be done to confirm sustained transmission which would lead to culling.
    - Sampling of environmental matrices (e.g. dust, aerosols, water, etc.), for virological surveillance, if found suitable in validation studies, presents potentially sensitive and cost-effective opportunities for early HPAI virus detection in vaccinated flocks before the onset of clinical signs or mortality.
    - Potential environmental samples for virological surveillance could include biofilm of poultry drinkers, swabs from boots used in the poultry house, swabs of ventilation louvers, swabs of egg belts, wastewater from processing plants, eggshell wash fluid, environmental samples used for regulatory testing for salmonella, etc.
    - There is a lack of general utility for surveillance sampling healthy chickens in a vaccinated population, but some potential for such use in ducks.
    - Surveillance must be cost-effective, efficient and sustainable.
- Serological surveillance, including use of DIVA-compatible vaccines, can at best only be part of a carefully balanced surveillance strategy in vaccinated poultry such as for assessing the presence of low infection rates before making major changes in or stopping a vaccination program.
- Virological surveillance, using qRT-PCR, is DIVA-compatible with any type of vaccine
- Undertake targeted research addressing uncertainty in surveillance and biosecurity to reassure trade partners
- The vaccination process should be assessed by monitoring for protective humoral immune response, especially if using inactivated vaccines. This informs the program on:
    - Effectiveness of the vaccination process to correctly apply vaccines and produce a protective immune response in most poultry, resulting in flock immunity,
    - Timing of booster vaccinations,

    - Focusing of virological surveillance to flocks with suboptimal immune responses because of much higher probability of infection and transmission, and
    - The need for investigating HPAI vaccines for antigenic updates in a timely manner
- The potential to create vaccination subpopulations whose existence would reduce inhibition of trade in non-vaccinated poultry and poultry products, should be explored.
- Inactivated vaccines that are a poor antigenic match to circulating strains should not be used and such vaccines should be updated. Vector vaccines can provide broader cross protection against antigenically diverse strains but protection against antigenically variant strains should be assessed especially if there is evidence of infection in vaccinated flocks.
- The registration of vaccines should be based on dossiers including quality, safety and efficacy data. Extrapolation of data for minor species should be considered, to avoid repetition in clinical trials already completed elsewhere.
- Development and adoption of multi-strain approaches in vaccine registration concepts should facilitate the exchange of vaccine antigens (e.g. replacement by new invading strains or the emergence of escape mutants) avoiding time-consuming and costly needs of a full licensing process, if the same vaccine platform is utilized. In countries where such a process exists, sharing of the expedited process between countries will accelerate adoption.
- Discussions with the biologics industry should be extended to the input into the design (not only Specificity and Sensitivity) of the tools used for surveillance. For example, an external positive control should be included in qRT-PCR kits to assist the end user in validating kits to new substrates, such as environmental samples or milk, thus facilitating more rapid adapting of surveillance tools while avoid repeating development and validation by the manufacturer.
- Vaccination of small and hobby poultry flocks should be considered to reduce risk of human infection, and because of low transmission risk to commercial poultry, surveillance of individual hobby poultry premises is not necessary.
- Publish Conclusions and Recommendations from the meeting on the IABS website and disseminated to partners.

- IABS commissions the writing of a concept paper for surveillance of vaccinated poultry populations against HPAI to be published in the peer-reviewed journal Biologicals. This will help meet the need for stronger international guidance to facilitate the updating of trade agreements when vaccination is implemented.
- Based on the outcome of the concepts paper, IABS, in consultation with OFFLU experts, will propose an update to the current WOAH Standards, particularly for vaccinated poultry, and if appropriate, develop guidelines to assist countries in biosecurity, surveillance and vaccination standards in support of safe trade.
- After 2 years, IABS convene a workshop on vaccination for prevention and control of HPAI, to discuss, analyze and disseminate information on the progress in surveillance development and implementation, and on utilization of vaccination for prevention and control of HPAI in poultry.