Modeling the effectiveness of avian influenza vaccination strategies in Vietnam: evaluation of the added value of day old chick vaccination in hatcheries

General context and objectives of the project
Vaccination against avian influenza (AI) is currently being implemented worldwide mostly using inactivated vaccines that are not applicable to day old chicks (DOCs). Since November 2012, a novel recombinant HVT (Herpes virus of Turkey) AI vaccine has been recently commercialized and applied in some industrial hatcheries in Vietnam. In principle, vaccination of DOCs at hatcheries, with the use of limited resources, would ensure sufficient vaccine coverage and protection levels. The objectives of this study were to assess the cost-effectiveness of AI DOC vaccination in hatcheries and feasibility of implementing AI DOC vaccination in the different production sectors in Vietnam.

A model of the Vietnam poultry production network was combined with a flock immunity model to simulate the distribution profile of AI immunity according to the different types of poultry farming (i.e. Grand Parents, breeders, layers or broilers) and production sectors (1 to 4); and vaccination scenario (including absence or presence of DOC vaccination). The model estimated the vaccination coverage (proportion of vaccinated birds from the total population considered), the protective sero-conversion level (birds with haemagglutinin inhibition (HI) titers greater than 4log2) and the duration of immunity (number of weeks where more than 70% of the birds had a protective sero-conversion level) for each node of the network and vaccination scenario.

Public private partnership (PPP) in Veterinary Public Health
This work is the product of a public-private partnership between CIRAD, a French research public institute for Agricultural development, the National University of Agriculture of Vietnam (VNUA) and CEVA. PPP aims to create conditions of partnership between Public and Private Stakeholders: to reach a common goal by developing complementary means and skills within a given perimeter supporting respective interests. CEVA contributes to the project in terms of vaccine development and private sector understanding; while CIRAD and VNUA brings in technical competency for scientific approach for evaluation of control strategies from the local to national level.
**Project organization**

A first mapping of the poultry industry was performed by CEVA in 2013. In 2014 a field study was implemented in collaboration between VNUA, CIRAD and CEVA experts to collect additional information on poultry production (type of poultry production(s), farm total capacity per year, total volume of DOC production per year, origin and destination of the DOCs) and AI vaccination strategy ((vaccine coverage, vaccine type, vaccination protocol and perception of AI vaccination (including DOC vaccination)). Quantitative data on avian influenza vaccine efficacy were collected from scientific and grey literatures (reports on laboratory and field evaluation in Vietnam) or obtained from VNUA, CIRAD and NIVR. The network analysis and immunity modeling was then performed by CIRAD and VNUA and the results were presented for validation during an expert workshop in October 2014 gathering experts from public and private sectors, from laboratory, epidemiology and poultry farmers from all sectors and from international organisations.

**Vaccination scenarios**

Six vaccination scenarios were identified based on centrality and connectivity analysis of the structure of the poultry production network and age at vaccination (vaccination of birds > 7 days old and/or DOCs) (Table 1). DOC vaccination of long cycle birds (breeders and layers) was only considered as a prime-boost strategy (vaccination at day old in hatcheries and boost at 20 weeks in breeder farms); whereas DOC broiler vaccination was considered as one single shot of vaccine.

| Table 1: Description of the vaccination protocols considered within the different vaccination scenarios considered and tested by the model |
|---------------|-----------------------------------|---------------------------------|-----------------|-------------------|-----------------|
| DOC source    | Integrated hatcheries              | Non-Integrated hatcheries Large and medium | Government hatcheries | Non-Integrated hatcheries Small (native birds) |
| DOC destination | Integration (Sector 1) | Contract Farms (Sector 2 and 3) | Clients Small farms (Sector 3) | Medium and small farms (Sector 2 and 3) | Medium and small farms (Sector 2 and 3) |
| Scenario 1    | Farm vaccination                   | Farm vaccination                 | Farm vaccination   | Farm vaccination   | Farm vaccination |
| Scenario 2    | Hatchery                          | Hatchery                         | Farm vaccination   | Farm vaccination   | Farm vaccination |
| Scenario 3    | Hatchery                          | Hatchery                         | Hatchery           | Farm vaccination   | Farm vaccination |
| Scenario 4    | Hatchery                          | Hatchery                         | Hatchery           | Hatchery           | Farm vaccination |
| Scenario 5    | Hatchery                          | Hatchery                         | Hatchery           | Hatchery           | Hatchery         |
| Scenario 6    | Hatchery                          | Hatchery                         | Hatchery           | Hatchery           | Hatchery         |
Network analysis of Vietnam chicken production system

Models of the Vietnam broiler and layer production networks were developed based on type of poultry production (i.e. Grand Parents, breeders, layers or broilers) and farm production sizes (number of heads and volume of production for a one year period) (Figure 1). Each node represented a type of poultry production; each link represented either the movement of eggs (between breeder farms and hatcheries) or the movement of DOCs (between hatcheries and commercial broiler/layer farms).

![Commercial Broiler Network](A)

![Commercial Layer Network](B)

![Native chickens network](C)

Figure 1. Vietnam broiler (A), layer (B) and native (C) poultry production network models. The types and colors of nodes represent the different types of productions: integrated (red); contract (green), government (light blue) or independent farms (black) of grand-parents (GP), commercial broilers (Bro) or layers (Lay). The size of the nodes represents the number of birds per nodes. The arrows represent the movement of eggs or day old chicks (DOC- between the nodes and the size of the arrows the volume of eggs or DOC for each movement.

Interest of using network analysis approach to display poultry production system in Vietnam:

- To present the dynamic model of DOC flow within the poultry production network
- To identify most important actors to target surveillance and control strategies
- To combine with other models (e.g. immunity or/and infection models) to predict outcomes of surveillance and control strategies
Added value of DOC vaccination for commercial broilers and layers

Under the current strategy (scenario 1= farm vaccination with inactivated vaccines), only a limited percentage of the total poultry population (<40%, only long cycle birds (GPs and breeders)) has sufficient level of immunity against avian influenza (vaccine coverage >80% and sero-protection >60%) (Figure 2A and 2B). With the introduction of hatchery vaccination of broiler DOC produced and raised in the integrated companies (Scenario 3), the model predicts that the immunity level for the whole broiler populations will rise above protective levels (Figure 2A and 2B). Moreover, the duration of sero-protection in the broiler population, under the current scenario (vaccinated at the farm with inactivated vaccine) is currently below 20% of the birds production time (Figure 2C). Hatchery vaccination of DOC will increase this protection time by 20-40% according to the type of production (Scenario 3 and 4) (Figure 2C).

Figure 2. Evolution of the vaccine coverage rate (A), the positive sero-conversion rate (B) and the duration of sero-protection (C) for broiler bird population, expressed as a percentage of the bird population per poultry production type and according to the different vaccination scenarios tested in the model: Sc1= no DOC vaccination (farm vaccination only with inactivated vaccine); Sc2= vaccination of DOC in integrated farms; Sc3= vaccination of all DOC produced by integration DOC (including sold clients); Sc4= Sc3 + DOC vaccination in large/medium hatcheries; Sc5= DOC vaccination in medium all hatcheries.
For the layer population similar results are observed (data not shown), with sufficient immunity and duration of immunity above 60% from Scenario 3.

The situation is different for the native population which is mainly produced by medium and small breeder farms: the immunity in the total native population will increase if hatchery vaccination was introduced up to the medium size independent breeder farms but will only reach sufficient levels is DOCs produced by small breeder farms were vaccinated (Figure 3).

![Figure 3. Evolution of the vaccine coverage rate (A), the positive sero-conversion rate (B) and the duration of sero-protection (C) for native bird population, expressed as a percentage of the bird population per poultry production type and according to the different vaccination scenarios tested in the model: Sc1= no DOC vaccination (farm vaccination only with inactivated vaccine); Sc2= vaccination of DOC in integrated farms; Sc3= vaccination of all DOC produced by integration DOC (including sold clients); Sc4= Sc3 + DOC vaccination in large/medium hatcheries; Sc5= DOC vaccination in medium all hatcheries; Sc6= All DOC vaccination.](image_url)

**Commercial poultry best scenario = Sc 3-4** (vaccination of all DOC produced by the integrations and large breeders)

- Total broiler and layer population vaccine coverage >80%
- Total boiler population sero-protection >60%; layer population sero-protection ~80%
- Total broiler population duration sero-protection >50%; layer duration sero-protection ~60%

**Native poultry best scenario = Sc 5-6** (vaccination of DOC up to medium and small breeders)

- Total native population vaccine coverage =80%
- Total native population sero-protection =60%
- Total native population duration sero-protection >40%
Spatial distribution of AI immunity according to the different vaccination strategies

As the poultry population density is not homogeneous within the country it is important to assess the distribution of the immunity levels at the spatial level (Figure 4). The spatial distribution profile of AI immunity was heterogeneous across the provinces, which reflected this spatial cluster distribution of the different poultry production types. However, the best scenario to ensure sufficient protection in the areas classified at high risk of infection was the same as for the homogeneous population model outputs described before (Scenario 3 and 4) (Figure 4).

Figure 4. Spatial distribution of the bird population immunity against AI according to the different vaccination scenario tested in the model. For each scenario the percentage of vaccine coverage, protective sero-conversion and duration of immunity (model outputs) were weighted according to the poultry density (for each production type) per province. The area classified at high risk of HPAI infection (according to the cumulated number of poultry outbreaks since 2004) are circled in red.
Conclusion

This study demonstrated the interest of combining network analysis and immunity modeling to assess the efficacy of AI vaccination scenarios. The model predicted that targeting DOC AI vaccination would increase immunity levels in the overall poultry population up to sufficient levels to improve HPAI disease control in commercial poultry. The model predicted that targeting DOC AI vaccination in integrated hatcheries would increase immunity levels in the overall poultry population and especially in small commercial poultry farms. DOC vaccination strategy was shown to be more efficient than the current strategy using inactivated vaccines. Improving HPAI control in commercial poultry sector could have positive spill over effect on the epidemiological situation of the disease in native and backyard poultry. This model could be applied for strategic management of other contagious diseases such as Newcastle Diseases.

- AI farm vaccination strategy (inactivated vaccine) (Sc1):
  - Allows for sufficient coverage and sero-protection in long cycle production (e.g. breeders and layers)
  - Provides limited duration of protection in long cycle birds
  - Not efficient for broilers and native birds

- DOC vaccination (vectored vaccine) (Sc3-Sc5):
  - Improves duration of sero-protection in long cycle birds
  - Provides sufficient vaccine coverage and immunity levels in broilers even in small farms
  - DOC vaccination targeted in large integrated hatcheries (Sc3) allows for sufficient immunity and duration of immunity in the total population especially in high HPAI risk areas.

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