Epidemiological and Financial Implications of HPAI Vaccination

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Preface

Since its emergence, H5N1 HPAI has attracted considerable public and media attention because the viruses involved have been shown to be capable of producing fatal disease in humans. While there is fear that the virus may mutate into a strain capable of sustained human-to-human transmission, the greatest impact to date has been on the highly diverse poultry industries in affected countries. In response to this, HPAI control measures have so far focused on implementing prevention and eradication measures in poultry populations, with more than 175 million birds culled in Southeast Asia alone.

Until now, significantly less emphasis has been placed on assessing the efficacy of risk reduction measures, including and their effects on the livelihoods of smallholder farmers and their families. In order to improve local and global capacity for evidence-based decision making on the control of HPAI (and other diseases with epidemic potential), which inevitably has major social and economic impacts, the UK Department for International Development (DFID) has agreed to fund a collaborative, multi-disciplinary HPAI research project for Southeast Asia and Africa.

The specific purpose of the project is to aid decision makers in developing evidence-based, pro-poor HPAI control measures at national and international levels. These control measures should not only be cost-effective and efficient in reducing disease risk, but also protect and enhance livelihoods, particularly those of smallholder producers in developing countries, who are and will remain the majority of livestock producers in these countries for some time to come.

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Keywords

Vaccination, Epidemiology, Economics, Highly Pathogenic Avian Influenza (HPAI), Poultry production systems, Chicken, Ducks.

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Executive Summary

Several HPAI vaccination campaigns have been implemented in Southeast Asian countries and have required substantial financial and veterinary resources. It thus appears warranted to assess both, the epidemiological as well as the economic implications of large-scale vaccination campaigns for HPAI control. This includes an assessment of the achievable immunization coverage with vaccination campaigns and the financial incentives for flock owners to use vaccination in their respective poultry production system. Based on the respective financial incentives for the use of vaccination in poultry production systems and their specific dynamics an evaluation of the potential achievable vaccination coverage and its contribution to overall disease control is conducted.

Vaccines

Many commercially available vaccines provide some level of protection from infection with virulent virus and significantly reduce morbidity and mortality in infected chicken. Although virus excretion of vaccinated and infected birds is significantly reduced some level of virus excretion usually remains. In contrast to the poultry owner, from an national animal health planner perspective the most important characteristic of vaccines is the reduction of virus excretion to stop disease transmission. Properly vaccinated birds have been shown to shed less virus but at the same time the probability of detecting outbreaks decreases due to a lack or reduction of clinical signs which may lead to the silent spread of virus.

The efficacy of most commercially available vaccines has been determined in studies with Specific Disease Free (SPF) chickens or turkeys reared under laboratory conditions, the results of which cannot necessarily be extrapolated to field conditions. In many developing countries other species such as ducks, muscovy ducks and quails represent significant parts of the poultry sector. The contribution of ducks to the maintenance and spread of HPAI virus has been shown in several studies. Thus, effective vaccines and vaccination strategies are required for ducks and other species to stop viral transmission.

Several risk factors can be identified during the vaccine delivery and administration process which may reduce the effective immunization rate of vaccinated birds. All currently available commercial HPAI vaccines require administration to poultry via injection with a syringe. Generally a two dose vaccination schedule is required to achieve satisfactory protection against HPAI in any poultry species which results in an unprotected time period after vaccination. Available field study results have shown that HPAI vaccine becomes fully effective only about 13-21 days after the first of two vaccine injections. A cold chain is required to maintain vaccine efficacy, which poses logistical challenges for the delivery organization. Genetic and antigenic shifts have been observed in vaccinated poultry populations. Sampling and testing requirements for seroconversion, virus and serum identification represents a challenge for the capacity of most laboratories in developing countries.

Vaccination Coverage with Routine Vaccination Campaigns

Poultry production system characteristics can be used to identify the maximal achievable vaccination coverage with mass vaccination campaigns and whether this coverage is capable of reducing disease transmission. Important characteristics are the average lifespan of poultry in the respective production system, origin of replacement birds (home bred vs.
bought), and the disease status and immuno-competency. An additional flock characteristic with high importance for the effectiveness of any disease control measure is the contact rate between flocks. Although flock characteristics such as contact rates differ substantially between flocks in different production systems, they are usually rather similar for flocks of the same type of production system.

Within the poultry sector, four main production systems can be identified: Breeder flocks, layer flocks, broiler flocks and backyard multi-purpose flocks. This production system classification roughly applies to both chickens and ducks. However, in some Southeast Asian countries free-range grazing duck systems prevail that are a mixture of layer and breeder systems.

Financial Incentives to Use Vaccination and Alternatives

The costs and benefits of vaccination differ depending on the perspective of the decision maker. Vaccination can be seen as an ‘insurance scheme’ by poultry keepers and their main interest is to prevent private financial losses from poultry mortality and morbidity at a minimum of private cost. An animal health policy maker would be interested in a vaccination strategy that reduces the risk of HPAI transmission between flocks and to humans at the lowest public cost. Nevertheless, the private financial incentives of individual flock owners are important for the success of any vaccination strategy. Without sufficient motivation at the poultry owner level, compliance with vaccination schemes and sufficiently high immunization rates are not likely.

The flock owner’s decision on whether to contract a ‘vaccination insurance policy’ depends on the vaccination costs (‘insurance premium’), the expected economic loss in case of an outbreak and the perceived probability of an outbreak. Ratios of vaccination costs to outbreak losses (‘breakeven outbreak risks’) indicate the probability of flock infection at which expenditure on vaccination in a specific production system would be profitable for a risk neutral flock owner.

Grandparent and layer chicken flock owners have the highest incentive to adopt vaccination. However, for relatively profitable laying hens with an estimated potential HPAI outbreak loss of 3 – 5 USD per bird the breakeven risk of 1 - 3% would not financially justify the use of vaccination for a risk neutral poultry keeper. Even under high infection risk conditions such as those during the peak incidence in 2004 in Thailand, only 0.2% of all poultry farms were infected with HPAI. An estimated breakeven risk level of 7 - 75% for short-lived industrial broiler flocks indicates an even lower private incentive to use vaccination, which only protects against infection for a small proportion of a broiler lifespan. Vaccination of an average backyard chicken flock of 16 birds would be profitable for a risk neutral flock owner, if the annual risk of HPAI infection were higher than 17%. Since such a high infection risk level is very unlikely, the average benefits of free of charge vaccination for backyard chicken flock owners would be marginal. If other vaccines to prevent more financially relevant diseases were delivered in addition and HPAI vaccinated flocks would be exempted from culling, subsidized HPAI vaccination would be a pro-poor disease control intervention.

In view of the relatively low private incentives to use vaccination, flock owners may consider other protection measures such as improvements of production hygiene and investments in cleaning and disinfection equipment. For a flock of 1,000 industrial broilers the annual vaccination costs vary between 325 and 651 USD. Detailed assessments of the specific risk
factors for the entry of the disease agent into these production systems would be essential to estimate the potential feasibility, costs and effectiveness of achieving a higher disease protection level for the respective flocks. Nevertheless, simple improvements, such as cleaning and disinfection equipment for poultry selling, cages, and work clothes are likely to cost less than the above estimated costs for vaccination.

Broilers represent the largest share of poultry which is marketed through live poultry markets and in contact with a magnitude of consumers in many Southeast Asian countries. Effective immunization of broilers would reduce the exposure of live bird market customers to HPAI virus and therefore reduce the public health risk. However, the required vaccination costs to supply a medium size live bird market with a daily trade volume of 1,000 broilers would amount to 1,151 – 1,707 USD per month. Similar to the situation on broiler farms a detailed assessment of the costs, effectiveness and feasibility of other market hygiene improvements and behaviour changes need to be considered in order to choose the most cost-effective public health risk reduction strategy.

**Conclusion**

The objective of routine vaccination would be to interrupt the infection chain, i.e. achieve a between-flock reproductive number $R_0<1$. The resulting required coverage depends on the infection dynamics in the absence of control measures. $R_0$ has been estimated for several situations in the range of 2 to 3. Thus, under ideal conditions, vaccination of between half and two thirds of flocks would be sufficient to stop between-flock transmission. While this may be achievable for a point in time, the problem remains that flock immunity rapidly decreases requiring relatively frequent repeat vaccination tailored to the specific dynamics of production systems, further constrained by the challenging logistics of vaccination campaigns.

The vaccination cost-effectiveness estimations for different poultry production systems and common infection risk levels in endemically infected countries indicate low private financial benefits for poultry owners to use HPAI vaccination. Vaccination of more valuable breeder and layer flocks is generally more profitable from the flock owners perspective, but at the same time the feasibility and costs to upgrade biosecurity in these systems is likely to be lower than in other production systems. The cost-effectiveness of other protection measures, such as trade and market hygiene interventions, should therefore be taken into consideration in order to identify cost-effective HPAI protection options.

Once a larger scale routine vaccination strategy has been adopted by the government several political responsibility and economic issues arise from considering the continuation or exit of vaccination. A high political risk could be expected from the decision to withdraw vaccination, if subsequently human cases of HPAI were reported. During a transition period prior to withdrawing vaccination additional resources would be required for increased surveillance and outbreak response systems to monitor disease status and rapidly control outbreaks when vaccination is not used anymore.

The question remains, whether the short to medium term gains in risk reduction through vaccination result in a cost-effective long-term control approach, i.e. does vaccination use and incentives on flock owner level lead to a minimum control cost solution for the whole sector?
I. Introduction

Since its emergence in 1996 in China, highly pathogenic avian influenza H5N1 virus has infected sixty-one countries, been associated with more than 260 human fatalities, and resulted in disease mortality and culling of several hundred million domestic birds. In most of the affected countries, the H5N1 virus could be eliminated through swift and determined interventions of national animal health systems. In some countries, however, the virus appears to have become endemic in specific eco- and production systems, leading to resurgence of infection in poultry and humans the moment control efforts are relaxed. The major countries in which HPAI H5N1 virus can currently be considered endemic comprise China, Egypt, Indonesia and Vietnam, all of which have included vaccination as part of their national control strategy.

Under laboratory conditions, vaccination trails against highly pathogenic avian influenza (HPAI) have shown that a variety of commercially available vaccines protect against clinical signs and reduce virus shedding in the case of contact with field virus but do not prevent infection in all vaccinated birds. (Swayne et al. 2008, Peyre et al. 2008). However, prior to the massive epidemics of H5N1 in Southeast Asia, only very few attempts to control HPAI outbreaks in domestic poultry populations by vaccination have been reported. Pre-H5N1 experience in the use of vaccination in large-scale HPAI control programmes was gained in Mexico (H5N1, 1994), Italy (H7N1, 2000), and Pakistan (H7N3, 2003) (van den Berg et al. 2007). In the course of the current H5N1 avian pandemic, several large-scale HPAI vaccination campaigns have been implemented by national animal health authorities in China, Hong Kong, Vietnam, Indonesia and Egypt. Experience has shown that despite the theoretical potential of vaccination to control HPAI epidemics (Swayne 2000b, van den Berg et al. 2007), this potential is in practice not fully realized in large-scale vaccination efforts due to the numerous constraints to delivering and administering vaccine in large and heterogeneous poultry populations (van den Berg et al. 2007).

Large-scale vaccination campaigns require substantial financial and human resources and therefore are unlikely to be sustainable over long time periods. It thus appears warranted to assess the technical, epidemiological as well as the financial implications of large-scale vaccination campaigns for HPAI control, both from a theoretical as well as from a practical perspective. This paper reviews existing data and literature on HPAI vaccines, HPAI epidemics, and large-scale HPAI H5N1 vaccination programmes and draws on calculations carried out by the authors to assess and evaluate the potential contribution and the financial implications of mass vaccination in the control of HPAI H5N1 in domestic poultry in developing countries.

The paper starts by reviewing the literature on various characteristics of commercially available HPAI vaccines which determine their utility as a tool for the control of HPAI in different poultry species. The following section presents the three HPAI vaccination strategies proposed by the Office International des Epizooties (OIE) and provides an overview of estimates of immunization rates that would be necessary to suppress H5N1 virus transmission to a level where infection dies out. Estimates of the maximum vaccination coverage that would be achievable in different poultry production systems through mass vaccination campaigns carried out under ideal conditions are presented in Section V. The following section summarizes common challenges for the implementation of large-scale
vaccination programmes and experiences with the implementation of such programmes are compiled in Section VI. Section VII provides assessments of the costs and returns of vaccination from a production systems perspective as well as considering the broader public aspects of embarking on vaccination as part of a national HPAI control programme. Finally, the last section discusses the advantages and drawbacks of large-scale vaccination programmes and their potential contribution to HPAI control.
II. Characteristics of Commercial HPAI Vaccines

Route and schedule of vaccine administration

All commercially available HPAI vaccines require administration to poultry via injection with a syringe. Vaccines for administration via other routes, such as aerosols, drinking water or injection during egg incubation are not currently available (Swayne et al. 2008b). Generally, a two-dose vaccination schedule is required to achieve satisfactory protection against HPAI in any poultry species. Application of the booster vaccination is often inconvenient and may not be ensured in all production systems for a number of reasons. Also, in many commercial production systems it is most efficient to vaccinate birds at one day of age. Trovac, a recombinant live H5N1 vaccine (A/Turkey/Ireland/83 recombinant Fowlpox vector) is the only commercially available vaccine purposely developed for a one-shot at day-old age vaccination schedule.

Vaccine efficacy

From a technical and biological perspective, for individual birds, vaccination efficacy can be measured using the following three parameters: (i) degree of protection from infection when exposed to a given amount of infectious virus, (ii) the degree of reduction of morbidity and mortality given infection occurred, and (iii) the level of reduction of virus excretion by infected poultry.

The efficacy of most commercially available vaccines has been determined in studies with chickens or turkeys, since, from an economic perspective, globally they represent the most important poultry species. However, in many developing countries, particularly in Southeast Asia, other species such as ducks, muscovy ducks and quails also represent significant parts of the poultry sector. Thus, vaccination strategies for poultry populations with significant shares of species other than chicken and turkeys require vaccines with proven efficacy in these species to contain viral transmission.

Peyre et al. (2008) have compiled a list of commercially available H5 and H7 vaccines with information on reductions in mortality and viral shedding based on experimental results from challenge trials under laboratory and controlled field conditions. Although almost all commercially available vaccines provide some level of protection from infection with virulent virus and significantly reduce morbidity and mortality in infected chicken, no HPAI vaccine has so far proved to satisfactorily perform on all three of the above parameters (Swayne 2006; van den Berg et al. 2007).

Challenge trial results on the efficacy of Trovac are conflicting. Inui 2008 conducted challenge trials with Trovac and observed 90% - 100% mortality 3, 4 and 6 weeks post vaccination in chickens when challenged with several clades of the Asian lineage HPAI H5N1 virus (Clades 1(08), 2.3.4 (08), 1(04)). By contrast, Swayne et al. 1997, in a challenge trial with H5N2 virus isolated in Mexico, observed 90% - 100% protection against morbidity and mortality, and significant reductions in virus shedding in chickens vaccinated at one day of age. Bublot et al. 2007 challenged Trovac-vaccinated chicken with HPAI H5N1 A/chicken/Vietnam/0008/2004 and observed full protection against morbidity and mortality. This diversity of challenge trial results with different HPAI H5N1 field strains for Trovac...
indicates a limited breadth of protection of Trovac vaccine, and most likely of other HPAI vaccines as well, against field strains that change over time.

Unpublished results of challenge trials carried out by the Friedrich-Loeffler Institute in 2008 showed that vaccinated layer chicken reared under commercial conditions did not attain sterile immunity and that infection with HPAI virus may facilitate bacterial infections which can then dominate the clinical disease picture (Rudolf et al. 2008).

In a vaccination trial with goose parents and a low pathogenic avian influenza virus strain vaccine (A/duck/Potsdam/1402/86 (H5N2)), Rudolf et al. (2009) found that vaccinated geese became infected and transmitted challenge virus (A/Cygnuscygnus/Germany/R65/06 (H5N1)) to non-vaccinated geese. The contribution of ducks to the maintenance and spread of HPAI H5N1 virus has been shown in several studies (Chen et al. 2004, Gilbert et al. 2006, Hulse-Post et al. 2005).

Several vaccines with proven efficacy in domestic ducks and geese are commercially available. A H5N3 reverse-genetics vaccine has been shown by Webster et al. 2006 to control clinical signs and virus shedding in Peking ducks challenged with a duck-lethal H5N1 virus after the application of two doses of vaccine. A H5N1 inactivated vaccine was used by Beato et al. 2007 to vaccinate Peking ducks at one and 30 days of age. The vaccinated ducks were subsequently challenged with an Asian-lineage H5N1 virus and neither clinical signs nor virus shedding were detected. After one shot of a recombinant H3N3 or H5N1 vaccine administered to two-week-old SPF Peking ducks and a challenge with duck lethal HPAI Dk/Laos/25/06 (clade 2.3.4), no clinical signs or virus shedding were detectable (Kim et al. 2008).

A specific challenge in developing vaccines for ducks and monitoring the effectiveness of duck vaccination campaigns is the lack of correlation between the serum antibody levels of vaccinated ducks and their degree of immunity. Kim et al. 2008 found complete protection in vaccinated ducks in the absence of detectable antibody responses. This may indicate that cell-mediated immune response is important in protecting ducks from HPAI and would constitute a major gap in the current capacity of assessing HPAI vaccine efficacy in this species, which constitutes a major part of the poultry population in a number of developing countries.

**Onset and duration of immunity**

The time lag between vaccination and protective immunity and the respective duration of protection depends on the vaccine used, timing of vaccination, number of doses given, species, immunologic condition of the birds, and the challenge virus. The literature is dominated by studies with SPF birds reared under laboratory conditions, the results of which cannot safely be extrapolated to field conditions, and in which protection is often assessed by serology, the assumption being that birds with a specified antibody level (e.g. a haemagglutination inhibition (HI) titre ≥16) are protected. However, under conditions of antigenic variability and diversity of the HPAI viruses circulating in the field, a given titre found under laboratory conditions cannot unequivocally be interpreted as protective against field virus challenge, and the observed variation in the level and length of protection also makes generalizations on vaccine efficacy problematic. Despite these limitations, some
examples of published literature on vaccine efficacy and the duration of protection under field and laboratory conditions are summarized in the following.

Field studies with a killed oil-adjuvanted H5N2 (A/chicken/Mexico/232/94/CPA) vaccine in Hong Kong showed effective protection by 13 to 18 days post-vaccination (Ellis et al., 2005; Ellis et al. 2004). Serologic response monitoring after vaccination of 3 flocks of white leghorn layer chicken in commercial farms in California, USA with two doses of killed LPAI H6N2 (CK/CA/0379/02) vaccine at 7.5 - 9 and 11 - 13 weeks of age showed significant differences in the onset and duration of immunity. In one flock 72% (15/21) of the tested chicken were sero-positive, based on agar gel immunodiffusion tests, within 21 days after the first vaccination and 100% were sero-positive four days after the second vaccination, but by 20.5 weeks after the second vaccination all chicken were sero-negative again. In two other flocks, situated on a different farm, serologic response monitoring only began 13 weeks after the first vaccination. Nearly 100% of the tested 32 chicken were sero-positive from 13 – 19 weeks post vaccination. Sixty-nine weeks after the second vaccination, the proportion of seropositive chicken had declined to 22.9% (Cardona et al. 2006).

Under laboratory conditions, vaccination experiments with 6-week-old white leghorn SPF chicken, using a single vaccination with H7N1 (A/Chicken/Italy/99) and H7N3 (A/Chicken/Pakistan/95) vaccines resulted in HI titres ≥16 eleven days post vaccination. In challenge experiments with a H7N7 virus (A/Chicken/Netherlands/621557/03) two weeks post vaccination, virus could not be recovered from tracheal and cloacal swabs and chicken did not infect unvaccinated chicken that were in close contact (van der Goot et al. 2005).

Qiao et al. 2006 vaccinated 4-week-old white leghorn SPF chicken once with a vaccine derived from A/Harbin/Re-1/2003 (Re-1) and conducted challenge trials with A/goose/Guangdong/1/96 (GSGD/96). Two weeks post vaccination and 3 days post challenge shedding of 0.9 log10 EID50 was detected in one chicken out of a group of eight. Five days after challenge, no virus shedding was detectable in groups of chicken that had been vaccinated two or 43 weeks before the challenge trial.

An ex-ante assessment of control strategies in case of H5N1 outbreaks in Great Britain, based on a mathematical simulation model, assumes a period of 21 days for vaccination to become effective (Truscott et al. 2007). During the HPAI outbreaks in the Netherlands in 2003, van Boven et al. 2003 based their advice on the use of vaccination on the assumption that it takes 2 to 4 weeks until vaccination offers effective protection and therefore concluded that ring vaccination in a radius < 50 km would have little effect in reducing the size of an outbreak. No conclusions were provided for vaccination in a radius > 50 km.
Vaccine cost and storage requirements

Legok and Harbin Werke vaccines purchased in large quantities for use in vaccination programmes in Indonesia and Vietnam cost about USD 0.02 – 0.03 per dose. Swayne et al. 2008b provide a wholesale price for HPAI vaccines of USD 0.05 – 0.15 per dose. Avian influenza vaccines have to be stored within a temperature range of 2 – 8° Celsius (Amorij et al. 2008) and cold storage and a cold chain is required to maintain the efficacy of all commercially available vaccines (CAST 2007).

Antigenic drift and long-term vaccine efficacy

Avian influenza viruses vary antigenically and evolve rapidly, which poses a major challenge for the use of vaccines as an effective and sustainable HPAI control measure. H5N1 virus isolates from human cases in Vietnam show evidence of antigenic drift (WHO 2005). Although several studies demonstrated cross-protection for HPAI viruses with regard to morbidity and mortality, a correlation between virus shedding and antigenic differences of vaccine and field strains was shown by Lee et al. 2004 for the Mexican lineage H5N2 virus and by Swayne et al. 2000 with nine different H5 HPAI viruses representing 87.3% – 100% deduced amino acid identity in the HA1 between the vaccine and challenge virus. During and after the extensive use of about 2 billion doses of H5N2 vaccine in commercial poultry farms in Mexico, molecular drifts with a yearly trend have been shown (Escorcia et al. 2008, Lee et al. 2004). Antigenic drift of avian influenza viruses was observed in the USA after vaccination programmes for LPAI in commercial poultry (Suarez et al. 2006). H5N1 HPAI outbreaks in Hong Kong in December 2008 were speculated to be the result of the vaccine used being ineffective due to antigenic shift of circulating field virus. Variant field strains that escaped the protection by the used vaccines emerged in Shanxi China during 2006, in Egypt in late 2006 and in Indonesia early 2007 (Swayne et al. 2008b).
III. HPAI Vaccination ‘Strategies’ and Effective Immunization Rates

OIE (2007) lists three HPAI vaccination ‘strategies’ with distinct objectives: (i) preventive vaccination, (ii) emergency vaccination and (iii) routine vaccination. A summary of the objective, time frame and critical success factors of these HPAI vaccination strategies is given in Table 1.

**Preventive vaccination**

Preventive vaccination is proposed as an option to prevent the infection of poultry flocks in a country or region that is free of disease but at ‘high’ risk of virus introduction and in which early detection and elimination of infection may not be feasible or realistic. Incorporation of DIVA\(^1\) is recommended as part of such a strategy. For example, in the Netherlands vaccination of free-range laying hens and hobby poultry with inactivated H5N9 vaccine was permitted as an alternative risk reduction measure to indoor housing in 2006. In Hong Kong, a killed oil-adjuvanted H5N2 vaccine is used in broiler chicken farms since the HPAI outbreak in 2002 to reduce the likelihood of outbreaks, if introduction of infection were to occur from mainland China (EFSA 2007).

**Emergency vaccination**

This vaccination strategy is considered an option for the control of HPAI introduced into the national flock when the epidemiological situation suggests an immediate and high risk of massive and rapid spread of infection, which cannot be contained by culling and movement restrictions. Emergency vaccination includes ‘ring’ vaccination of flocks located within a pre-defined (but not further specified) radius around detected outbreaks to create a ‘buffer zone’. This strategy was applied in northern Pakistan within a 3 km ring after H7N3 outbreaks in 2003 when layer and breeder flocks were vaccinated (EFSA 2007).

**Routine vaccination**

Routine vaccination is listed as an appropriate measure in “countries and regions where the disease is endemic and where the classical control cannot be effectively implemented to eliminate the virus”. It can achieve a reduction in poultry mortality and in the longer term decrease the prevalence of infection to a level where surveillance and stamping out could be applied cost-effectively. Eradication of HPAI virus is not stated in the OIE (2007) document as an objective that is achievable solely through routine vaccination\(^2\). In addition the contribution of vaccination to reducing the risk of human cases via reducing the virus load is mentioned in OIE (2007) as a potential result of any vaccination strategy.

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1 DIVA: Differentiating Infected from Vaccinated Animals, i.e. vaccinated birds can be distinguished from (vaccinated and subsequently) infected birds.

2 ‘Routine vaccination’ was successfully used for the eradication of other transboundary diseases such as Rinderpest in Africa (Normile 2008) and FMD in parts of South-America (Melo 2002).
Table 1. Vaccination strategies, objectives, time frame, critical success factors and alternative / complementary control measures

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<tr>
<th>Vaccination strategy</th>
<th>Objective</th>
<th>Time frame</th>
<th>Critical factor</th>
<th>Alternatives</th>
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<tbody>
<tr>
<td>Preventive</td>
<td>Protect individual / specific flocks / birds</td>
<td>Variable, depending on risk of exposure to infectious virus</td>
<td>Accuracy of the exposure risk assessment</td>
<td>Improve bio-security, limit contact to secure sources</td>
</tr>
<tr>
<td>Emergency</td>
<td>Curtail potential of an acute epidemic after virus introduction</td>
<td>Short-term</td>
<td>Time to achieve immunity</td>
<td>Movement control and preemptive depopulation</td>
</tr>
<tr>
<td>Routine</td>
<td>Reduction of mortality/production losses in endemic situations; in longer term, may facilitate eradication of HPAI virus presence in domestic poultry</td>
<td>Medium-to long-term</td>
<td>Effective immunization coverage (reduction of between-flock $R_n&lt;1$)</td>
<td>Passive and active surveillance with rapid stamping out</td>
</tr>
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All three of the above ‘strategies’ can be applied in different ‘tactics’, i.e. either in a ‘mass or a targeted manner’, targeting specific sub-populations (age, species, location, production systems) and / or times within production cycles.

Effective immunization rates

Whichever the applied vaccination strategy, its effectiveness depends on the proportion of poultry which are rendered immune and will therefore not significantly contribute to virus transmission in the case of exposure. As poultry populations are segregated into flocks (or other types of management units), both within-flock and between-flock transmission need to be sufficiently contained to avoid sustained virus transmission and potential development of endemicity.

A number of studies estimated the minimum within-flock immunization rate required to stop virus transmission within a poultry flock. Depending on the assumptions made, the
calculated within-flock immunization rate required to avoid disease spread range from 50% to 90%: Tiensin et al. (2007) analysed within-flock HPAI transmission data from the 2004 epidemic in Thailand and conclude that 80% of birds need to be immunized to avoid major within-flock disease spread. Bouma et al. (2009) estimated that a within-flock immunization rate of 60% to 80% was necessary to avoid major outbreaks, which they defined as more than 50 infected birds. Mathematical modelling conducted by Savill et al. (2006) indicated a required 90% within-flock coverage to reduce the outbreak probability by 50%. According to Lesnoff et al. (2009) a flock immunity rate between 50% and 67% is necessary to completely interrupt within-backyard-flock virus transmission.

A factor of high importance for disease control is the contact rate between flocks and the level of risk of each contact to transmit infection (Beach et al., 2007). The objective of emergency and routine vaccination would be to interrupt the infection chain between flocks / farms, i.e. achieve a between-flock / farm-to-farm ‘reproductive number’ (R_n) that is below unity. The required proportion of flocks that would have to be immunized within an affected region can be derived from the infection dynamics in that region in the absence of control measures. For HPAI outbreaks in Holland, Canada and Italy, Garske et al. (2007) estimated mean farm-to-farm reproductive numbers prior to the introduction of control measures to range from 1.1 to 2.4. For Vietnam and Romania, countries with less industrialized poultry sectors, R_n was estimated to have been in the order of 2 to 3 prior to the introduction of control measures (Walker et al. 2009; Ward et al. 2009). Under the ideal condition of full protection of vaccinated flocks, immunization of between half and two thirds of flocks would be necessary to stop sustained between-flock transmission under the situation prevailing in Vietnam (based on the fraction of 1-1/R_0 (Anderson 1992)). Under conditions where only partial immunity of vaccinated flocks is achieved a higher proportion of immunised flocks would be required to interrupt disease transmission to the extent needed to control an outbreak.
IV. Maximum Vaccination Coverage Achievable with Vaccination Campaigns

As pointed out by Alders et al. (2007) production system characteristics need to be considered to estimate the potential vaccination coverage and whether this coverage is capable of preventing, or at least significantly reducing, virus transmission. Important characteristics are the average lifespan of poultry, origin of replacement birds (home-bred vs. bought), synchronization of flock age, and the disease status and immuno-competency of flocks in the respective production system. Furthermore, poultry owners’ incentives to vaccinate against HPAI strongly influence potential vaccination coverage. Although incentives are generally similar for owners of flocks of the same type of production system, they may still vary depending on their flocks point in the production cycle. It would for example be very unlikely that a broiler farmer would allow vaccination of a flock close to the point of sale because of fear that the vaccination will affect the birds and potentially kill a proportion.

Poultry production systems

Within the poultry sector, four main production systems can be identified: (i) Breeder flocks, (ii) layer flocks (iii), broiler flocks and (iv) backyard multi-purpose flocks. This production system classification roughly applies to both chickens and ducks (Rushton et al., in press). Sub-systems, such as short- and long-lived broiler production and free-range grazing duck production systems prevail in some countries. The main poultry production systems are briefly described in the following to provide an overview of the main characteristics relevant for the effectiveness of HPAI vaccination campaigns.

Breeder flocks (grandparent and parent) are kept in closed houses and cages and the birds are bought from specialized poultry genetic supply companies. Several batches of birds of differing ages are required to meet the continuous demand for DOCs. The average lifespan of breeder chicken for the production of DOCs varies between 63 and 65 weeks. The production period of breeder duck flocks varies between 52 and 104 weeks. Breeder ducks are kept in houses with outdoor access (Desvaux et al. 2008).

Layer chicken are typically kept in cages in open or closed housing without outdoor access. Hens start laying eggs at 23 – 25 weeks of age and are kept for 63 – 74 weeks. Continuous egg supply requires a layer flock with chickens of several age groups. Either DOCs or pullets (at 16 - 25 weeks of age) are bought to replace spent hens, which are either sold for immediate slaughter or for fattening. In Asia, layer ducks are kept between one and three years and for a varying proportion of this time flocks are free-ranging in rice fields to use left over rice, weeds and snails as a feed resource. Semi-confined fishponds with temporary or permanent shelters are used to house the ducks when they are not left to range in rice fields (Desvaux et al. 2008).

Two broiler chicken production systems need to be distinguished, namely long- and short-finish systems. Short-finish, ‘industrial’, broilers are usually kept indoors on the ground, whereas long-finish, crossbred broilers are kept under semi-confined conditions to utilize some feed resources from the natural environment. The attention to hygiene and animal health management is normally lower than in breeder and layer flocks. Chicken broilers are
kept for a relatively short life span. ‘Industrial’ broilers are kept in batches of the same age for 5 – 7 weeks while ‘crossbred’ broilers are kept for 9 – 26 weeks and achieve a premium price in local markets. Similar to broiler chicken production systems, the production cycle length of broiler ducks varies depending on the breed and feeding system used. Scavenging broiler ducks are reared under similar conditions to layer ducks and are usually sold for slaughter after about 80 days. Confined and intensively fed ducks, usually of specific meat type breeds, are finished in about 60 days (Desvaux et al. 2008, Seng 2007, Songserm 2006).

Mixed backyard poultry production systems are characterized by scavenging indigenous birds that consume left over feed and produce their own replacement chicks with very little cash investment of the owner (Otte 2006). The systems typically have high mortality rates in the early stages of life due to predation, poor diets, and diseases (Dessie 1996; Gunaratne et al. 1993; Rushton et al. 1998; Spradbrow 1993). Due to the high mortality rates, particularly in young birds, a relatively high population turnover is common, in which birds get replaced by newly hatched chicks. This high population turn over significantly limits the duration of flock immunity that can be maintained with vaccination campaigns.

The potential coverage of HPAI or Newcastle disease vaccination in backyard poultry with uncontrolled but more or less continuous replacement dynamics has been modelled by several authors (e.g. Lesnoff et al. 2009; Taylor 2008; Udo et al. 2006). For non-backyard poultry production systems, in which birds are periodically replaced by controlled reproduction, and which in most countries constitute a significant share of the standing poultry population, no estimates of the maximum vaccination coverage achievable through mass vaccination was available in the literature. The authors therefore had to make their own estimates, which are based on the simplifying assumption that the birds within a specific flock and production system are of the same age (i.e. all-in/all-out flock management) and that the age of all flocks in a region is uniformly distributed (i.e. no seasonal production). The maximum flock vaccination coverage with a vaccination campaign, in which vaccination teams visit each farm once only (or twice in case of booster application) is then theoretically given by the time a particular flock is eligible for vaccination within its production cycle (including the idle time between batches). The estimated maximum achievable vaccination coverage applies to the area that can be vaccinated within a day. For areas which require more than one day for vaccination teams to visit all flocks, the theoretical maximum vaccination coverage is lower due flock turnover. The results of the calculations are displayed in Table 2.
Table 2. Estimated flock vaccination coverage and time until flocks are fully susceptible again after an HPAI vaccination campaign

<table>
<thead>
<tr>
<th></th>
<th>Length of production cycle (days)</th>
<th>Idle time between batches (days)</th>
<th>Time eligible for 1st shot (days)</th>
<th>Time eligible for 2nd shot (days)</th>
<th>Proportion of flocks eligible for 1st shot (%)</th>
<th>Proportion of flocks eligible for 2nd shot 14 days later (%)</th>
<th>Time until all flocks are 100% naïve again after 1st shot (days)³</th>
<th>Time until all flocks are 100% naïve again after 2nd shot (days)³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Layer chicken; vaccination during laying period</td>
<td>490</td>
<td>0</td>
<td>476</td>
<td>462</td>
<td>97</td>
<td>94</td>
<td>180</td>
<td>180</td>
</tr>
<tr>
<td>Layer chicken; no vaccination during laying period</td>
<td>490</td>
<td>0</td>
<td>140</td>
<td>126</td>
<td>29</td>
<td>26</td>
<td>147</td>
<td>133</td>
</tr>
<tr>
<td>Broiler chicken; industrial</td>
<td>32</td>
<td>14</td>
<td>18</td>
<td>4</td>
<td>39</td>
<td>9</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td>Broiler chicken; crossbred</td>
<td>120</td>
<td>14</td>
<td>106</td>
<td>92</td>
<td>79</td>
<td>69</td>
<td>113</td>
<td>99</td>
</tr>
<tr>
<td>Broiler ducks; intensive confined</td>
<td>60</td>
<td>21</td>
<td>46</td>
<td>32</td>
<td>57</td>
<td>40</td>
<td>53</td>
<td>39</td>
</tr>
<tr>
<td>Broiler ducks; scavenging</td>
<td>80</td>
<td>-</td>
<td>66</td>
<td>52</td>
<td>83</td>
<td>65</td>
<td>73</td>
<td>59</td>
</tr>
</tbody>
</table>

Source: authors’ calculations

Maximum vaccination coverage of breeder and layer flocks

Chicken breeder and layer flocks: In theory, relatively high vaccination coverage could be achieved for chicken layer flocks with a production cycle length of 490 days, assuming owners would allow vaccination during the egg laying period (Table 2). Since layer flocks usually comprise of birds of several age groups (are not kept under all in and all out management), the coverage of 94% for a single shot campaign and 92% for a double shot campaign is a reflection of the share of birds that could be vaccinated at any point in time within a flock of heterogeneous age composition. It should however be recognized that in most layer flocks birds are vaccinated before point of lay and owners are reluctant to revaccinate during egg laying periods. If vaccination during the laying period is not accepted, within-flock vaccination coverage would not exceed 26% in a double shot vaccination campaign.

³ Protection assumed to be lost 180 days after vaccination due to waning immunity.
Scavenging layer duck flocks: The age distribution and the number of layer duck flocks are related to the rice harvest seasons. Vaccination coverage similar to those in layer chicken could be achieved with well-timed vaccination campaigns that take into account the seasonality of rice harvest and laying period. However, the poor accessibility of scavenging duck flocks in rice paddies makes the administration of vaccine, especially the second booster shot, very difficult and experience from China shows, that scavenging duck breeder and layer flocks usually don’t receive a booster vaccination (Chen 2009).

Maximum vaccination coverage of broiler flocks

Short-lived industrial chicken broiler flocks: During the average 32-day production cycle of an industrial batch of broiler chicken, vaccine can be administered over a period of 18 days, since vaccination should only be applied at a minimum age of 7 days and requires at least 7 days to confer protection, i.e. needs to be applied more than 7 days prior to slaughter to have any effect. Due to an assumed average idle time of 14 days for cleaning and disinfection between batches, a significant proportion (18/46) of broiler houses in a country or region will either be empty or not be populated by birds eligible for vaccination on any given day. Hence the maximum achievable vaccination coverage with a single injection in a one-day visit vaccination campaign is 39% of all industrial broiler flocks within a country or region. As described in Section II, two injections are required to achieve full protection in domestic poultry. Therefore, if each broiler flock needs to be given a booster shot 14 days after the initial vaccination, only the flocks that received their first injection during the first 4 days of the 18 day window will be eligible for the booster shot 14 days later. Although some previously non-eligible farms will have become available for the first vaccination in the 14-day interval, only 9% of all broiler flocks would have received the two injections required to achieve full protection. All industrial broiler flocks would be naïve again within 25 days after a single injection vaccination campaign since vaccinated birds will have been slaughtered and replaced.

Intensively raised duck broiler flocks: The relatively short production cycle length of about 60 days for duck broilers in intensive closed systems results in a low maximum coverage of 40% for a two-injection a 14 day interval HPAI vaccination campaign. However, experience from China shows, that flock owners usually don’t vaccinate these birds due to their short life span (Chen 2009).

Long-lived crossbred chicken broiler flocks: The maximum achievable vaccination coverage for crossbred broiler flocks would be 79% and 69% for a one- or two-injection campaign, respectively. The higher coverage compared to industrial broiler flocks results from the considerably longer production cycle. All crossbred broiler flocks would be naïve again within 113 days after a single injection vaccination campaign.

Scavenging duck broiler flocks: Seasonal peaks of available rice in harvested paddies are utilized by raising broiler ducks around the time of rice harvests. Therefore the timing of vaccination campaigns should take into account this seasonality. The maximum achievable vaccination coverage by a vaccination campaign will depend on the age distribution of duck broiler flocks within a region. However, under the assumption that the start of broiler flock raising in a region is uniformly distributed over a time period of at least 80 days, 65 % of all flocks can be vaccinated in a two shot campaign. It should be noted that the delivery of a
second shot is a challenge due to the difficult accessibility of scavenging ducks in rice paddies and will require significantly higher vaccinator time inputs for travelling and catching ducks.

**Immunization rates in extensively reared, mixed backyard flocks**

Based on a spreadsheet poultry population model, Taylor (2008) estimates that a maximum immunization rate of 52% of all backyard birds can be achieved with a two-shot vaccination campaign under the assumption that 80% of all chicken older than 4 weeks are caught for an initial vaccination and a booster shot 14 days later. Immunization coverage would fall to 19% within 17 weeks due to replacement. These results assume a vaccine efficacy of 80% and that 50% of the eggs are used for human consumption and the remaining 50% are hatched. Also under a two-shot vaccination scenario, vaccinating all poultry \( \geq 14 \) days and assuming 80% vaccine efficacy, Lesnoff *et al.* (2009) estimate a maximum achievable population immunity rate of 55%. Seventeen weeks after the vaccination campaign, the population immunity rate is estimated to have dropped to 25%.

**Maximum vaccination coverage of national poultry populations**

The maximum vaccination coverage of national poultry populations achievable through vaccination campaigns is determined by the specific mix of flock types in the national poultry industry and the time required to carry out a campaign. Given that in most countries broilers are the most common type of poultry followed by backyard birds, while layer and breeder flock comparatively rare, immunization rates needed to break infections chains will be difficult to achieve unless vaccination campaigns are complemented by restocking bans.
V. Practical Challenges of Large-Scale HPAI Vaccination Programmes

There are three main steps in the process of implementing vaccination programmes: (a) planning, which includes estimation of vaccine needs, identification of vaccine source, storage, delivery, as well as procedures and schedules of administration, and respective budget allocation (b) information campaigns and monitoring of vaccine quality, delivery, and administration, and (c) programme evaluation which covers technical and cost elements and would lead to a revision of the programme if necessary. For this purpose long(er)-term performance indicators are required.

Depending on whether the public veterinary staff are responsible for the implementation of vaccination campaigns or whether their role is restricted to monitoring and ensuring the efficacy of the campaign, public agents are involved in all or a part of the following tasks: selection of vaccines, monitoring the production or importation of vaccine, organizing the timely distribution of vaccines, and monitoring of field virus strains and the efficacy of the vaccine(s) employed. It needs to be emphasized that due to scarce veterinary staff and animal health funds the inevitable effect of large-scale vaccination campaigns is a detraction of public animal health services from other disease control activities, both with respect to HPAI and other diseases (e.g. FMD outbreaks increased in Vietnam during and after HPAI campaigns).

It has been emphasized by several authors that the achievable protection through vaccine use in the field is unlikely to reach the potential shown under experimental studies with SPF chicken (Swayne et al. 2000, van den Berg et al. 2007). Since commercially available HPAI vaccines are not thermostable, maintaining the cold chain from production to administration is crucial for obtaining high levels of immunization in vaccinated birds in the field. This represents a significant challenge in many developing countries with high daytime temperatures and shortages of cold storage capacity. A list of factors which compromise the effectiveness of avian influenza vaccination campaigns are provided by Wooldridge (2007) and Alders et al. (2007):

- Inappropriately matched field and vaccine strains
- Vaccines which are inappropriate for the species or age group vaccinated
- Spoiled (ineffective) vaccine
- Inadequate hygiene during vaccine administration to birds (clean needle, disinfectants)
- Vaccine administration to inappropriate tissues of the birds
- Infection of birds with immunosuppressive disease agents

Assessments of Rinderpest (Normile 2008) and Classical Swine Fever (Taylor et al. 2003) vaccination campaigns have identified similar risk factors to those mentioned above for avian influenza vaccination campaigns. The results of an evaluation of the cold chain for Newcastle vaccination in Mozambique have been documented by Chicamisse et al. (2005). All transport and storage systems exceeded the recommended temperatures. Some reasons for non-optimal storage temperature were: storing too much vaccine in the refrigerator, too high temperatures in vaccine storage rooms, and old refrigerators.

In addition to the above listed practical and technical issues, the perception of poultry owners and vaccinators with respect to the benefits of vaccination is a crucial factor for
vaccination to be effective. If owners and vaccinators are not convinced of the need for vaccination they are unlikely to be cooperative, which increases the risk of not achieving immunization targets. Information and communication campaigns are therefore necessary to ensure the preparedness and optimal cooperation of all stakeholders. The target audience comprises of a wide range of stakeholders with different information requirements, e.g. senior government decision makers, veterinary staff, local authorities, poultry owners and poultry traders (Alders et al. 2007). Properly trained and motivated (paid) vaccinators and cooperative poultry keepers are key to achieve high vaccination coverage and immunization levels.

Wooldridge (2007) describes a formal risk assessment for vaccination campaigns which serves for identifying different risk pathways and risk reduction measures. Identification of the necessary data to quantify the risk linked to each pathway facilitates the planning and monitoring of vaccination campaigns. An effective tracing and monitoring scheme for the vaccines used, storage locations and temperature, vaccinator, poultry flocks and post-vaccination protection rate is necessary to accurately determine the cause of poor performance and implement the appropriate corrective measures. While such a standardized approach to vaccination campaign monitoring is seductive in its apparent accuracy it appears to lack the necessary appreciation of the importance of the people involved in a vaccination campaign and their incentives to collaborate. The assumption is that their interest and willingness is a given, something that is rarely if ever the case.

Due to the changing nature of HPAI virus strains circulating in the field, the need for post-vaccination monitoring of vaccine efficacy is stressed in the HPAI literature. Virus isolation and sequencing should be an essential part of any vaccination strategy to detect potential genetic shifts and to monitor vaccine efficacy. The possibility that the efficacy of the vaccine(s) used in the programme decreases over time needs to be considered in the planning process because the frequency with which a new representative master-seed for the production of adapted vaccines needs to be found directly influences the profitability of commercial vaccine production. Producers need a certain level of security about the potential scale and duration of market demand for their vaccine to embark in vaccine development and production. The recommended number of blood samples to test for seroconversion and swab samples to test for virus presence and potentially isolate field virus represents a major challenge for the capacity of most laboratories in developing countries.
VI. Experiences from Large-Scale HPAI H5N1 Vaccination Programmes

**China**
Since the introduction of vaccination in China in 2004, the national vaccination policy has evolved. Until the end of 2005 all waterfowl and terrestrial poultry near waterways and wetlands were vaccinated (EFSA 2007). Eight billion birds (60% of China’s domestic poultry population) were vaccinated between the onset of vaccination in 2004 and November 2005 (Cyranoski 2005). In 2006, compulsory vaccination of all poultry was mandated and 8.2 billion head of poultry were vaccinated from January to September 2006 (MoA China 2006). A vaccination coverage of 20% – 50% was achieved in mainly backyard poultry (Peyre et al. 2008). Since then a twice-yearly vaccination campaign is estimated to result in the annual administration of 11 billion doses of vaccine (FAO 2009). Relatively low vaccination rates have been observed in waterfowl. The required booster vaccination for layer and breeder ducks is not actually administered in most flocks and broiler ducks are usually not vaccinated due to their short life span (Chen 2009). Testing of 1,113 chicken sera from Guangdong and Guiyang Provinces collected at markets in 2005 and 2006 revealed that only 180 (16%) were positive against Ck/HK/YU22/02 (H5N1) and that 55 of the positive sera had low or no neutralizing antibodies against the predominant FJ-like sub-lineage (Smith et al., 2006).

**Hong Kong**
A killed oil-adjuvanted H5N2 (A/chicken/Mexico/232/94/CPA) vaccine was used in Hong Kong after HPAI outbreaks in February-April 2002. HPAI vaccination was introduced after a 12-month vaccination field trial in commercial broiler chicken (yellow meat) flocks to evaluate its effectiveness. All broiler chicken between 8 and 55 days of age were vaccinated followed by a booster 4 weeks later. In 75.8% (188/248 for a total of 1.35 million broilers) of the batches vaccinated, results were considered successful (≥ 70% of chickens per batch had a HI titre of ≥ 16 and a geometric mean batch titre ≥ 20, see results in Table 4). Some HPAI outbreaks occurred on farms shortly after vaccination. In one farm, where chicken developed clinical HPAI 9 days after vaccination, vaccination had not yet induced a protective immune response. In a few other farms which became infected it was shown that vaccination provided protection form disease and reduced virus excretion by 13-18 days post-vaccination (Ellis et al. 2005).

Compulsory vaccination was introduced for local chicken farms in June 2003 and by the end of 2003 all chicken from Hong Kong entering the live poultry were vaccinated using the killed H5N2 vaccine. The farm bio-security enhancements introduced between 1998 and 2002 were not sufficiently effective to prevent the spill over of circulating virus from markets to farms. The contact rates between broiler chicken farms and live poultry markets were relatively high due to rearing of several batches of different ages on the same farm. HPAI vaccination was introduced as an obligatory condition for poultry farms to have market access, which required substantial enforcement and laboratory capacity (Sims, personal communication). In addition to vaccination, bio-security measures were further enhanced on farms and live poultry markets (EFSA 2007), No outbreaks were detected until 2008. Surveillance results showed that virus circulation in live poultry markets had ceased for the 5-year period after the introduction of vaccination (OIE 2009). The re-emergence of an HPAI
outbreak on a vaccinated chicken farm in Hong Kong in December 2008 led to speculation about vaccine efficacy.

**Egypt**

Voluntary vaccination with registered vaccines was permitted by the government in 2006. Over 750 million birds were vaccinated with H5N2 and 150 million with H5N1 in commercial farms (Samaha 2007). For backyard or household village poultry, vaccine was provided by the government since mid 2007 (FAO 2008b). 70 million birds were vaccinated with H5N1 in backyards and 11 million day old chicks (DOCs) were vaccinated with H5N2.

**Indonesia**

By March 2008 twenty vaccines were registered for use in poultry in Indonesia. Vaccine seed strains include a highly pathogenic local strain, A/chicken/Legok/2003 (H5N1), A/chicken/Mexico/94 (H5N2), A/turkey/Wisconsin/69 (H5N9) and A/turkey/England/73 (H5N2). The widely used Legoc/03 strain is not fully protective against all circulating viruses. The OFFLU network is therefore collecting HPAI virus isolates and screening these to identify a new vaccine seed strain, which affords better protection against circulating HPAI viruses (FAO 2008c).

A compulsory vaccination policy for all poultry was adopted by the Government of Indonesia in June 2004. Poultry classified as sector 4 (backyard) and sector 3 (small-scale commercial) up to maximum flock size of 5,000 birds were to be vaccinated free of charge by government services. Problems were reported with respect to vaccine availability and confidence of flock owners in the benefits of vaccination (Sawitri Siregar et al. 2007). Vaccination coverage assessed by the Ministry of Agriculture rarely exceeded 30% of the poultry population. Post-vaccination monitoring of HI-titres ranged from 11% with protective titres (HI-titre ≥ 16) in native chicken populations in Bali to 78% protected in industrial breed chicken populations in Medan (Sawitri Siregar et al. 2007).

The commercial poultry sector implemented vaccination programmes using a variety of protocols mainly in chicken layer flocks (including grandparent and parent flocks) until point of lay. Short-lived broilers were not vaccinated except in areas considered to be at high risk and was based on a half dose shot at 7 days of age (Sawitri Siregar et al. 2007). No information was available on vaccination in long-lived broilers and male layers (90 - 120 day finish) which make up a substantial proportion of the poultry raised for meat.

A vaccination pilot study in semi-intensive and native chicken layer farms coupled with the use of sentinel chicken was conducted in Sukabumi to assess the efficacy of locally produced homologous vaccines. Farmers were reluctant to have sentinel birds in their systems. After receiving two doses of vaccine, 75% of the semi-intensive layer chicken hens developed HI-tires ≥ 32, while only 15% - 40% of the native layer chicken hens in 4 vaccinated flocks showed a titre ≥ 16. Blood samples from sentinel birds remained sero-negative for HI (Sawitri Siregar et al. 2007).

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4 The China Post cited Guan Yi from University of Hong Kong on December 12, 2008, based on a press release on 9 December 2008 by Dr York Chow, Secretary for Food & Health Bureau, Hong Kong.
Vaccination of backyard poultry was conducted under a World Bank and USAID funded operational research project. A total of 2.9 million birds in 425 villages located in 32 sub-districts in the provinces West Java, Yogyakarta and Central Java received two doses of vaccine. It took three weeks each to administer the first and second shots of Legok 2003 H5N1 vaccine and required 64 community vaccinator coordinators and 1,088 community vaccinators. The campaign was estimated to have covered only 32% of the 9.0 million poultry reported by official livestock statistics to be in the sub-districts where vaccination was implemented (FAO 2009b). About 18,000 blood samples from vaccinated backyard chicken and ducks were taken for sero-monitoring, of which 33.1% showed a protective HI titre ≥ 16 (McLaws, 2009, Table 4).

The participatory disease surveillance and response (PDSR) project also vaccinated poultry. The PDSR teams visited 9,326 villages, detected HPAI infection in 494 of them, and vaccinated poultry flocks in 56 (11.3%) of the infected villages (FAO 2008b).

**Pakistan**

Strategic vaccination and increased biosecurity was used in 1995 to control outbreaks of H7N3 HPAI. The outbreak was controlled within 4 months. However, H7N3 HPAI virus re-emerged in November 2003. The HPAI virus originated from an LPAI outbreak in April 2003. Breeder and layer flocks were vaccinated prophylactically and no H7N3 virus has been isolated since January 2005 (Naem et al. 2007).

The vaccination strategy in the area affected by HPAI H5N1 in 2007 has been to vaccinate all flocks within 3 km of the outbreak with a water-based vaccine. Ten days after the first vaccination a second vaccination with an oil-based vaccine was given. Breeder and layer flocks were vaccinated prophylactically and infected flocks were destroyed by immediate burial. Mild clinical signs with some mortality have been observed in vaccinated flocks (EFSA 2007).

**Vietnam**

A large scale vaccination programme of domestic poultry against HPAI based on twice yearly vaccination campaigns has been conducted since mid 2005 by public veterinary services. This vaccination programme was combined with supplementary age-based vaccination of larger commercial poultry flocks between the main campaigns (Cristalli 2006).

The vaccination policy, in terms of the eligible poultry population and cost-recovery schemes, has evolved over time. Currently, all domestic chicken and ducks older than 7 and 15 days respectively are eligible for vaccination. However, broiler chickens and ducks kept for less than 70 days until slaughter and for broiler chicken to be slaughtered within 15 days are exempted. Vaccine delivery has required immense labour inputs from public veterinary services and contracted commune animal health workers. According to a survey conducted by Cristalli in 2006, about 25,000 commune animal health workers were involved in administering vaccine during the 2005 and 2006 campaigns (Cristalli 2006, EFSA 2007, MARD 2007). Farm labour inputs to these campaigns have not been estimated. Initially, flocks with less than 2,000 birds were vaccinated free of charge. This flock size cut off point for free vaccination has been reduced to 500 birds for the 2009 campaigns.
Each campaign, comprising of two injections within a four week interval, required about 60 days to be completed. In 2005, 158 million chicken and 72 million ducks were vaccinated while for 2006 the respective numbers were 177 million and 28 million (Taylor et al. 2007). In 2007, 164 million poultry were vaccinated during the first campaign, comprising of 87 million chicken and 74 million ducks plus 42 million doses of vaccine administered by private livestock firms (FAO 2008d, Cristalli 2006, Taylor et al. 2007). Vaccination costs have been estimated at USD 20 million annually (McLeod et al. 2007b). In 2008 the use of 500 million doses of HPAI vaccine was planned.

Vaccination coverage estimations based on the number of vaccinated domestic poultry in relation to available domestic poultry census have been conducted by Taylor 2007 (Table 3) and To et al. 2007. The data shows a decreasing trend in vaccination coverage, which could be related to increasing vaccination fatigue of vaccinators and reduced vaccination acceptance of poultry owners. Post-vaccination monitoring results with regard to the prevalence of protective antibody levels in vaccinated poultry are provided in Table 4. The proportion of tested poultry with protective antibody levels varied between 33% and 72 %.

### Table 3. Estimated vaccination coverage in Vietnam, 2005 and 2006 HPAI vaccination campaigns

<table>
<thead>
<tr>
<th>Year</th>
<th>Campaign</th>
<th>Shot</th>
<th>Chicken population vaccinated (%)</th>
<th>Duck population vaccinated (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>1st</td>
<td>1st</td>
<td>66</td>
<td>79</td>
</tr>
<tr>
<td>2005</td>
<td>1st</td>
<td>2nd</td>
<td>58</td>
<td>73</td>
</tr>
<tr>
<td>2006</td>
<td>1st</td>
<td>1st</td>
<td>51</td>
<td>58</td>
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<tr>
<td>2006</td>
<td>1st</td>
<td>2nd</td>
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</tr>
<tr>
<td>2006</td>
<td>2nd</td>
<td>1st</td>
<td>47</td>
<td>72</td>
</tr>
<tr>
<td>2006</td>
<td>2nd</td>
<td>2nd</td>
<td>22</td>
<td>26</td>
</tr>
</tbody>
</table>

Source: Taylor 2007, based on poultry population census data

No outbreaks of avian influenza were reported in Vietnam between December 2005 and December 2006. However, assessment of the contribution of vaccination to the absence of reported outbreaks is challenging, since vaccination has not been implemented as an isolated control measure. Other factors, such as improved hygiene practices together with a significant reduction in the susceptible poultry population subsequent to culling and market reactions in 2004, probably also have contributed to the reduction of outbreaks. However, in 2005, at the time the decision to embark on mass vaccination campaigns was taken, a reduction of the human infection risk rather than disease eradication was the main goal in an emergency situation with several human cases (MARD 2006).

Table 4 provides a compilation of post-vaccination sero-monitoring results obtained in different countries which have embarked on large-scale HPAI vaccination programmes. In individual birds, the prevalence of antibody levels regarded as protective ranges from 16% to 72.1%.
### Table 4. Prevalence of protective HPAI antibody levels in poultry after vaccination campaigns

<table>
<thead>
<tr>
<th>Country</th>
<th>Species</th>
<th>‘Protected’</th>
<th>Comment(s)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>n.s.</td>
<td>69% (n=n.s.)</td>
<td>In 2004</td>
<td>EFSA (2007)</td>
</tr>
<tr>
<td>China</td>
<td>chicken</td>
<td>16% (n=1,113)</td>
<td>sera collected from Nov. 2005 to April 2006 in Guangdong and Guiyang Provinces; HI titre ≥ 20</td>
<td>Smith et al. (2006)</td>
</tr>
<tr>
<td>Egypt</td>
<td>n.s.</td>
<td>25.6% (n=160)</td>
<td></td>
<td>CIRAD (2008)</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>broiler chicken</td>
<td>75.8% (n=248 batches)</td>
<td>1 month after second vaccination, HI titre ≥ 16</td>
<td>Ellis et al. (2005)</td>
</tr>
<tr>
<td>Indonesia</td>
<td>chicken and ducks</td>
<td>33.1% (n=18,000)</td>
<td>1-2 months after campaign ended, H5N1 HI titre ≥ 16</td>
<td>McLaws (2009)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>n.s.</td>
<td>53.8% (n=364)</td>
<td>1-2 weeks after end of 1(^{st}) round of 2005 campaign</td>
<td>Nguyen Van Long (2007)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>n.s.</td>
<td>44.9% (n=203)</td>
<td>3-4 weeks after end of 1(^{st}) round of 2005 campaign</td>
<td>Nguyen Van Long (2007)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>n.s.</td>
<td>56.2% (n=269)</td>
<td>1-2 weeks after end of 1(^{st}) round of 2006 campaign</td>
<td>Nguyen Van Long (2007)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>n.s.</td>
<td>33.3% (n=43)</td>
<td>3-4 weeks after end of 1(^{st}) round of 2006 campaign</td>
<td>Nguyen Van Long (2007)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>n.s.</td>
<td>72.1% (n=1,263)</td>
<td>1 month after end of 1(^{st}) round of 2007 campaign</td>
<td>Nguyen Van Long (2007)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>ducks (n=182)</td>
<td>55% (n=182)</td>
<td>4-6 weeks after end of the 1(^{st}) round of the 2007 campaign</td>
<td>Henning et al. (2008)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>chicken (n=30)</td>
<td>40% (n=30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vietnam</td>
<td>ducks (n=302)</td>
<td>63% (n=302)</td>
<td>&gt;12 weeks after end of the 1(^{st}) round of the 2007 campaign</td>
<td>Henning et al. (2008)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>chicken (n=57)</td>
<td>37% (n=57)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

n.s.: not specified
VII. Costs and Incentives for HPAI Vaccination

Costs of large-scale vaccination campaigns in Indonesia and Vietnam

Essential cost components of any mass vaccination programme comprise of: (i) planning, monitoring and communication, (ii) vaccinator labour and equipment, (iii) storage and distribution of vaccine and equipment, (iv) post-vaccination sero-monitoring and (v) vaccine. The recurrent and investment costs differ between countries due to different economic and (veterinary) infrastructure conditions and due to differences in the structure of the poultry industry. Unfortunately, comprehensive cost estimates vaccination campaigns are only available for Indonesia and Vietnam.

The vaccination costs presented in Table 5 are derived from ex-ante assessments for a government run mass vaccination campaign in Vietnam and a planned mass vaccination campaign in Western Java, Indonesia. The total costs per vaccination vary between USD 0.03 in broiler flocks and USD 0.12 in backyard flocks in Indonesia. HPAI vaccination costs per bird differ between production systems due to varying accessibility and flock size related differences in achievable vaccinations per vaccinator and day\(^5\). Predominantly scavenging extensive backyard flocks in remote areas demand significantly higher labour input for vaccination than confined chicken broiler production systems. The relatively high storage and distribution costs for the vaccination of backyard poultry in Indonesia result from necessary investments in motorbikes to supply vaccinators with vaccine.

Table 5. Mass vaccination campaign costs per vaccination (USD/100 birds)

<table>
<thead>
<tr>
<th>Cost component</th>
<th>Layer</th>
<th>Broiler</th>
<th>Backyard</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Indonesia</td>
<td>Vietnam</td>
<td>Indonesia</td>
</tr>
<tr>
<td>Vaccine</td>
<td>3.18 (77%)</td>
<td>4.06 (85%)</td>
<td>3.18 (77%)</td>
</tr>
<tr>
<td>Vaccinator (labour, equipment)</td>
<td>0.84 (21%)</td>
<td>0.36 (8%)</td>
<td>0.84 (21%)</td>
</tr>
<tr>
<td>Storage &amp; distribution</td>
<td>0.04 (1%)</td>
<td>0.01 (0%)</td>
<td>0.04 (1%)</td>
</tr>
<tr>
<td>Post-vaccination monitoring</td>
<td>0.02 (0%)</td>
<td>0.02 (0%)</td>
<td>0.02 (0%)</td>
</tr>
<tr>
<td>Planning &amp; communication</td>
<td>0.03 (1%)</td>
<td>0.31 (6%)</td>
<td>0.03 (1%)</td>
</tr>
<tr>
<td>Total</td>
<td>4.12 (100%)</td>
<td>4.75 (100%)</td>
<td>4.12 (100%)</td>
</tr>
</tbody>
</table>

Source: authors’ calculations

\(^5\) 115 (300) birds per day and vaccinator assumed in backyard systems and 500 (500) birds per day and vaccinator assumed in broiler and layer systems in Indonesia (Vietnam).
Private incentives for HPAI vaccination

If poultry owners see an economic advantage in vaccinating their flock against HPAI compared to (or in addition to) applying other control measures, they are more likely to comply with a compulsory national vaccination strategy and a higher level of vaccination coverage can be achieved (McLeod et al. 2007). Whether poultry owners regard vaccination as a financially worthwhile risk reduction measure not only depends on the infection risk and cost of vaccination, but also on the overall profitability of their respective poultry enterprise. Indicative values for production inputs, prices of inputs and outputs, performance indicators, and production margins for the various production systems in Southeast Asia are provided in Table 6. As market prices for feed and poultry products have been highly volatile and differ between countries in the region, the presented values and prices reflect the price range since 2006. The gross margins for the production systems are calculated per production cycle and only account for feed costs and the costs of replacement birds.

From a flock owner’s perspective vaccination represents a protective measure against the economic impact of a HPAI outbreak. The decision on whether to contract the ‘vaccination insurance policy’ depends on the vaccination costs (‘insurance premium’), which also include production impacts of vaccination such as decreased egg laying, the expected economic loss in case of an outbreak, and the perceived probability of an outbreak. The ratio of vaccination costs to outbreak losses (‘breakeven outbreak risk per year’ in Table 7), adjusted for an average 80% vaccine efficacy, indicates the probability of flock infection at which expenditure on vaccination would be profitable for a risk neutral flock owner. The expected absolute loss in case of an outbreak varies during the production cycle. The applied absolute losses for the calculations of the break even risks in Table 7 are based on the assumption of a 50% loss of the maximum bird value and a 4-week gross margin loss due to production downtime subsequent to an outbreak. In case outbreaks occur when birds are of lower value than assumed in Table 7 or a salvage value can be derived from selling sick birds, the calculated breakeven risks are underestimated.

The breakeven risks presented in Table 7 are underestimates due to several other reasons. In all production systems the ‘background’ mortality requires vaccinating more birds than will eventually be produced. Vaccination can depress production leading to revenue foregone. In Vietnam, layer chicken reportedly showed a decrease in egg production of 5% over three weeks following vaccination (Cristalli 2006). This cost component has not been accounted for in the estimation of vaccination costs for layer flocks. The vaccination campaign costs in Table 5 were used to calculate vaccination costs per production cycle in Table 7 while an age-based vaccination scheme to achieve the maximum immunization coverage of the birds during the production cycle is assumed. Especially for short production cycle broiler flocks this is not achievable through mass vaccination campaigns. A more continuous vaccination delivery system would be required, for which the costs are likely to be higher, than the cost estimates from vaccination campaigns used to calculate the figures in Table 7.
Table 6. Chicken values and gross margins in different production systems in Southeast Asia

<table>
<thead>
<tr>
<th>Production system</th>
<th>Bird input (USD)</th>
<th>Mortality (%/prod. cycle)</th>
<th>Prod. cycle length (weeks)</th>
<th>Feed (kg/prod. cycle)</th>
<th>Feed costs (USD/kg)</th>
<th>Bird output (USD)</th>
<th>Eggs (no.)</th>
<th>Egg price (USD)</th>
<th>Gross margin (USD/bird &amp; week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOC to grand parent (meat purpose) layer spent hen</td>
<td>38.00</td>
<td>74.00</td>
<td>5</td>
<td>63.0 - 65.0</td>
<td>52.0</td>
<td>0.23 - 0.46</td>
<td>3.86 - 4.89</td>
<td>160</td>
<td>6.00 - 18.00</td>
</tr>
<tr>
<td>DOC to parent (meat purpose) layer spent hen</td>
<td>10.00</td>
<td>30.00</td>
<td>5</td>
<td>63.0 - 65.0</td>
<td>52.0</td>
<td>0.23 - 0.46</td>
<td>3.86 - 4.89</td>
<td>160</td>
<td>0.22 - 0.48</td>
</tr>
<tr>
<td>DOC to pullet</td>
<td>0.37</td>
<td>0.80</td>
<td>5</td>
<td>16.0 - 25.0</td>
<td>10.0</td>
<td>0.25 - 0.46</td>
<td>2.26 - 3.14</td>
<td>-0.13</td>
<td>0.02</td>
</tr>
<tr>
<td>Pullet to spent hen</td>
<td>2.26</td>
<td>3.14</td>
<td>5</td>
<td>45.0 - 54.0</td>
<td>43.0</td>
<td>0.23 - 0.46</td>
<td>3.86 - 4.89</td>
<td>320</td>
<td>0.09 - 0.15</td>
</tr>
<tr>
<td>DOC to spent hen</td>
<td>0.37</td>
<td>0.80</td>
<td>5</td>
<td>61.0 - 79.0</td>
<td>53.0</td>
<td>0.23 - 0.46</td>
<td>3.86 - 4.89</td>
<td>320</td>
<td>0.09 - 0.11</td>
</tr>
<tr>
<td>DOC to broiler (industrial)</td>
<td>0.37</td>
<td>0.74</td>
<td>5</td>
<td>4.6 - 6.7</td>
<td>5.0</td>
<td>0.44 - 0.62</td>
<td>3.09 - 5.71</td>
<td>-0.12</td>
<td>0.68</td>
</tr>
<tr>
<td>DOC to broiler (crossbred)</td>
<td>0.31</td>
<td>0.37</td>
<td>10</td>
<td>8.6 - 25.7</td>
<td>4.4</td>
<td>0.44 - 0.62</td>
<td>3.55 - 5.68</td>
<td>0.02 - 0.39</td>
<td></td>
</tr>
<tr>
<td>Backyard grower to spent hen</td>
<td>3.84</td>
<td>4.86</td>
<td>12</td>
<td>39.0 - 41.0</td>
<td></td>
<td>4.29 - 5.44</td>
<td>40 - 0.12</td>
<td>0.06 - 0.15</td>
<td>0.15</td>
</tr>
<tr>
<td>Backyard grower to cock</td>
<td>3.84</td>
<td>4.86</td>
<td>12</td>
<td>39.0 - 41.0</td>
<td></td>
<td>4.29 - 5.44</td>
<td>40 - 0.12</td>
<td>-0.03 - 0.22</td>
<td></td>
</tr>
<tr>
<td>Backyard chick to grower</td>
<td>0.25</td>
<td>0.41</td>
<td>20</td>
<td>21.0 - 23.0</td>
<td></td>
<td>3.84 - 4.86</td>
<td>0.15 - 0.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Backyard egg to chick</td>
<td>0.09</td>
<td>0.26</td>
<td>46</td>
<td>3.0 - 5.0</td>
<td></td>
<td>0.25 - 0.37</td>
<td>-0.03 - 0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Backyard flock6</td>
<td>14.38</td>
<td>19.55</td>
<td></td>
<td></td>
<td></td>
<td>38.20 - 48.70</td>
<td>120 - 0.35</td>
<td>0.92 - 2.17</td>
<td></td>
</tr>
</tbody>
</table>

Source: Poultry production survey data from May 2008 in Vietnam (FAO 2008); International egg production costs comparison data from Thailand, Vietnam and Indonesia for June 2006 (World Poultry 2007); Backyard production parameters and costs from Otte (2006); Aviagen* & Hy-Line* poultry management guides; own calculations for selected examples of existing production systems.

6 ‘Standard flock’ of 16 birds including 5 chicks, 6 growers, 4 hens, 1 cock
Table 7. Financial breakeven outbreak risks for HPAI vaccination (authors’ calculations)

<table>
<thead>
<tr>
<th>Production system</th>
<th>Vaccinations required / production cycle</th>
<th>Vaccination costs per prod. cycle (USD cents)</th>
<th>Vaccination costs per year (USD cents)</th>
<th>HPAI outbreak loss (USD)</th>
<th>Breakeven outbreak risk per year (%)</th>
<th>Breakeven outbreak frequency in years</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOC to grandparent (meat purpose) layer spent hen</td>
<td>4</td>
<td>16</td>
<td>19</td>
<td>13</td>
<td>15</td>
<td>55</td>
</tr>
<tr>
<td>DOC to parent (meat purpose) layer spent hen</td>
<td>4</td>
<td>16</td>
<td>19</td>
<td>13</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>DOC to pullet</td>
<td>3</td>
<td>12</td>
<td>14</td>
<td>24</td>
<td>41</td>
<td>1</td>
</tr>
<tr>
<td>Pullet to spent hen</td>
<td>1</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>DOC to spent hen</td>
<td>4</td>
<td>16</td>
<td>19</td>
<td>11</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>DOC to broiler (crossbred)</td>
<td>2</td>
<td>5</td>
<td>8</td>
<td>10</td>
<td>40</td>
<td>2</td>
</tr>
<tr>
<td>DOC to broiler (industrial)</td>
<td>2</td>
<td>5</td>
<td>8</td>
<td>33</td>
<td>65</td>
<td>1</td>
</tr>
<tr>
<td>Backyard grower to spent hen</td>
<td>1</td>
<td>4</td>
<td>11</td>
<td>5</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>Backyard grower to cock</td>
<td>1</td>
<td>4</td>
<td>11</td>
<td>5</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>Backyard chick to grower</td>
<td>1</td>
<td>4</td>
<td>11</td>
<td>8</td>
<td>28</td>
<td>3</td>
</tr>
<tr>
<td>Backyard egg to chick</td>
<td>2</td>
<td>7</td>
<td>23</td>
<td>77</td>
<td>394</td>
<td>0.02</td>
</tr>
<tr>
<td>Backyard flock</td>
<td>72</td>
<td>219</td>
<td>453</td>
<td>2,191</td>
<td>23</td>
<td>33</td>
</tr>
</tbody>
</table>

7 A potential outbreak is assumed to occur in the middle of the production cycle which would lead to the loss of 50% of the bird value at the production cycle end and 4 weeks of lost gross margin due to subsequent downtime for cleaning and disinfection.

8 Based on 80% vaccine efficacy.
Grandparent and layer chicken production systems have a relatively low estimated breakeven outbreak risk. Compared to vaccination in other production systems, vaccination in these production systems would be most cost-effective and flock owners have a relatively high private incentive to adopt vaccination and HPAI vaccination is commonly used by parent stock keepers in Indonesia (Sawitri Siregar et al. 2007). However, even for relatively valuable laying hens with an estimated potential HPAI outbreak loss of USD 3 – 5 per bird the breakeven risk of 1% – 3% would not economically justify the use of vaccination for a risk neutral poultry keeper under infection risk conditions similar to the peak HPAI H5N1 incidence in 2004 in Thailand and Vietnam, which was around 0.2% (Otte et al. 2008). Nevertheless, HPAI vaccination is reportedly widely used by layer flock owners in Vietnam and Indonesia (Sims, pers. comm.), which indicates that these poultry producers are risk averse and regard vaccination as an important component of their strategy to reduce the likelihood of the high economic losses of an HPAI outbreak would cause.

Although the value of broiler flocks increases over their relatively short lifespan, broiler producers have a relatively small financial incentive to vaccinate against HPAI with a vaccine that becomes fully effective only about 13 to 21 days after the first of two injections, since they only keep chicken for a short time thereafter. The financial incentive to vaccinate duck broilers, despite their longer production cycle is also low as they normally only show mild clinical signs of disease when infected with HPAI (Hulse-Post et al. 2005).

Vaccination of an average backyard chicken flock would only be ‘profitable’ for a risk neutral flock owner, if the annual risk of HPAI infection were higher than 17% and resulted in a loss USD 1 to 3 per bird. Since such a high infection risk is very unlikely, the average benefit of free of charge vaccination for backyard chicken flock owners would be marginal. Notwithstanding the relatively high gross margins of backyard poultry production, poultry keepers have shown little motivation to vaccinate against HPAI or other more prevalent diseases such as Newcastle disease. A survey on the willingness to pay for HPAI vaccination in Vietnam showed that only 32% out of the surveyed 62 poultry owners used Newcastle vaccine at an average price of USD 0.026 per chicken (FAO 2008). If other vaccines to prevent more financially relevant diseases were delivered in addition to HPAI vaccination and if HPAI-vaccinated flocks would be exempted from culling, subsidized HPAI vaccination might be a pro-poor disease control intervention.

The breakeven outbreak frequency is given by the reciprocal of the breakeven outbreak risk per year (per production cycle) and indicates the time period in years (in production cycles) within which the use of vaccination is expected to result in the same costs as the disease itself. The breakeven outbreak frequency for an industrial broiler flock owner would be one outbreak every 10 to 82 production cycles, depending on the assumed vaccination costs and losses. However, outbreak risk and absolute loss of an outbreak are not equally distributed over the time period of a production cycle. The economic value at risk is correlated with the feed investments in growing broilers. Broilers within a batch usually don’t grow homogenously and are therefore not finished at exactly same time, which leads to the sale of smaller batches over several days. The interaction with traders is likely to increase the infection risk of the remaining birds towards the end of a production cycle. Protection through vaccination for this specific time point however needs to be started early in the production cycle.
If market access of poultry producers is made conditional on the proven use of vaccination, as is the case in Hong Kong and Ho Chi Minh City, Vietnam, vaccination is likely to be used by producers supplying these markets. However, this only holds, if the capacity to control market access and the diagnostic capacity to test for antibodies is sufficiently high. The higher the difference between the calculated break even outbreak risk and the actual outbreak risk, the higher is the incentive for flock owners to ‘bypass’ market access restrictions.

Flock owners may consider other available protection measures such as improvements of production hygiene and investments in cleaning and disinfection equipment. The calculated vaccination costs to achieve the maximum achievable protection through vaccination could be considered as a benchmark for the maximum expenditure on other protection measures. For a flock of 1,000 industrial broilers the annual vaccination costs vary between USD 325 and 651. Annual vaccination costs would rise to between USD 106 and 157 for an integrated layer production system with a flock size of 1,000 birds. Detailed assessments of the specific risk factors for the entry of HPAI virus into these production systems would be essential to estimate the potential feasibility, costs and effectiveness of achieving a higher disease protection level for the respective flocks. Nevertheless, simple improvements, such as cleaning and disinfection of equipment, cages, and work clothes are likely to cost less then the above estimated costs for vaccination. It is recognized that the ease of applying such measures will differ between systems and the quality of housing. For example, layer units with multi-age flocks may not be in a position to regularly disinfect units and may have difficulty in cleaning egg trays, whereas an all-in/all-out broiler system with concrete flooring may be in a better position to apply cleaning and disinfection measures. Such measures require significant investments in training and then need to be followed with management so that they are continuously applied. Production hygiene improvements would also likely have additional benefits from reduced mortality and morbidity and subsequently increased productivity.

Public ‘returns’ to vaccination

Positive externalities from vaccinating poultry flocks result from the reduced probability of secondary outbreaks and the public health benefits from reduced exposure to HPAI virus, neither of which is taken into account in the estimated financial incentives for vaccination presented in Table 7.

The main benefit of vaccination for the community of poultry producers stems from the expectation that vaccinated flocks will act as ‘dead ends’ of infection chains and thereby also indirectly ‘protect’ non-vaccinated flocks. This indirect benefit is deemed to outweigh the ‘direct’ benefits of vaccination, but, given the uncertainty surrounding prevented infections / outbreaks, the inclusion of prevented outbreaks in public cost-benefit analyses is problematic. For Vietnam, Soares Magalhaes et al. (2006) estimated that vaccination of all commercial smallholder farms would more than halve ‘secondary’ outbreaks by reducing $R_n$ from 2.24 in the case of culling of infected premises and pre-emptive cull in a 3-km zone to 1.05 in the case of the same measures complemented by vaccination. Additional immunization of 25% of backyard flocks was estimated to further reduce secondary outbreaks from 1.05 to 0.23 per infected premises. These major reductions in secondary outbreaks would result in much higher public cost-benefit ratios than those that can be
derived from Table 7 for individual producers, the order of magnitude depending on the
generations of cases avoided. Assuming three successive generations of cases resulting from
one HPAI H5N1 outbreak, vaccination of commercial smallholder farms (in addition to
standard culling of infected and surrounding premises) would theoretically lead to a 90% reduction of the outbreak size, i.e. a ten-fold increase in cost-effectiveness. Dis-incentives are needed to counter the ‘free-rider’ problem that results from the above positive externalities that reduce overall disease risk, from which farmers, who do not vaccinate benefit without incurring respective costs.

To reduce the public health risk it would be essential to limit the contact of humans with infected poultry. Broilers represent the largest share of poultry which is marketed through live poultry markets and in contact with a magnitude of consumers in many developing countries. Effective immunization of broilers would reduce the exposure of live bird market customers to HPAI virus. However, high immunization coverage of marketed broilers is not likely to be achieved due to the low economic incentive for flock owners to vaccinate their birds. Subsidised vaccination in these flocks may be justified for public health reasons, but even if the vaccine delivery was entirely free, owners’ willingness to participate may be affected by their perception of risk and the impact of a vaccination campaign on production in terms of potential losses of birds and their condition. In addition these costs need to be assessed against market hygiene interventions. The required vaccination costs to supply a medium size live bird market with a daily trade volume of 1,000 broilers would amount to USD 1,151 – 1,707 per month. Similar to the situation on broiler farms, a detailed assessment of the costs, effectiveness and feasibility of other market hygiene improvements and behaviour changes need to be considered in order to choose the most cost-effective risk reduction strategy.
VIII. Discussion and Conclusions

The available literature on field vaccination experiments with commercially available vaccine indicates that antibody titres considered as protective can develop within 13 days after the first vaccination. However, with the exception of Trovac, two injections at two-week intervals are required to achieve full protection and one of the few long-term serologic response studies indicates that immunity is lost in most chicken 20.5 weeks after vaccination. In general, vaccinated birds have been shown to shed less amounts of virus than unvaccinated controls at specific times post challenge. Thus, most commercial vaccines have the potential to reduce the level of circulating virus in infected chicken populations. However, a crucial factor for achieving significant reductions in circulating virus in poultry flocks are sufficiently high vaccination coverage levels (50% to 90% immunization of at least 50% of all flocks at risk of infection) with a vaccine that protects against the circulating virus(es).

Both theoretical considerations as well as field observations show that such high immunization rates are difficult to attain in large poultry populations through vaccination campaigns and that they are even more difficult to maintain over a longer time period due to the high population turn over in short-lived commercial broiler and mixed-age backyard poultry flocks. There are also problems of maintaining immunity levels in long-lived commercial layer and parent flocks as the currently available vaccines do not lead to lifetime immunity. The short to medium term gains in reducing the virus load with vaccination are not likely to result in a cost-effective long-term control approach, if no additional measures are in place, because infection chains are unlikely to be totally interrupted and virus will not be eliminated from the entire poultry population.

A major drawback of vaccination is that the probability of detecting outbreaks may decrease due to a lack or reduction of clinical signs, which could lead to the silent spread of virus (Savill et al. 2006). Incentives for disease reporting are relatively low and masking disease signs through vaccination further depresses an already low level of reporting. For northern Vietnam, Walker et al. (2009) estimated a 45% effective vaccination coverage achieved by mass vaccination campaigns, leading to a greatly reduced transmission of virus between communes but also to an increase in the commune-level infectious period due to outbreaks remaining unreported for a longer duration. The same authors estimated that, had detection levels been maintained at pre-vaccination levels, around two-thirds of outbreaks which occurred in the 2007 wave in northern Vietnam would have been prevented. This highlights the fact that, regardless of the underlying reasons for less rapid reporting of outbreaks, in order to translate the reductions in disease transmission following vaccination into greater gains in disease control, more effective reporting and surveillance strategies are required.

Another drawback of the extensive use of vaccination is the increased likelihood of genetic drift as seen in Mexico (Escorcia et al. 2008, Lee et al. 2004) and the US (Suarez et al. 2006). Therefore close virus monitoring of circulating field strains, continuous vaccine testing via challenge trials, and subsequent development of new vaccines that protect from infection with evolving field strains are an inevitable component of any longer-term routine

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9 Theoretically close to 50% of all vaccinated broilers have been replaced by non-vaccinated birds in the 60 days required by the Vietnamese animal health system to conduct one national vaccination campaign.
vaccination programme. This requires considerable financial resources and supporting activities have to be based on surveillance systems that have a high probability of detecting circulating HPAI viruses even in the absence of significant clinical disease. It also requires the sharing of isolates with laboratories capable assessing the suitability of the vaccines used. At present these significant ‘collateral’ investments to vaccination are rarely found in countries with problems of HPAI endemicity. In Indonesia, a donor-funded OIE/FAO network of expertise on Avian Influenza (OFFLU) is monitoring avian influenza virus variants and the efficacy of vaccines used in commercial poultry production systems (Domenech et al. 2009).

Short-lived broilers, mainly chicken but also ducks, constitute a relatively large share of the standing poultry population of most countries, which, due to their rapid turnover, provide a constant and ample supply of susceptible avian hosts. Campaign-based vaccination programmes can only achieve a very low coverage in these systems, particularly if two injections are required to achieve immunity. An age-based vaccination schedule for broilers would be an option to achieve higher vaccination coverage and its maintenance over time, but the logistical requirements for age-based vaccine delivery and associated costs differ significantly from those of vaccination campaigns. The private incentives for owners of broiler flocks to regularly vaccinate replacements are low and even if owners do vaccinate, broiler flocks will remain at least partially susceptible for two to three weeks, i.e. most of their lifespan (unless Trovac is used and protects against circulating virus strains). Broilers thus represent the ‘Achilles heel’ of any HPAI control strategy that relies, at least to some extent, on the use of vaccination.

Although vaccination of more valuable breeder and layer flocks is generally more ‘profitable’ from the flock owners’ perspective, the incentives to vaccinate are not constant over the production cycle and immunity of birds might have waned towards the end of their productive life. Also, as breeder and layer flocks have relatively high contact rates with other flocks and as HPAI vaccination is frequently used in these production systems, postponed detection of infection due to potential masking of symptoms by vaccination may undermine the success of a vaccination strategy in these systems. Upgrading of bio-security is likely to be safer and more cost-effective in these production systems than vaccination.

From a public health and national health security perspective the reduction of human cases of avian influenza as a means of reducing the risk of a national panic and global pandemic is most important. Human cases of avian influenza receive high media attention and the political pressure to act is high. The impact of poultry vaccination on human health risk is controversially debated in the scientific community. Human cases of H5N1 infections in China in January 2009 raised concerns about the role of vaccination in increasing the virulence of HPAI virus and masking its symptoms in poultry (FAO 2009). Hygiene practices and awareness of risk factors for poultry to human transmission are possibly as important for preventing human infections as reducing virus shedding by vaccination.

The cost-effectiveness of national vaccination efforts need to be weighed against those of alternative measures to reduce disease spread in the national flock. In Vietnam for example the culling strategy employed during the first wave of outbreaks led to the destruction of about 44 million birds (20% of the standing poultry population) and caused major losses to poultry owners and costs to the government. However, even this extensive depopulation of poultry flocks was not sufficient to break the chain of infection in all locations (Tuan 2007).
As a consequence, the government decided to use vaccination as an additional control measure, which, in combination with a modified culling policy, reduced the number of culled poultry, but added substantial vaccination costs. On the other hand, Thailand managed to very significantly reduce or even eliminate the circulation of H5N1 virus in its domestic poultry population within 2 years without resorting to vaccination, largely through intensive active and passive surveillance combined with, progressively restricted, culling in case of outbreaks.

The high and recurrent costs, technical difficulties, and epidemiological drawbacks of large-scale, open-ended blanket vaccination programmes in national efforts to control HPAI call for careful targeting of vaccination in national control strategies, which ‘intelligently’ combine available disease control measures. In principle, vaccination can be targeted spatially, temporally, and / or by production system to maximise its impact and cost-effectiveness. Effective targeting however requires sound risk assessments, for which data and expertise are often lacking. Strengthening of the epidemiological capacity of national animal health systems would thus be a major prerequisite for large-scale use of vaccination in the control of HPAI.
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