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Assessment of national strategies for control of high-pathogenicity avian influenza and low-pathogenicity notifiable avian influenza in poultry, with emphasis on vaccines and vaccination

D.E. Swayne [1, 2]*, G. Pavade [1], K. Hamilton [1], B. Vallat [1] & K. Miyagishima [1]

(1) World Organisation for Animal Health (OIE), 12 rue de Prony, Paris 75017, France
(2) World Organisation for Animal Health (OIE) Collaborating Centre for Research on Emerging Avian Diseases, Exotic and Emerging Avian Viral Diseases Research Unit, Southeast Poultry Research Laboratory, Agricultural Research Service, United States Department of Agriculture, 934 College Station Road, Athens, Georgia 30605, United States of America
*Corresponding author

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Summary

Twenty-nine distinct epizootics of high-pathogenicity avian influenza (HPAI) have occurred since 1959. The H5N1 HPAI panzootic affecting Asia, Africa and Eastern Europe has been the largest among these, affecting poultry and/or wild birds in 63 countries. A stamping-out programme achieved eradication in 24 of these epizootics (and is close to achieving eradication in the current H5N2 epizootic in South African ostriches), but vaccination was added to the control programmes in four epizootics when stamping out alone was not effective. During the 2002 to 2010 period, more than 113 billion doses of avian influenza (AI) vaccine were used in at-risk national poultry populations of over 131 billion birds. At two to three doses per bird for the 15 vaccinating countries, the average national vaccination coverage rate was 41.9% and the global AI vaccine coverage rate was 10.9% for all poultry. The highest national coverage rate was nearly 100% for poultry in Hong Kong and the lowest national coverage was less than 0.01% for poultry in Israel and the Netherlands. Inactivated AI vaccines accounted for 95.5% and live recombinant virus vaccines for 4.5% of the vaccines used. Most of these vaccines were used in the H5N1 HPAI panzootic, with more than 99% employed in the People's Republic of China, Egypt, Indonesia and Vietnam. Implementation of vaccination in these four countries occurred after H5N1 HPAI became enzootic in domestic poultry and vaccination did not result in the enzootic infections. Vaccine usage prevented clinical disease and mortality in chickens, and maintained rural livelihoods and food security during HPAI outbreaks. Low-pathogenicity notifiable avian influenza (LPNAI) became reportable to the World Organisation for Animal Health in 2006 because some H5 and H7 low-pathogenicity avian influenza (LPAI) viruses have the potential to mutate to HPAI viruses. Fewer outbreaks of LPNAI have been reported than of HPAI and only six countries used vaccine in control programmes, accounting for 8.1% of the total H5/H7 AI vaccine usage, as compared to 91.9% of the vaccine used against HPAI. Of the six countries that have used vaccine to control LPNAI, Mexico, Guatemala, El Salvador and Italy have been the biggest users. In countries with enzootic HPAI and LPNAI, development and implementation of exit strategies has been difficult.

Keywords

Animal disease – Avian disease – Avian influenza – Avian influenza virus – High-pathogenicity avian influenza – Immunity – Low-pathogenicity avian influenza – Low-pathogenicity notifiable avian influenza – Poultry – Vaccination – Vaccine – Vaccine bank.

Introduction

High-pathogenicity avian influenza (HPAI) and low-pathogenicity notifiable avian influenza (LPNAI) in poultry are reportable to the World Organisation for Animal Health (OIE) by its 178 Member Countries (56). The causal agents of LPNAI are limited to the H5 and H7 haemagglutinin subtypes of low-pathogenicity avian influenza (LPAI) viruses. Reporting HPAI and LPNAI outbreaks is necessary for animal health transparency (to minimise the risk of international disease spread), for fair trade and for the enhancement of our knowledge of the worldwide avian influenza (AI) outbreak situation in animals, which enables the development of effective, common control strategies. Traditionally, HPAI control strategies have used various components, including rapid diagnostics and accurate surveillance, elimination of infected flocks, enhanced biosecurity, and education/training of poultry workers (50). Such combinations of components have been effective in eradicating most outbreaks when implemented to a high level, especially within stamping-out or culling programmes.

Since 1959, there have been 29 HPAI epizootics (45, 59). Twenty-four have been handled with stamping-out strategies without vaccination, which has resulted in eradication. However, the largest HPAI epizootic or, more appropriately, panzootic of the last 50 years has been the H5N1 HPAI that emerged in the People's Republic of China (hereafter referred to as China), first reported in 1996, and has since spread to poultry and wild birds in 63 countries or regions (16, 60). In many of these countries, the H5N1 HPAI poultry outbreaks have been eradicated through traditional stamping-out programmes but, in some countries, stamping out alone has not achieved infection control or eradication. Thus, vaccination has been added as an additional control component to maintain rural livelihoods and reduce the number of clinical outbreaks.

The number of H5/H7 LPNAI outbreaks since 1959 remains unknown because LPNAI was not an OIE-listed disease before 2006. Low-pathogenicity notifiable AI became reportable because of the unpredictable ability of H5 and H7 LPAI viruses to mutate and become HPAI viruses, as occurred in the United States of America (USA) in 1983 (H5N2), Mexico in 1994 (H5N2), Italy in 1999 (H7N1), Chile in 2002 (H7N3) and Canada in 2004 and 2007 (H7N3) (47). Thus, H5 and H7 LPAI viruses were unique and needed special status for surveillance, control and eradication in poultry, as compared to non-H5/H7 LPAI viruses, hence their reclassification as LPNAI viruses.

Vaccination has been used as a tool to control and eradicate multiple subtypes of LPAI in poultry since the late 1970s, with the licensing and use of oil-emulsified inactivated AI vaccines (48). Most recently, vaccines have been used against H5 and H7 LPNAI in the USA, Italy, Mexico, Guatemala and El Salvador, with and without controlled slaughter (3, 48, 53). The latter three countries have used both oil-emulsified inactivated AI vaccines and recombinant fowl poxvirus-vectored vaccine with an H5 AI gene insert. For HPAI, the first field uses of poultry vaccination were in Mexico against H5N2 HPAI (1995) (53) and Pakistan against H7N3 (1995) (35). Vaccination for H5N1 HPAI was first implemented during 2002 in Hong Kong and soon thereafter in Indonesia and China (2004) (48). Poultry vaccination programmes against H5N1 HPAI have been reported in Russia, Egypt, the Netherlands, France, Vietnam and Pakistan (48). The current study examines the control components used in HPAI and LPNAI outbreaks from 2002 to 2010 and in current emergency plans, primarily focusing on vaccines and vaccination as a single tool in a comprehensive AI control strategy.

Materials and methods

Questionnaire on avian influenza vaccines and vaccination

A questionnaire survey was conducted, using the official channel of communication between the OIE and its Delegates, in the 80 countries that had reported HPAI and/or LPNAI outbreaks in poultry or wild birds between 2002 and 2010. The objective was to determine what lessons countries have learned from their past experiences in AI control and how they have modified ongoing AI control strategies to improve control and eradication.

The questionnaire was in two formats. A shorter format of 20 questions was sent to 42 countries, focusing principally on overall AI control strategies, with a few questions on AI vaccines and vaccination. A longer format, consisting of the initial 20 questions, plus an additional 17 that focused on how AI vaccines had been used, was sent to 38 countries that had or potentially had used H5 and/or H7 AI vaccines, based on information contained in the OIE World Animal Health Information Database (WAHID), published reports or field intelligence information. This longer-format questionnaire covered various topics, namely: general AI vaccine use policy, AI vaccine bank questions, vaccine usage, vaccination strategy, including exit strategy, and vaccine licensing. The questionnaire was available in English and French versions. The latter was sent to Francophone countries in Europe and Africa. The English version of the questionnaire is available as an appendix at the end of this paper. The responses for each question were grouped and compiled in a database (Access, Microsoft, Seattle, Washington, USA) and for numerical data analysis (Excel, Microsoft, Seattle, Washington, USA). The responses were analysed and interpreted.

Other data sets

The national poultry population data were obtained from one of three sources, in order of preference:

i) the OIE WAHID Interface, Animal Population (59)

ii) staff of the Veterinary Services of individual countries

iii) the statistical database of the Food and Agriculture Organization of the United Nations (FAOSTAT) (15).

From FAOSTAT, national poultry production was calculated by summing the figures of poultry slaughtered for meat (chickens, ducks, geese, guinea fowl, turkeys and others) and poultry for egg production (chickens and others). National poultry density was based on information about stocks of poultry and agricultural land, as obtained from FAO (http://kids.fao.org/glipha/). Poultry data were collected from the WAHID database for HPAI and LPNAI outbreaks and the species of birds affected (59).

Avian influenza vaccine coverage (%) was calculated for selected poultry species in selected countries, based on the data available on doses of vaccine administered (from the current survey), vaccination protocol and poultry production data, generated as above (15). The percentage of coverage was calculated using an estimated average of two doses of vaccine per bird per year if poultry species were not specified or the country did not specify the vaccination programme. If vaccination was conducted only in layers or breeders, three doses were used for annual use calculations.

For selected countries with vaccine usage, Chief Veterinary Officers and their staff, and field veterinarians were interviewed and secondary information was collected to supplement the original questionnaire.

Results and discussion

All countries (short and long questionnaires)

General avian influenza control strategies and components

A total of 69 out of 80 (86%) countries completed and returned the questionnaire. Responses were received from countries on all six inhabited continents:
– Asia (24 countries)
– Africa (10 countries)
– North America (5 countries)
– South America (1 country)
– Europe (28 countries)
– Australia and Oceania (1 country).

Of these 69 countries, 27 (39%) had experienced HPAI outbreaks in poultry only, 11 (16%) experienced HPAI outbreaks in wild birds only and 26 (38%) had HPAI outbreaks in both poultry and wild birds. Five (7%) countries had LPNAI outbreaks only while 14 (20%) had both HPAI and LPNAI outbreaks in poultry. Not all of the 69 responding countries completed every question in the survey.

For all countries, a national AI control programme was in place. The most frequently mentioned components in the plans included:
– quarantine and additional movement restrictions or controls
– tracing poultry in the outbreak area
– enhanced biosecurity measures
– farmer and public education and awareness about the disease
– active and passive surveillance of poultry and wild birds
– monitoring
– rapid diagnostics
– culling (stamping out) of positive cases
– disinfection of facilities and equipment
– decontamination and disposal of infectious materials
– compensation.

Some countries also listed a crisis management framework, high-throughput rapid diagnostic testing, early processing of at-risk non-infected poultry, emergency vaccination and, occasionally, pen-side testing as a screening tool. The criteria for deciding which group of poultry should be culled varied greatly between individual countries (59). For some countries, culling was only practised on infected premises, while other countries also culled dangerous contacts, epidemiologically linked farms or all poultry in a village. Some used a zone approach to culling, covering 0.5, 1 or 3 km in radius. Risk zones were also implemented in some countries, which incorporated varying levels of movement restriction and surveillance.

For HPAI, culling poultry in flocks, farms and villages was consistently used as a method for eliminating infected poultry or those suspected to be infected. For LPNAI, culling and disposal were most frequently used, but some alternatives were practised, including:

– slaughter of unknown/undiagnosed infected commercial poultry without recall of products; time-delayed marketing or controlled slaughter of commercial infected poultry to allow recovery from acute LPNAI virus infections

– quarantine of recovered layer farms with marketing of washed eggs

– release of quarantined egg layer flocks if demonstration of LPNAI virus was negative (59) (data from current survey).

Two developing countries allowed slaughter of clinically normal village poultry and/or commercial poultry that were infected with LPNAI (data from current survey) (59). Seropositive flocks without recovery of the virus or detection of the viral genome have a low risk of disseminating the virus if specific management and biosecurity procedures are used (25). Payment for destruction of such flocks by national governments through compensation programmes is fair to the farmer and causes the lowest risk to animal health, but requires a large outlay of financial and physical resources. However, if compensation is not available, marketing virus-negative flocks that have recovered from LPNAI is of low risk for disease spread to other flocks and to public health, if adequate biosecurity processes are used.

Compensation programmes were present in 48 of 69 (70%) countries and were linked to stamping out of infected flocks. The funding was provided by the government in 41 countries (85%) and via a government/industry partnership in six countries (13%). One country (2%) did not specify a funding source.

Vaccines and vaccination were included as an option for 58% and 39% of the countries in their HPAI and H5/H7 LPNAI control strategies, respectively, with 58% of the countries having written plans with specific criteria for vaccine usage. However, only 14% had actually completed AI vaccine and vaccination simulation exercises or worked out the logistics of implementing a vaccination programme. Table-top exercises were conducted twice yearly in the USA, annually in Australia, and every two years or at unspecified time periods in most other countries. In 2010, Chinese Taipei conducted three table-top exercises. Only 21 countries have used AI vaccine to control HPAI or LPNAI in poultry, eight countries have used vaccine in preventive programmes, 14 in emergency programmes and eight in routine vaccination programmes. Eight countries have used AI vaccines in more than one type of vaccination programme. For example, China initiated an emergency vaccination programme in 2004, vaccinating poultry in buffer zone or outbreak areas, but in late 2005 this was changed to a routine (mass) vaccination programme for all poultry in the country (10).

However, the specific control components were only listed qualitatively as traits, and no assessment was included of the quantitative implementation and practice of each component in the comment section of the questionnaire. In the WAHID database on H5N1 HPAI outbreaks (59), the components listed in control measures were very similar between different countries, but the outcomes varied dramatically: some countries declared the disease to have been eradicated three months after the last flock had been stamped out and the premises disinfected (with the lack of infection attested by proper surveillance [55]), but other countries reported that enzootic infection had become established. Such outcome variations suggest that qualitative implementation of specific components, along with epidemiological, environmental and geographical factors, varied with individual countries, resulting in inconsistency in stopping the spread of the AI virus. This had a severe impact upon the total number of cases and outbreaks and, ultimately, the time it took to control and eradicate the disease.

A companion study indicated that the strength of the country's Veterinary Services, as measured by the scores achieved in an OIE Evaluation of Performance of Veterinary Services (PVS), had an impact on HPAI control; i.e. higher PVS scores were associated with a decreased AI eradication time, mortality rate, culling rate and occurrence of outbreaks (39). In addition, countries that were Members of the Organisation for Economic Co-operation and Development (OECD) had fewer HPAI outbreaks, shorter outbreaks, earlier eradication times, lower poultry mortality rates and higher poultry culling rates than non-OECD countries (39). This indicates that countries that are transparent, and provide adequate funding for the development and maintenance of efficiently performing Veterinary Services, have better control of HPAI.

Avian influenza vaccine and vaccination from 2002 to 2010

Field trials had been conducted with H5 vaccines in 25% and H7 vaccines in 7% of the countries before the implementation of field vaccination programmes or their inclusion in emergency response plans. In field implementation of vaccination, 30% of countries had used vaccines for HPAI control: 16% in poultry, 10% in zoological and other collections of birds and 4% in both categories. By contrast, 12% had used vaccines to control H5/H7 LPNAI and 17% to control non-H5/H7 LPAI but, in both of these virus categories, the vaccine was only used in poultry. For non-H5/H7 LPAI, H9N2 was the most common subtype for which vaccine was used as a control tool, and was reported by ten countries. Vaccine was also used, although to a lesser extent and in a restricted/targeted population or geographic region, against other LPAI subtypes in poultry. They included subtypes causing swine influenza in Canada (H3) and the USA (H1 and H3) in breeder turkeys; H6 in Germany, South Africa (ostrich breeders only) and the USA; and H2, H4 and H10 in the USA. In the USA, the vaccines were mostly used in turkeys, especially turkey breeder hens.

Avian influenza vaccine bank

Vaccination against AI can be used as a preventive, emergency or routine practice in control programmes for HPAI and LPNAI (30). Vaccine banks are a necessary part of any emergency vaccination plan when other disease control measures alone are insufficient to contain the outbreak. In addition, implementation of an effective emergency vaccination programme also requires fully developed application plans and an understanding of the logistics of a vaccination campaign in the field. Preventive vaccination programmes may take a slightly longer time to implement than emergency vaccination programmes but are most effective when kept small in size and targeted to high-value or high-risk populations, such as genetic stocks of commercial poultry, zoo birds, rare birds or endangered species. Preventive vaccination programmes require less planning in advance than emergency vaccination programmes, but a vaccine bank and some logistical infrastructure may be necessary for rapid implementation, should an outbreak occur in the border area of a neighbouring country. If the HPAI or LPNAI becomes widespread and enzootic, routine vaccination may assist in reducing disease incidence and allow the continuation of poultry production in rural settings, to maintain the livelihoods and food security of the rural poor. A routine vaccination programme requires a steady, direct supply of commercial vaccine and cannot rely upon an emergency AI vaccine bank.

With the spread of H5N1 HPAI from south-east and eastern Asia across central Asia to Eastern Europe, the Middle East and Africa during 2005 to 2006, many countries began to develop emergency vaccination plans and vaccine banks. This development, alongside targeted preventive plans, accelerated with the appearance of dead wild birds infected with H5N1 HPAI virus in Europe during the winter of 2006 (26).

In the survey, 13 countries (19%) reported development of an H5 and/or H7 national AI vaccine bank containing frozen virus (4 of 13), processed antigen (1 of 13) and/or final oil-emulsified product (10 of 13). The vaccines or pre-vaccine products were held by governments (8 of 13), private companies (2 of 13) or both (3 of 13). The seed strains used in the inactivated oil-emulsified vaccines included:

– H5 and H7 LPNAI viruses from previous outbreaks in poultry (H5N2, H5N7, H5N9, H7N2 and H7N3)

– an H5N1 HPAI virus

– an H5N1 classic reassortant LPAI virus with the haemagglutinin gene from an H5 wild waterfowl virus

– reverse-genetic-generated LPAI viruses (two H5N1 viruses and an H5N3 virus).

Ten countries had only H5 in the vaccine bank while three countries had both H5 and H7 vaccines in the bank. The quantity of vaccine ranged from 0.5 to 55 million doses per subtype, but most countries had ≤3.5 million doses of each subtype. Such modest quantities would limit emergency vaccination programmes to zoo birds, endangered bird species and valuable genetic collections of poultry, or targeted vaccination to high-risk poultry groups within a small geographic region. Such a small number of doses would not support a massive or routine vaccination campaign. Many of the first doses in the banks were acquired in 2006 (n = 4), when the risk of introducing the H5N1 HPAI virus from infected migratory wild birds was perceived as high in Europe and western Asia (42). Some countries acquired vaccines for their banks during 2007 (n = 1), 2008 (n = 1), 2009 (n =1) and 2010 (n = 3). The vaccines' expiration dates ranged from one to four years. A few countries indicated that future vaccines would be purchased as rotating stocks from commercial vaccine manufacturers, but most countries did not have plans to purchase replacement vaccines for their bank. Some countries have opted out of vaccine banks, perceiving the cost of replacing and maintaining a vaccine bank to be unsustainable when the perceived risks of introduction from migratory birds have declined and significant improvements have been made in biosecurity for poultry production systems, as well as in rapid diagnostics and surveillance programmes.

The cost of vaccines and vaccination is mainly covered by federal and/or state or provincial governments but, in some countries, the commercial sector has responsibility for vaccine and vaccination costs within private companies. For emergency vaccination in the European Union (EU), 50% of the cost of vaccination is covered by the EU and 100% of the vaccine cost.

In 2006, the OIE set up a regional vaccine bank for AI vaccines in Africa, funded under the EU Pan-African Programme for the Control of Epizootics, and in 2007 it also established a global vaccine bank for AI vaccines

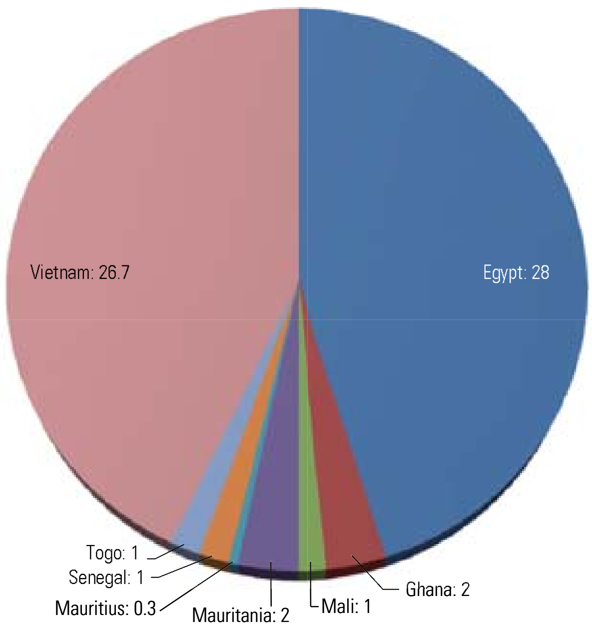

Fig. 1
Countries that used the World Organisation for Animal Health H5N2 avian influenza vaccine bank and number of doses employed

funded by the Canadian International Development Agency (Fig. 1) (58). Only 39 (57%) respondents indicated that they were aware of the OIE H5 vaccine bank. Eight countries obtained vaccine doses from the OIE vaccine bank, totalling 62 million H5N2 doses. The vaccines were provided to Egypt, Ghana, Mali, Mauritania, Mauritius, Senegal, Togo and Vietnam, but Egypt and Vietnam accounted for the majority of the doses: 28 million and 26.7 million doses, respectively (Fig. 1). In Egypt and Vietnam, these AI vaccine doses were used in the field, but the doses provided to the other six countries (7.3 million) have not been used. The OIE AI regional and global vaccine banks are virtual entities.

Thirty-two countries listed several circumstances for potentially using the vaccine bank or AI vaccines in general, including:

– a rapid eradication in poultry not achieved using other measures, including stamping out (28%)

– risk assessments indicating significant and immediate threat of spread, either from a neighbouring country or within the country (19%)

– the presence of enzootic AI in poultry (13%)

– the occurrence of an HPAI outbreak (6%)

– the presence of virus strains with a high risk for zoonotic infection (3%)

– the difficulty of rapidly destroying infected poultry (3%)

– infections in endangered or rare species of birds (3%)

– changes in the international spread pattern of the AI virus (3%)

– structural changes in a country's poultry industries (3%)

– changes in the clinical presentation of the disease (3%).

Factors associated with use or non-use of avian influenza vaccines in control programmes

Fifty-eight countries reported on why they had not used or would not use AI vaccines. The most consistent responses focused on a few common themes:

– traditional control measures, including stamping out, to control and eradicate HPAI and LPNAI in sporadic to widespread outbreaks had proved successful

– there were negative aspects to AI vaccines and vaccination, such as:

i) the potential for silent infections and subclinical shedding of the AI virus

ii) difficulty in identifying infections in a vaccinated population

iii) the high cost of vaccines and their labour-intensive administration, especially when individually injecting birds using inactivated vaccines

iv) the delay in protection for seven to 14 days after administration

v) trade restrictions imposed by importing countries (Table I).

Table I

Responses of 58 countries concerning why they had not or would not use avian influenza vaccines to control high-pathogenicity avian influenza or low-pathogenicity notifiable avian influenza

Reasons for not using vaccines in avian influenza control	Responses
Eradication is possible or has been successful using stamping out and other control measures	24%
Vaccination does not prevent infection and creates clinically silent shedders	22%
Difficulty of differentiating the non-infected from infected birds in vaccinated populations (i.e. DIVA)	17%
High cost of vaccines and vaccination	16%
Vaccination would result in trade restrictions	14%
Presence of small or sporadic outbreaks, or low risk of spread of outbreak	10%
Lack of vaccination plan or policy	9%
No outbreaks or freedom from outbreaks	5%
Seven to 14 days are needed to induce an adequate level of immunological protection in a large poultry population	5%
Vaccination would mask detection of other avian influenza infections	3%
Vaccination in rural sector is difficult due to inability to trace movements of live poultry	3%
Lack of adequate human resources for vaccination	3%
Vaccines have to be injected individually to each bird and some require two doses	2%
Lack of public acceptance	2%
Vaccination promotes enzootic disease	2%
Vaccination results in increased laxity in biosecurity	2%
Vaccination is less efficient than depopulation	2%
Avian influenza outbreak only in low-density poultry production area	2%

By contrast, 45 countries would consider using AI vaccines in the future or had used AI vaccines in the past. Their most consistent reasons for doing so included:

– the inability to control or eradicate an HPAI or LPNAI outbreak using stamping out and other control measures

– a large outbreak with a high risk of spread

– positive aspects of the vaccine, such as:

i) decreasing the susceptibility of poultry to infection

ii) decreasing virus shedding

iii) preventing clinical disease and mortality in birds (Table II).

Long questionnaire only

General vaccine usage

The survey indicated that countries have used H5/H7 AI vaccines in the past eight years (2002–2010) in emergency, preventive and routine vaccination programmes (Tables III to VII). The majority of the countries used AI vaccines in an emergency programme after an outbreak of AI had occurred within the country (80%). Less frequently, some countries used vaccine in a preventive programme before AI had entered their borders (42%), or as routine vaccination after AI became enzootic in their country's poultry population (36%). Countries have vaccinated and/or were vaccinating different types of birds to control or eradicate AI. Most frequently, it was chickens (meat chickens, broiler breeders, egg chickens and layer breeders), ducks (meat ducks and breeder ducks) and turkeys (meat turkeys and turkey breeders) that were vaccinated. However, other poultry species, including meat geese, breeder geese, quail, guinea fowl, pheasants, peacocks, grouse and ostriches, have all been vaccinated. In addition, zoo, hunting, companion, conservation and endangered birds received a minimal quantity of AI vaccine (Table V). The doses used per year, vaccination coverage rates, national poultry populations, and national poultry densities are summarised in Tables III, IV and V for HPAI and in Tables VI and VII for LPNAI.

When it is stated that a country has a vaccination programme for poultry, the general public and public health officials may incorrectly assume that 100% of the poultry within the country have been vaccinated. However, the availability of vaccine and logistics of vaccination dictate how close a country can come to 100% coverage. In addition, many countries do not need mass vaccination campaigns and can target only high-risk poultry for vaccination. The FAO has classified poultry production into four systems, often called sectors. For this study, the authors used the FAO classification system:

– sector 1: high biosecurity, industrial, vertically integrated production

– sector 2: moderate-to-high biosecurity, commercial poultry, non-vertically integrated production, using both slaughterhouses and live markets

Table II
Responses of 45 countries concerning the conditions under which they would consider using or had already used avian influenza vaccines to control high-pathogenicity avian influenza or low-pathogenicity notifiable avian influenza

Reasons for using vaccines in avian influenza control	Responses
Stamping out and other measures not adequate for control	29%
Widespread outbreaks	24%
High risk of spread	13%
To protect valuable birds, such as poultry breeders or endangered bird species	9%
To decrease animal susceptibility through improved immunity	7%
Enzootic disease	7%
To reduce virus shedding and infection pressure	4%
To decrease clinical infections and mortality	4%
In high-risk areas because of neighbouring infections	4%
As low-level support for stamping out by industry or citizens	4%
To control localised infection	2%
Persistence of avian influenza in a population of one species	2%
To prevent low-pathogenicity avian influenza virus from mutating into a high-pathogenicity avian influenza virus	2%
To decrease economic losses	2%
For a geographic 'immunity ring' to prevent spread	2%
Presence of adequate resources for vaccination programme	2%
Animal welfare concerns	2%
Against high-risk zoonotic avian influenza viruses	2%

Table III
Number of doses of H5 or H7 avian influenza vaccine used in poultry against high-pathogenicity avian influenza and the coverage rate for 15 countries from 2002 to 2010

Country	Year	Species	National poultry population (1,000s)[(a)]	Dose (1,000s)[(b)]	Subtype	Vaccine coverage (%)	Poultry density (birds/km² of agricultural land)[(c)]	Global usage (%)
China	2004	Poultry	**e** 14,862,137	5,266,885[(d)]	H5	17.4	933	
	2005	Poultry	15,203,486	12,889,931[(d)]	H5	41.6	n/a	
	2006	Poultry	15,544,835	18,905,901[(d)]	H5	59.6	971	
	2007	Poultry	14,597,919	20,361,127[(d)]	H5	68.4	985	
	2008	Poultry	15,503,531	22,603,952[(d)]	H5	71.5	n/a	
	2009	Poultry	**e** 15,971,298	23,687,824[(d)]	H5	72.8	n/a	
	2010	Not available	**e** 16,439,065	n/a	H5	n/a	n/a	
	Subtotal		**108,122,271**	**103,715,621**		**47.1**	**963**	90.99
Côte d'Ivoire	2006	Broiler & layer breeders & other Galliformes[(e)]	31,995	8,000	H5	12.5	158	<0.01
Egypt	2006	Poultry	534,060	496,000	H5	43.0	3,633	
	2007	Poultry	598,807	1,235,000	H5	65.2	3,667	
	2008	Poultry	551,154	1,300,000	H5	83.3	n/a	
	2009	Poultry	548,100	1,350,000	H5	75.8	n/a	
	2010	Poultry	**e** 545,046	917,926	H5	82.0	n/a	
	Subtotal		**2,777,167**	**5,298,926**		**69.9**	**3,650**	4.65
France	2006	Meat & breeder ducks & breeder geese	832,049	816	H5	0.05	778	<0.01
Hong Kong	2002	Meat chickens	8,406	1,400	H5	11.1	n/a	
	2003	Meat chickens	10,154	10,400	H5	68.3	124,714	
	2004	Meat chickens	7,821	12,600	H5	107.4	125,000	
	2005	Meat chickens	11,676	18,600	H5	106.2	n/a	
	2006	Meat chickens	9,155	13,700	H5	99.8	148,333	
	2007	Meat chickens	7,273	10,500	H5	96.2	149,167	
	2008	Meat chickens	4,662	6,348	H5	90.8	n/a	
	2009	Meat chickens	3,510	5,793	H5	110.0	n/a	
	2010	Meat chickens	**e** 4,000	6,233	H5	103.9	n/a	
	Subtotal		**66,657**	**85,573**		**86.2**	**136,804**	0.08
Indonesia	2004		**e** 1,266,124	398,000	H5	15.7	2,370	
	2005		1,283,702	443,400	H5	17.3	n/a	
	2006		**e** 1,301,280	402,900	H5	15.5	2,518	
	2007		1,318,858	398,500	H5	15.1	2,703	
	2008		1,526,819	370,000	H5	12.1	n/a	
	2009		1,350,858	300,000	H5	11.1	n/a	
	2010		**e** 1,382,858	330,000	H5	11.9	n/a	
	Subtotal		**9,430,499**	**2,642,800**		**14.0**	**2,530**	2.32
Israel	2006	Ostriches	379,644	6[(f)]	H5	<0.01	8,470	<0.01
Kazakhstan	2006	Village poultry	58,823	7,000	H5	6.0	12.6	
	2007	Village poultry	67,678	7,000	H5	5.6	n/a	
	2008	Village poultry	62,061	7,000	H5	5.6	n/a	
	2009	Village poultry	73,402	7,000	H5	4.8	n/a	
	2010	Village poultry	78,262	7,000	H5	4.5	n/a	
	Subtotal		**335,226**	**35,000**		**5.2**	**12.6**	0.03

e: estimate based on surrounding years
DPR Korea: Democratic People's Republic of Korea
n/a: not available
a) Population data source: China, Indonesia, and the Netherlands (WAHID, Animal populations); Hong Kong, Mongolia and Russia (Chief Veterinary Officer staff); Côte d'Ivoire, Egypt, France, Israel, Kazakhstan, DPR Korea, Pakistan, Sudan and Vietnam (FAOSTAT); national poultry populations: low <25 million, moderate <250 million, high <2.5 billion, very high ≥2.5 billion
b) Data sourced from current survey questionnaire
c) National poultry density was based on information on poultry/agricultural land (km^2) available from FAO (kids.fao.org/glipha/). National poultry density: low <75, moderate <750, high <7,500, very high ≥7,500 birds/km^2

Table III (cont.)
Number of doses of H5 or H7 avian influenza vaccine used in poultry against high-pathogenicity avian influenza and the coverage rate for 15 countries from 2002 to 2010

Country	Year	Species	National poultry population (1,000s)[(a)]	Dose (1,000s)[(b)]	Subtype	Vaccine coverage (%)	Poultry density (birds/km² of agricultural land)[(c)]	Global usage (%)
DPR Korea[(g)]	2005	Chickens	55,550	2,202	H7	1.98	819	<0.01
Mongolia	2005	Chickens	142	357	H5	83.8	n/a	
	2006	Chickens	212	377	H5	59.3	0.1	
	2007	Chickens	295	475	H5	53.7	0.2	
	2008	Chickens	360	517	H5	47.9	n/a	
	2009	Chickens	399	661	H5	55.2	n/a	
	2010	Chickens	426	412	H5	32.2	n/a	
	Subtotal		**1,834**	**2,799**		**50.9**	**0.2**	<0.01
Netherlands	2006	Hobby poultry and free-range layers	92,584	32	H5	0.02	4,807	
	2007	Hobby poultry and free-range layers	92,763	21	H5	0.01	4,951	
	2008	Hobby poultry and free-range layers	95,129	15	H5	0.01	n/a	
	Subtotal		**280,476**	**68**		**0.01[(h)]**	**4,879**	<0.01
Pakistan	2004	Layers, broiler & layer breeders	434,940	12,100	H7	0.7	701	
	2005	Layers, broiler & layer breeders	443,383	14,100	H7	0.8	n/a	
	2006	Layers, broiler & layer breeders	534,603	21,400	H5/H7	1.0	871	
	2007	Layers, broiler & layer breeders	575,688	21,400	H5/H7	0.9	932	
	2008	Layers, broiler & layer breeders	618,809	21,400	H5/H7	0.9	n/a	
	2009	Layers, broiler & layer breeders	667,662	18,400	H5/H7	0.7	n/a	
	2010	Layers, broiler & layer breeders	**e** 716,515	23,400	H5/H7	0.8	n/a	
	Subtotal		**3,991,600**	**108,800**		**0.8**	**835**	0.12
Russia	2006	Poultry	**e** 372,581	107,000	H5	14.4	164	
	2007	Poultry	**e** 409,429	97,900	H5	12.0	171	
	2008	Poultry	**e** 449,922	82,000	H5	9.1	n/a	
	2009	Poultry	**e** 494,420	79,000	H5	8.0	n/a	
	2010	Poultry	543,319	59,427	H5	5.5	n/a	
	Subtotal		**2,269,671**	**425,327**		**9.4**	**168**	0.37
Sudan	2006	Broilers, layers & broiler & layer breeders	34,576	3,177	H5	4.6	27	
	2007	Broilers, layers, & broiler & layer breeders	36,150	3,149	H5	4.4	26	
	Subtotal		**70,726**	**6,326**		**4.5**	**27**	<0.01
Vietnam	2005	Chickens & ducks	322,590	244,500	H5	63.7	n/a	
	2006	Chickens & ducks	343,696	274,630	H5	67.9	2,129	
	2007	Chickens, ducks & geese	358,000	353,930	H5	75.2	2,243	
	2008	Chickens & ducks	419,100	268,000	H5	49.4	n/a	
	2009	Chickens & ducks	476,700	272,570	H5	42.2	n/a	
	2010	Chickens & ducks	**e** 534,300	212,880	H5	31.1	n/a	
	Subtotal		**2,454,386**	**1,626,510**		**52.3**	**2,186**	1.43
	Total		**131,099,262[(i)]**	**113,982,174[(i)]**		**41.9**		100.00

d) Reported in ml for inactivated avian influenza vaccine and by dose for recombinant vaccines; one dose was 0.5 ml for chickens and 1 ml for ducks and geese. Calculations for coverage rate were based on population distribution of ducks, geese and meat chickens (80%) and egg-type chickens (20%), with two doses for ducks, geese and meat chickens and three doses for egg-type chickens. One exception was Hong Kong where the native breed chicks are smaller than commercial chicks and received 0.25 ml as a first dose (half the manufacturer's recommended dose) and 0.5 ml as the second dose

e) Other Galliformes: quail, guinea fowl, pheasants, peacocks, grouse, etc.

f) 6,020 ostriches on one commercial farm were vaccinated with one dose per bird, 1 ml vaccine per dose

g) Autogenous avian influenza vaccine was used in chickens in DPR Korea against H7N7 high-pathogenicity avian influenza during 2005. Vaccine doses were estimated at two doses per bird and 1,101,000 birds were vaccinated (59). The poultry density was not available for 2005 and was estimated based on the average for the years 2004 and 2006

h) In 2006, 2007 and 2008, 0.27%, 0.14% and 0.07% of the 3 million national hobby poultry population were vaccinated, respectively, compared to <0.01% of the 90–92 million national commercial poultry population over the same period

i) World poultry production 2002–2010 = 520,030,922,000 birds; at-risk population = 25.2% of world poultry production; vaccinated proportion of world's poultry population = 10.9%. Of total vaccines used, 95.5% were inactivated H5 and/or H7 vaccines and 4.5% were live recombinant vaccines

Table IV
Number of doses of H5 and/or H7 vaccine used and vaccine coverage rates for specific poultry categories in Egypt, Pakistan and Vietnam based on available data (2004 to 2009)

Country	Years	Species	Poultry population (1,000s)[a]	Dose (1,000s)[b]	Vaccine coverage (%)
Egypt	2006–2009	Meat & breeder chickens	1,860,552	1,469,162	78.2
		Meat & breeder ducks	60,000	27,007	15.0
		Meat & breeder geese	40,000	1,686	1.4
		Meat & breeder turkeys	8,105	1,686	10.4
		Other meat poultry & breeders[c]	172,000	1,359	0.5
		Layers & layer breeders	91,464	86,715	31.6
		Subtotal	**2,232,121**	**1,587,615**	**67.0**
Pakistan	2004–2009	Broiler & layer breeders	54,000	55,800	25.8
		Layers	474,000	53,000	2.8
		Broilers	2,707,600	0	0.0
		Subtotal	**3,235,600**	**108,800**	**0.8**
Vietnam	2005–2009	Broilers	1,327,890	826,250	51.7
		Meat ducks	322,000	580,380	90.1
		Subtotal	**1,649,890**	**1,406,630**	**58.1**

a) Population data source: Egypt (FAOSTAT, Production, Livestock Primary); Pakistan (FAOSTAT, Production, Livestock Primary); Vietnam – data from current survey for broiler and layer breeders
b) Data sourced from current survey questionnaire
c) Other Galliformes: quail, guinea fowl, pheasants, peacocks, grouse, etc.

– sector 3: minimal-to-low biosecurity, smallholder, commercial, including waterfowl, and sold mainly through live markets

– sector 4: low-to-minimal biosecurity, mainly village and backyard production.

The ease with which a national poultry population can be vaccinated depends on the number of premises and the size of the population. The survey indicated that the more poultry in sectors 1 and 2, the higher the coverage rate, because there are fewer farms to organise for vaccination and, since all aspects of production are integrated, cooperation between management and the farmer is easier. By comparison, if there are more poultry within sectors 3 and 4, which have more premises and independent management systems, there tends to be a lower coverage rate. With both LPNAI and HPAI, most of the world's AI vaccine use occurs in developing and transition countries.

High-pathogenicity avian influenza vaccine use

Chickens, ducks, geese, turkeys and other poultry

Vaccination was first used against HPAI in Mexico during 1995, when 383 million doses of inactivated oil-emulsified vaccine, made from a 1994 precursor H5N2 LPNAI virus, were used (53). The combined use of the vaccine and other control measures were associated with the eradication of the H5N2 HPAI virus by mid-1995 and Mexico's declaration of freedom from HPAI in December 1995 (53). However, the predecessor H5N2 LPNAI virus has continued to circulate in central Mexico, resulting in the continued use of vaccines in the H5N2 LPNAI control programme (Table VI).

The second use of vaccine for HPAI control began in Pakistan in 1995, against H7N3 HPAI (35). This programme used a homologous inactivated HPAI virus in an aqueous vaccine, principally in broiler breeders. However, the greatest use of vaccine for HPAI control has been against the H5N1 HPAI panzootic that began with a first report in domestic geese from Guangdong, China, in 1996, was first detected outside China in 2001 in the live poultry markets of northern Vietnam, and caused large outbreaks in poultry in Indonesia and the Republic of Korea in 2003 (28, 36, 43, 60). After 2003, the H5N1 HPAI virus spread to infect poultry and wild birds in 63 countries on the Asian, African and European continents (16).

From 2002 to 2010, over 113 billion doses of AI vaccine were used in the at-risk poultry population of more than 131 billion birds to protect against H5 or H7 HPAI in 15 countries (Table III). Programmes initiating AI vaccination against the H5N1 panzootic began in 2002 in Hong Kong, 2004 in Indonesia and China, 2005 in the Democratic People's Republic of Korea (DPR Korea), Vietnam and Mongolia, and in 2006 in the nine remaining countries/regions (Table III). The years 2002 to 2005 were growth years for vaccine use, as AI vaccine-manufacturing capacity and inventories increased to meet demand, and vaccination logistics were developed to implement programmes in the field, especially in China (Table III) (Fig. 2). The yearly use of vaccine was at its highest from 2006 to 2009, at over 26 billion doses per year, when all 15 countries had fully implemented vaccine programmes (Fig. 2). The top four users of AI vaccine were China (90.99%), Egypt (4.65%), Indonesia (2.32%) and Vietnam

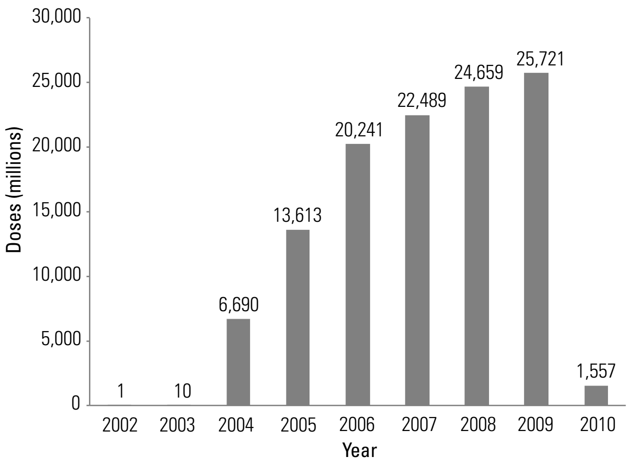

Fig. 2
Number of doses of avian influenza vaccine used between 2002 and 2010 against high-pathogenicity avian influenza
Data for China in 2010 were not available.

(1.43%), all of which had enzootic H5N1 HPAI infections in poultry. The remaining 11 countries had minor usage, accounting for less than 0.7% in total, as follows:
– Russia (0.37%)
– Pakistan (0.12%)
– Hong Kong (0.08%)
– Kazakhstan (0.03%)
– Côte d'Ivoire (<0.01%)
– DPR Korea (<0.01%)
– France (<0.01%)
– Israel (<0.01%)
– Mongolia (<0.01%)
– the Netherlands (<0.01%)
– Sudan (<0.01%).

The majority of vaccine (>99.5%) was used in the ten countries with a high (≥750 birds/km^2) to very high (≥7,500 birds/km^2) national poultry density, while less than 0.5% was used in the five countries with a moderate (<750 birds/km^2) to low (<75 birds/km^2) national poultry density.

Five countries/regions had routine AI vaccination programmes: China, Egypt, Hong Kong, Indonesia and Vietnam (Table III). These countries had high to very high national poultry densities (963; 3,650; 136,804; 2,530 and 2,186 birds/km^2, respectively) and low to very high national poultry populations (14.6–16.4 billion, 534–599 million, 3.5–11.7 million, 1.3–1.4 billion and 323–534 million birds, respectively).

Hong Kong had the highest vaccination coverage rate at more than 90.8%, after full implementation of its vaccination programme in 2004, but the numbers of poultry involved were quite small: 3.5 to 11.7 million per year, when compared to the production figures of other countries in Table III, excluding Mongolia. The calculated coverage rate exceeded 100% for four years because of variations in chick placements, the number of chicks sold on multi-age farms for long rearing periods with normal chick mortality and culling during grow-out, and wastage of vaccine in large dose bottles. Poultry in Hong Kong were raised by the small commercial systems of sector 3. Currently, only 30 registered farms are allowed to produce chickens for the live poultry market, with tight government control of the process. Hong Kong lacks the big commercial poultry systems of sectors 1 and 2, as well as the village or household poultry of sector 4. It is the only country/region whose mass vaccination policy approached 100% implementation in the field. In addition to vaccinated locally grown birds, vaccinated commercial live poultry were imported daily into Hong Kong from mainland China through a single wholesale market.

In the four countries that accounted for over 99% of vaccination use (China, Egypt, Indonesia and Vietnam) the peak vaccination coverage rate was 83.3% (Egypt in 2008) and the lowest rate was 11.1% (Indonesia in 2009) (Table III). Most of the production in all four of these countries takes place in sector 3 (small commercial farms) and sector 4 (village or backyard poultry), and both sectors have inherent logistical problems in applying any type of vaccine to such a large number of premises/households with low numbers of birds per premises. For example, surveys of vaccination coverage rates, based on H5 haemagglutination inhibition (HI) antibodies, showed vaccination rates of between 20% and 40% in sector 4 in Indonesia (33), and less than 20% in sector 4 in Egypt (21). By contrast, sectors 1 and 2 have a much higher vaccination compliance rate because fewer farms are involved, the owners are better educated on animal health issues and these sectors have the funds to implement economically oriented vaccination programmes, including hiring professional vaccination crews.

Interestingly, estimates of poultry production in developing countries vary significantly, especially for poultry produced on small farms (sector 3) and in the village/backyard (sector 4). For example, in Egypt, the vaccine coverage rates were based on a conservative 550 million poultry per year from FAOSTAT (15), but one domestic source (21) estimated poultry production of between 800 million and 1.4 billion birds per year, which suggests the average coverage rate would be much lower than the authors calculated; i.e. between 27.8% and 48.6%, instead of the 69.9% reported in Table III. In China, the annual H5 AI vaccine usage was the highest of all countries, with between 18.9 and 23.7 billion doses used per year from 2006 to 2009. This number was slightly below the semi-quantitative number of 25 billion doses produced for domestic use yearly (34), but double the previously published range of 11.5 to 13.2 billion doses per year (10).

From the survey, all the vaccines used have been inactivated AI vaccines, except in China, where 4.5% (5.1 billion) have been live recombinant fowl poxvirus (rFPV) vaccine with H5 and N1 AI gene inserts (rFPV-AIV-H5N1: 613 million doses) and recombinant Newcastle disease virus (rNDV) with H5 AI haemagglutinin gene inserts (rNDV-AIV-H5: 4.4 billion doses). A previous report listed recombinant vaccine usage in China between 2004 and 2008 at 5.7 billion doses (rFPV-AIV-H5N1 = 613 million; rNDV-AIV-H5 = 5.1 billion doses) (10). The reason for such discrepancies is not clear, but the numbers used in this study were based on the questionnaire from the OIE Delegate in China and were reported in ml for inactivated vaccine, which had to be converted into doses, based on the volume for a dose in each species, and the percentage of the species in the poultry population.

Some countries used a targeted AI vaccination approach in their emergency control programmes; Pakistan, for example, which has a high national poultry population (435 to 717 million/year) and a high national poultry density (835 birds/km^2), conducted ring vaccination around outbreaks, resulting in vaccination of 0.7% to 1.0% of poultry per year. Similarly, Russia, with a high national poultry population (373 to 543 million/year) and a moderate national poultry density (168 birds/km^2), targeted its vaccination at village (sector 4) and small commercial flocks (sector 3), primarily in Siberia and eastern Russia, resulting in vaccination coverage rates of between 5.5% and 14.4% of poultry per year (Table III). Pakistan has had cases of both H5 and H7 HPAI in poultry and, since 2006, has used a bivalent H5/H7 vaccine (58).

France and the Netherlands, which have high and moderate national poultry populations (832 million and 93–95 million birds/year, respectively) and high national poultry densities (778 and 4,879 birds/km^2, respectively), used a targeted preventive vaccination approach for poultry that could not be brought indoors during a high-risk period, i.e. when migratory waterfowl were dying of H5N1 HPAI in 2006. France vaccinated flocks of geese and ducks (816,000 doses, covering 0.05% of the national poultry population) during 2006 (Table III). The Netherlands vaccinated hobby poultry (26,000 doses) and free-range commercial layers (42,000 doses on eight farms) between 2006 and 2008 (Table III). The Netherlands programme resulted in vaccination of 0.01% to 0.02% of the national poultry population. However, the proportion of vaccinated birds from the national hobby population (0.27%, 0.14% and 0.07% of three million birds for 2006, 2007 and 2008, respectively) was slightly greater than the proportion of vaccinated birds from the national commercial poultry population (<0.01% of 90–92 million) (Table III). The use of vaccine was discontinued as the risk and interest decreased in France and the Netherlands. Israel vaccinated 6,020 ostriches on a commercial farm after outbreaks in galliform poultry during 2006, but no vaccination was conducted in chickens, turkeys, ducks or other poultry species (Table III) (59). The vaccinated ostriches were used for breeding or destroyed; none were slaughtered for food.

Côte d'Ivoire, Kazakhstan, Mongolia and Sudan were exceptions to the generalisation that AI vaccine was used mainly by countries with high national poultry populations (≥250 million) and/or high poultry densities (>750 birds/km^2) (Table III). Mongolia had a very small national poultry population (142,000 to 426,000 poultry/year) and low poultry density (0.1 to 0.2 birds/km^2), but chose to conduct a preventive vaccination programme in small commercial layer flocks and backyard poultry around three human population centres because of perceived transmission risks from the presence of H5N1 HPAI virus infections and deaths in migratory waterfowl. Mongolia has a very low population of village poultry: only 8% of rural households keep poultry. To date, Mongolia has not experienced H5N1 HPAI viral infections in poultry. Kazakhstan also conducted preventive vaccination in village poultry, beginning in two geographic regions in 2006, in response to deaths in wild birds caused by H5N1 HPAI virus, but has not experienced outbreaks in poultry. Côte d'Ivoire, DPR Korea and Sudan have moderate poultry populations (32, 55.6 and 35–36 million, respectively) and low-to-high poultry densities (158, 819 and 27 birds/km^2, respectively), but chose to conduct targeted emergency vaccination programmes following outbreaks of H7N7 HPAI during 2005 (DPR Korea) and H5N1 HPAI during 2006 (Côte d'Ivoire and Sudan). Côte d'Ivoire vaccinated sector 2 commercial and sector 4 village poultry while Sudan vaccinated 90% of sector 1 and 80% of sector 2 commercial farms, respectively. The Côte d'Ivoire programme ended in 2006. The Sudanese programme ended in December 2007, after vaccinating poultry on 99 farms and no additional HPAI cases in poultry for 15 months. The Democratic People's Republic of Korea had an outbreak of H7N7 in layers during 2005 and implemented an H7N7 AI vaccination programme, using an autogenous vaccine, with 1.1 million chickens being vaccinated (59).

Most countries did not provide a detailed breakdown of the types of birds in their poultry population, so it was not always possible to accurately determine what percentage of the various poultry species had been vaccinated. However, semi-quantitative data were available for some countries and these provided evidence of vaccination programmes being targeted towards particular types of poultry within a country. In Egypt, outbreaks have occurred in both commercial and village poultry, affecting mainly meat and egg-producing chickens (1). Using available estimates of poultry populations and their types between 2006 and 2009 (Table IV), the highest AI vaccine coverage rate was achieved in meat (78.2%) and layer (31.6%) chickens,

Table V
Number of doses of H5 or H7 avian influenza vaccine used in zoo, hunting, companion, conservation or endangered birds to protect against high-pathogenicity avian influenza viruses

Country	Year	Number of premises	Vaccine doses (number of birds vaccinated)	Subtype	References
Austria	2005–2006	2	596[a] (298)	H5	(13)
Belgium	2003	NR	NR	H7	(13)
	2005–2006	10	2,350[a] (1,175)	H5	Survey (13)
	2007	NR	900	H5	Survey
	2008	NR	300	H5	Survey
Denmark	2005–2006	12	2,170[a] (1,085)	H5	(13)
Egypt	2006	NR	30,000	H5	Survey
	2007	NR	30,000	H5	Survey
	2008	NR	31,000	H5	Survey
	2009	NR	31,000	H5	Survey
	2010	NR	31,000	H5	Survey
Estonia	2005–2006	1	520[a] (260)	H5	(13)
France	2005–2006	138	54,000[a] (27,000)	H5	(13, 27)
	2007–2009	NR	NR	H5	Survey
Germany	2003	NR	NR	H7	(13)
	2005–2006	32	NR	H5	(13)
	2007	10	NR	H5	Survey
	2008	4	NR	H5	Survey
	2009	5	NR	H5	Survey
Hong Kong		2	NR	H5	Survey
Hungary	2005–2006	8	2,782[a] (1,391)	H5	(13)
Ireland	2005–2006	2	426[a] (213)	H5	(13)
Israel	2006	NR	11,681 (11,681)	H5	Survey
Italy	2005–2006	4	1,850[a] (925)	H5	(13)
	2007	NR	6,000	H5	Survey
	2008	NR	1,000	H5	Survey
Kuwait	2007	NR	NR	H5	Survey
Netherlands	2003	NR	400	H7	Survey
	2004	NR	4,000	H7	Survey
	2005–2006	23	8,000 (6,444)	H7+H5	Survey
	2007	NR	4,000	H5+H7	Survey
	2008	NR	3,000	H5+H7	Survey
	2009	NR	2,000	H5+H7	Survey
Portugal	2005–2006	2	400 (197)	H5	Survey (13)
	2006	NR	200		Survey
Singapore	2005	1	179 (118)	H5	(38)
Spain	2005–2006	21	9,680[a] (4,840)	H5	(13)
Sweden	2005–2006	9	1,284[a] (642)	H5	(13)
Switzerland	2005–2006	4	730[a] (365)	H5	(19)
United Arab Emirates	2006–2007	2	242[a] (121)	H5	(37)
Total		**292**	**271,690**		

NR: not reported
a) Estimate based on two doses per bird reported

while meat ducks had 15%, turkeys 10.4% and other poultry had less than 1.4% coverage rates (Table IV). By contrast, Pakistan has mainly focused its vaccination programme on long-lived poultry, i.e. breeders and layers (35). The highest AI vaccine coverage rate was in broiler and layer breeders (25.8%). There was low coverage (2.8%) among layers and no AI vaccine use at all among broilers (Table IV). Finally, Vietnam had higher AI vaccine

Table VI
Number of doses of H5 or H7 avian influenza vaccine used in poultry against low-pathogenicity notifiable avian influenza and coverage rate for individual countries from 2002 to 2010

Country	Year	Species	National poultry population (1,000s)[(a)]	Dose (1,000s)[(b)]	Subtype	Vaccine coverage (%)	Poultry density (birds/km² of agricultural land)[(c)]	Global use (%)
El Salvador	2002	Chickens	53,700	64,865	H5	60.4	n/a	
	2003	Chickens	53,068	68,680	H5	64.7	812	
	2004	Chickens	62,980	66,278	H5	52.6	789	
	2005	Chickens	77,495	70,297	H5	45.4	n/a	
	2006	Chickens	79,606	81,710	H5	51.3	888	
	2007	Chickens	83,655	81,106	H5	48.5	948	
	2008	Chickens	75,600	64,150	H5	42.4	n/a	
	2009	Chickens	76,566	68,238	H5	44.6	n/a	
	2010	Chickens	**e** 77,532	73,890	H5	47.7	n/a	
	Subtotal		**640,202**	**639,214**		**49.9**	**859**	1.95
Guatemala[(d)]	2002	Chickens	92,500	**e** 47,327	H5	25.6	n/a	
	2003	Chickens	88,310	**e** 57,327	H5	32.5	644	
	2004	Chickens	88,792	**e** 109,902	H5	61.9	681	
	2005	Chickens	88,955	120,795	H5	67.9	n/a	
	2006	Chickens	100,256	**e** 122,587	H5	61.1	859	
	2007	Chickens	89,360	123,729	H5	69.2	704	
	2008	Chickens	88,500	111,933	H5	63.2	n/a	
	2009	Chickens	88,503	131,798	H5	74.5	n/a	
	2010	Chickens	**e** 88,506	**e** 120,267	H5	67.9	n/a	
	Subtotal		**813,682**	**898,338**		**55.2**	**722**	6.33
Italy	2002	Poultry	574,279	7,849	H7	0.7	n/a	
	2003	Poultry	499,919	75,434	H7	7.5	839	
	2004	Poultry	512,340	51,047	H7 & H5/H7	5.0	839	
	2005	Poultry	505,725	36,162	H5/H7	3.6	n/a	
	2006	Poultry	462,720	12,313	H5/H7	1.3	845	
	2007	Poultry	529,891	10,625	H7 & H5/H7	1.0	900	
	2008	Poultry	**e** 562,455	3,905	H7 & H5/H7	0.4	n/a	
	Subtotal		**3,647,329**	**197,335**		**2.7**	**856**	9.36
Mexico[(e)]	2002	Chickens	1,389,182	**e** 938,492	H5	33.8	n/a	
	2003	Chickens	1,406,663	**e** 933,027	H5	33.2	397	
	2004	Chickens	1,492,904	**e** 927,594	H5	31.1	414	
	2005	Chickens	1,579,522	874,080	H5	27.7	n/a	
	2006	Chickens	1,631,009	837,854	H5	25.7	463	
	2007	Chickens	1,676,140	1,121,265	H5	33.5	477	
	2008	Chickens	1,715,640	820,335	H5	23.9	n/a	
	2009	Chickens	1,747,220	1,106,793	H5	31.7	n/a	
	2010	Chickens	**e** 1,778,800	755,792	H5	21.2	n/a	
	Subtotal		**14,417,080**	**8,315,232**		**28.8**	**438**	82.28

e = estimated
a) Population data source: FAOSTAT
b) Data sourced from current survey questionnaire
c) National poultry density was based on information about stocks of poultry/agricultural land (km^2) obtained from FAO (available at: kids.fao.org/glipha/)
d) Estimates of inactivated vaccine doses for 2002, 2003, 2004, 2006 and 2010 were based on the average for 2005 and 2007–2009; and combined with recombinant vaccine data
e) 2002–2004 vaccine doses were estimated from exponential regression analysis based on data from 2005 to 2010
f) Breeder mallards whose offspring are used for hunting release; national poultry population for 2007
g) National poultry density (2007)
h) 5.76 billion doses of inactivated vaccine (57%), and 4.35 billion doses of recombinant fowl poxvirus containing an H5 haemagglutinin gene insert from A/turkey/Ireland/1983 (43%)

Table VI (cont.)
Number of doses of H5 or H7 avian influenza vaccine used in poultry against low-pathogenicity notifiable avian influenza and coverage rate for individual countries from 2002 to 2010

Country	Year	Species	National poultry population (1,000s)[(a)]	Dose (1,000s)[(b)]	Subtype	Vaccine coverage (%)	Poultry density (birds/km² of agricultural land)[(c)]	Global use (%)
Portugal	2008	Mallard breeders[(f)]	205,444	9	H5	<0.01	n/a	
	2009	Mallard breeders	207,386	9	H5	<0.01	n/a	
	2010	Mallard breeders	**e** 209,328	9	H5	<0.01	n/a	
	Subtotal		**622,158**	**27**		**<0.01**	**1,273[(g)]**	<0.01
United States	2003	Layers	9,315,812	4,200	H7	0.02	527	
	2004	Layers	9,518,525	4,200	H7	0.02	544	
	Subtotal		**18,834,337**	**8,400**		**0.02**	**536**	0.08
	Total		**34,593,539**	**10,058,546**				

coverage rates in meat ducks (>90%) than in meat chickens (51.7%) (Table IV). With domestic ducks playing an important role as an asymptomatic reservoir of H5N1 HPAI virus in Vietnam (20), a higher vaccination rate in domestic ducks would assist in reducing environmental contamination with the H5N1 virus, resulting in a lower exposure and outbreak rate in galliform poultry.

Zoo, hunting, companion, conservation and endangered birds

No AI vaccines have been specifically licensed for zoo, hunting, companion, conservation or endangered species of birds, but H5 and H7 AI vaccines licensed for chickens are available and have been used in AI preventive vaccination programmes for non-poultry species. Such poultry AI vaccines were safe, producing only minor swellings at the injection sites of a few birds (41). However, the stress of catching and handling the birds for vaccination and blood sampling resulted in low mortality rates in some species (13).

From 2002 to 2010, a total of 20 countries used 271,690 doses of H5 or H7 AI vaccine in zoo, hunting, companion, conservation and endangered species of birds on over 292 premises (Table V), representing 0.000003% of the total number of AI vaccine doses used in birds (Table III). The largest vaccination programme of zoo and bird collections occurred in the EU. Seventeen countries were approved by the European Commission for preventive vaccination programmes against H5N1 HPAI among birds held in zoos and by other approved bodies, institutes and centres of Member States (13, 14). From 2005 to 2006, the programme was implemented in 13 Member States, with the use of five different H5N2 (A/duck/Potsdam/1402/86 and A/chicken/Mexico/232/94/CPA) or H5N9 (A/turkey/Wisconsin/68 and A/chicken/Italy/221/1998 [*n* = 2]) oil-emulsified inactivated vaccines, developed and licensed for chickens and turkeys (13). In these 13 countries, 44,721 birds were vaccinated between 2005 and 2006, representing 374 species and 19 taxonomic orders (13). Fifty percent of the birds seroconverted after a single vaccination and 82% after the second vaccination, as determined by HI titres ≥16 (13). Sero conversion rates varied with the species, family and order of birds, as well as the individual study country, but, in general, a booster vaccination significantly increased the serological titres, based on the HI test. Although challenge testing was not undertaken, the HI titres suggested protection rates of 71% (27), 80% (40), 82% (41), 84% (2, 38), 94% (37) and 96% to 100% (19) after a two-dose regime, depending on the species and assuming an HI protective titre of ≥16, ≥32 or ≥40. Birds from the orders Anseriformes, Ciconiformes, Falconiformes, Galliformes, Phoenicopteriformes and Psittaciformes had seroconversion rates of ≥82% after one immunisation (13). However, typically six months after vaccination, titres began to decrease, suggesting the need for an annual booster (13, 19). In addition to the EU programme, vaccination of zoo or captive-held non-poultry birds was conducted in Egypt and Israel (data from current survey), Hong Kong (current survey), Kuwait (current survey), Singapore (38), Switzerland ([19], current survey), and the United Arab Emirates (37). Furthermore, H7 vaccination programmes were used in zoos in Belgium, Germany and the Netherlands, after the 2003 H7N7 HPAI outbreaks in poultry (13).

In most zoos, an AI vaccination programme against H5N1 was not implemented as the principal method of protection from HPAI. The first line of defence was based on biosecurity measures (such as indoor housing, sanitation and hygiene programmes, the addition of netting to separate bird collections housed outdoors from wild birds, and isolation and quarantine facilities), veterinary care to ensure early detection of disease and screening birds before their entry into the collections (13).

Vaccination is not the cause of enzootic high-pathogenicity avian influenza virus infections

The authors would be cautious about suggesting that AI vaccine usage has resulted in enzootic infections. Multiple factors are associated with enzootic HPAI virus infections. Eleven countries/regions have used AI vaccine in poultry without the HPAI virus becoming enzootic:

– Côte d'Ivoire
– France
– Hong Kong
– Israel
– Kazakhstan
– Mongolia
– the Netherlands
– DPR Korea
– Pakistan
– Russia
– Sudan.

Côte d'Ivoire and Sudan used emergency AI vaccination in poultry, along with other measures in their comprehensive AI control programmes, after the H5N1 HPAI outbreaks occurred. This combination of control measures resulted in elimination of the virus and the discontinuation of vaccination after three months (for Côte d'Ivoire) and 16 months (for Sudan) (59) (data from current survey). The Netherlands and France conducted preventive targeted vaccination for outdoor-reared poultry that could not be brought indoors after cases of H5N1 occurred among wild birds in Europe in 2006. France had a single case of H5N1 HPAI in a turkey flock before the vaccination programme began. Neither France nor the Netherlands recorded cases of H5N1 HPAI in poultry during the vaccination programme. The programme was discontinued in France after 2006 and in the Netherlands after 2008 (Table III).

Kazakhstan and Mongolia conducted preventive vaccination programmes in poultry in response to H5N1 infections and deaths in wild birds in both countries. Mongolia's AI vaccination programme was implemented in 2005 and is scheduled to be discontinued in 2011, while Kazakhstan used vaccine throughout 2011 (Table III) (data from current survey). No cases of H5N1 HPAI have been reported in poultry, either from Kazakhstan or Mongolia (59). Israel only vaccinated a single ostrich flock in 2006 and H5N1 outbreaks were eradicated, based on a stamping-out programme in poultry. The eradication was confirmed by surveillance data.

Hong Kong implemented a routine national AI vaccination programme beginning in 2002, with full implementation by late 2003 (data from current survey). Extensive surveillance identified the H5N1 HPAI virus in dead wild birds from 2002 to 2010, but only one infected vaccinated poultry flock was identified during that period (2008) (59). The Democratic People's Republic of Korea had a single disease event on three farms in 2005 and eradication was achieved (59). Vaccine was used only during 2005, with no recurrence in 2006 or later years (59). Russia had 117 outbreaks in 2005, 93 in 2006, 23 in 2007 and one in 2008. It began a vaccination programme in 2006, and no poultry cases were reported between 2009 and 2011 (59). Pakistan had outbreaks of H7N3 HPAI during 2003 and 2004, and H5N1 in 2006 (14 outbreaks), 2007 (32 outbreaks) and 2008 (seven outbreaks), but no cases between 2009 and 2011 (59). Pakistan vaccinated poultry against H7N3 in 2004 and 2005, and against both H5N1 and H7N3 from 2005 to 2010 (data from current survey).

At present, there are four countries with enzootic H5N1 HPAI clinical disease in poultry (Bangladesh, Egypt, Vietnam and Indonesia). Two countries (China and eastern India) have recurring reports of H5N1 infections, especially in domestic ducks and poultry in the live poultry markets of China (9, 12, 22, 23, 29, 54, 59). Bangladesh had its first outbreak of H5N1 HPAI on 5 February 2007. It has not used vaccine in its control programme but has focused on targeted stamping out and other measures for individual outbreaks (59). Outbreaks of H5N1 HPAI were first reported in Egypt on 17 February 2006 and 343 outbreaks occurred all over the country before a nationwide vaccination programme was begun, one month after the first official report of the outbreaks. However, the full vaccination programme was not immediately implemented because of lack of vaccine-manufacturing facilities within Egypt and logistics delays in importing sufficient vaccine doses (18). Over 573 outbreaks occurred within the first five weeks after the first official reported outbreak. During those weeks, less than 1% of the poultry population had been vaccinated (7, 18). In Indonesia, the first cases occurred in July 2003, but the government AI vaccination programme was not established until June 2004 (43). By June, over 312 outbreaks had occurred, with over 10.9 million poultry deaths (57). Vietnam had its first three outbreaks in poultry during December 2003, followed by 1,747 outbreaks in 2004 (57). By the end of 2004, 24% of communes and 60% of towns had reported cases of HPAI in poultry and 17% of the poultry population had died as a result of infection or culling. The vaccination programme was implemented in Vietnam during October 2005 (44). In China, the first outbreak occurred on a small goose farm in Guangdong during 1996 (60). Infections were identified in domestic ducks from five eastern provinces between 1999 and 2002 (11). In the first two months of 2004, there were 48 H5N1 outbreaks across 16 provinces, extending from the eastern province of Zhejiang to the remote western province of Xinjiang; from the southern provinces of Guangxi and Guangdong to the northern province of Jilin (57). These geographically widespread outbreaks occurred during the eight years preceding the implementation of a vaccination programme in mid-2004. These data support the idea that enzootic H5N1 HPAI virus infections became established among poultry in China, Egypt, Indonesia and Vietnam before the implementation of official vaccination programmes.

Low-pathogenicity avian influenza vaccine usage

Between 2002 and 2010, the total number of vaccine doses used in poultry against H5 and H7 LPNAI was much smaller (10.1 billion, 8.1%) than that used for HPAI (>113 billion, 91.9%) (Tables III & VI). Vaccine was used in six countries with average national poultry densities ranging from 536 to 1,273 birds/km^2 (Table VI). The majority of vaccines used were oil-emulsified inactivated vaccines (5.76 billion doses, 57%), but a large amount of rFPV with an H5 haemagglutinin gene insert was also used (4.35 billion doses, 43%).

The top user was Mexico (82.28%), which has continued H5N2 vaccine use in broilers, broiler breeders, layers and layer breeders to control H5N1 LPNAI after eliminating H5N2 HPAI in 1995 (Table VI). In addition, H5N2 vaccine was used in El Salvador and Guatemala after H5N2 LPNAI outbreaks began there in 2001 and 2000, respectively, making them the third- (1.95%) and second- (6.33%) highest users of vaccine against LPNAI, respectively (45). All three countries used inactivated H5N2 vaccine, made from a 1994 H5N2 LPNAI field virus from an early Mexican H5N1 LPNAI outbreak. Since 1998, Mexico has used an rFPV vaccine with a haemagglutinin gene insert from A/turkey/Ireland/83 (H5N8).

The fourth-highest user of vaccine against LPNAI was Italy, which has a high national poultry density (856 birds/km^2) (Table VI). The Po Valley of north-eastern Italy, where the outbreaks occurred, raises 70% of Italy's meat turkeys (8). The regions of Veneto and Lombardy have 45 million poultry on 4,760 km^2 of land, making a densely populated poultry area of 9,500 birds/km^2 (31). Multiple incursions of H5 and H7 LPNAI have occurred, from 2002 to 2003 (H7N3), from 2004 to 2005 (H5N2 and H7N3), and from 2006 to 2011 (H7N3) (4, 8, 31) (data from current survey). Italy reported the use of 197 million doses of inactivated H7 or bivalent H5/H7 between 2002 and 2008 in northern Italy (Table VI). The vaccination programmes were targeted in two ways:

– geographically, at northern Italy

– at the most susceptible poultry species, primarily meat turkeys and some layers, along with vaccination of minimal numbers of cockerels and capons (32).

Previous studies have demonstrated that turkeys are more susceptible than chickens to the H7N2 LPNAI virus, which caused outbreaks in Virginia, West Virginia and North Carolina during 2002 (51). In addition, turkeys were more susceptible than chickens to infection by wild-bird LPAI viruses (49). Vaccinating turkeys increases their resistance to LPNAI virus infection: a vaccinated turkey requires at least $2\log_{10}$ greater exposure to the virus than a non-vaccinated turkey (5). According to the survey, on a national poultry population basis, only 2.71% of the poultry in Italy were vaccinated. However, when examining specific types of poultry, peak vaccine usage was in 2003, when meat turkeys had a coverage rate of 84%, layers 23% and meat chickens 0.23% (Table VII). The vaccine was used only in sectors 1 and 2 poultry, where the infections were focused, although, in the later outbreaks of 2006 to 2008, asymptomatic infections in village poultry were identified but AI vaccine was not used (4). The questionnaire indicated that vaccination ended in 2008 because of improvements in poultry management between 2000 and 2008, including:

– better biosecurity

– all-in, all-out rearing of turkeys in 'micro-areas'

– separate rearing of male and female turkeys, to eliminate partial load-out marketing of female turkeys at 19 weeks, while leaving males until 24 weeks.

As various other control measures were implemented, the need for vaccination decreased, as shown by the yearly decline in vaccine use between 2003 and 2008, and its complete cessation in mid-2008 (Table VII). Italy also developed and implemented a heterologous neuraminidase AI vaccine to allow differentiation of infected poultry in the vaccinated population, i.e. 'differentiation of infected from vaccinated animals' (DIVA) (6).

Since 1978, the USA has used targeted vaccination in Minnesota turkeys against various subtypes of LPAI viruses, including some H5 and H7 LPNAI epizootics (25). From 1979 to 2000, 22.7 million doses of LPAI vaccine were used to control 108 epizootics, of which 20 were due to H5 or H7 subtypes (24). Over time, as the industry learned the limitations of vaccination and as rearing moved from outdoors to indoors by 1998, AI vaccine use declined to minimal then to no use (25). By contrast, from 2004 to 2010, 13.4 million doses of bivalent H1N1 and H3N4 vaccines were used in turkey breeders as targeted vaccination to control the drops in egg production induced by swine influenza virus (D. Lauer, personal communication, 2011). In this present survey for LPNAI, the USA reported using H7 AI vaccine in only a single commercial enterprise, producing layers, in a low-density poultry state (261 birds/km^2) in 2003 and 2004. This, along with enhanced biosecurity measures and marketing changes, resulted in the eradication of the virus. Vaccine coverage was low, based on the national poultry population (i.e. 0.02% for all poultry and 0.62% for the national layer/pullet population) (Table VII). However, since the vaccination was targeted at a single, large, layer company in Connecticut, the coverage rate was actually 56% of the state's chicken inventory. Based on global usage,

Table VII
Variation in vaccination of different poultry types within a country against low-pathogenicity notifiable avian influenza during 2002 to 2010

Country	Year	Species	National poultry population (1,000s)[a]	Vaccine dose (1,000s)[b]	Vaccine coverage rate (%)
Italy	2003	Meat chickens	1,061	1,061	0.23
	2004		1,261	1,261	0.31
	2002	Layers	5,831	5,831	4.92
	2003		26,830	26,830	22.85
	2004		13,263	13,263	11.33
	2005		7,577	7,577	6.55
	2006		3,959	3,959	3.57
	2007		6,194	6,194	5.34
	2008		1,070	1,070	0.89
	2002	Meat turkeys	2,018	2,018	2.24
	2003		47,242	47,242	84.05
	2004		36,171	36,171	64.35
	2005		28,318	28,318	47.80
	2006		8,202	8,202	15.30
	2007		4,425	4,425	7.98
	2008		2,835	2,835	4.73
United States	2003	Layers	339,300	4,200	0.62[c]
	2004		342,500	4,200	0.61[c]

a) Population data source: FAOSTAT
b) Data sourced from current survey questionnaire
c) 56% vaccination coverage rate based on Connecticut state chicken inventory (available at: www.nass.usda.gov/Publications/Ag_Statistics/2005/05_ch8.PDF, Table 8-44. 3,745,000 chickens for 2003)

this was 0.08% of the vaccine used for LPNAI between 2002 and 2010. The programme used two different DIVA strategies:

– virological testing of mortality cases from non-vaccinated sentinel and vaccinated layers
– serology in non-vaccinated sentinel birds (52).

A similar targeted vaccination programme was used in 1995 in a single turkey production company in the Moroni Valley, Utah (17). The programme used two million doses of inactivated H7N3 vaccine over a four-month period.

Portugal experienced an outbreak of H5N2 LPNAI in a single game-bird holding of mallard ducks (*Anas platyrhynchus*) during September 2007, controlling it through depopulation of infected, outdoor-reared ducks. The unique genetics of the mallard strain were preserved through vaccinating the indoor-reared breeder ducks and monitoring for infection in non-vaccinated sentinel ducks. The progeny were not vaccinated, and were used for restocking wild game populations.

H5 and H7 AI vaccines have not been used in zoological or other collections of non-poultry birds to protect against LPNAI viruses. The lack of morbidity and mortality from infections by LPNAI viruses in non-poultry species makes the benefit of any vaccination questionable.

Vaccination protocols

Fourteen countries provided the vaccination protocols used in their campaigns. For the most part, two vaccinations were used across all poultry types, including meat ducks and geese, but three vaccinations were typical for chicken and duck layers and breeders, with semi-annual or yearly boosters. One country used four vaccinations in chicken layers and breeders before 20 weeks of age. Some countries vaccinated broilers with their first vaccination at seven to ten days and a booster at three to four weeks. However, two countries used only a single vaccination in broilers. One country used three vaccinations in ducks, turkeys, guinea fowl and larger poultry.

Post-vaccination strategies

Thirteen countries conducted post-vaccination surveillance, by serological assay, to assess field protection. The most common test was the HI test, using a minimum protective titre of 1:16 (in five countries), 1:32 (in one country), 1:64 (in one country) and 1:128 (in two countries). Two countries used the enzyme-linked immunosorbent assay to determine immunity status.

Identification of infected birds in vaccinated populations

Thirty countries responded to the question about identifying infected birds within a vaccinated population. Sixteen of these countries (53%) had a strategy to distinguish infected birds from vaccinated birds (i.e. a DIVA strategy). Fourteen of these 16 countries (88%) used non-vaccinated sentinels and clinical observation (14%), virological testing (50%) and/or serological testing (79%), ranging from every two weeks to four times per year. Seven (50%) countries employed heterologous neuraminidase vaccines and serological testing for anti-neuraminidase antibodies against the field virus in vaccinated birds, using a neuraminidase inhibition test or immunological detection of anti-neuraminidase antibody. Thirteen (93%) conducted examinations for the field virus in vaccinated birds by virus isolation (33%) and/or detection of the H5 or H7 genome (67%), through real-time reverse transcription polymerase chain reaction assay.

Vaccine licensing and registration

Twenty of 69 (29%) countries have licensed AI vaccines. Eight (12%) countries manufactured their vaccines, 12 (17%) countries imported them and two (3%) countries did both. All 20 countries required a challenge test for licensure or registration. The vaccine licence was most frequently valid for either five years (n = 8; 40%) or one year (n = 7; 35%), but three (15%) countries had no expiration date, one had a three-year licence (5%) and one did not respond (5%). A process was in place to allow the updating of vaccine seed strains in 14 (70%) countries. Most countries released each vaccine batch based on sterility, safety, stability and immunogenicity potency tests, but one country required a challenge test to release each vaccine batch. Eighteen countries have a regulatory method to license or register live recombinant (vectored) vaccines for AI, but only six have licensed such vaccines (Canada, China, France, Mexico, the USA and Vietnam).

Exit strategy

Twenty-eight countries replied to the question on exit strategies, 18 of which (64%) responded that they had an exit strategy from vaccine use. The exit strategy varied: some countries have a specific predetermined date for the cessation of vaccination (Pakistan: 2011; Mexico: 2013; Vietnam: 2015), while others carry out surveillance and wait until risk assessment data indicates that infection is absent, e.g. no infections in the previous six to three months. However, exit strategies in HPAI-enzootic countries have proved difficult to implement.

Conclusions

Between 1959 and 2010, 24 of 29 HPAI disease events were eradicated, primarily by comprehensive control programmes that included stamping out of infected and suspected to be infected poultry. In four of the 29 HPAI disease events, countries used vaccine as a component of their control programme to maintain poultry production by preventing poultry morbidity and mortality, reducing infection and virus shedding, buying time to re-organise their poultry production and maintaining rural livelihoods.

A survey of the OIE Delegates of 69 countries that had experienced HPAI and/or LPNAI outbreaks between 2002 and 2010, demonstrated that each country had a national AI control programme with common components, such as: rapid diagnostics/early detection, active and passive surveillance of poultry and wild birds, quarantine and movement restrictions, tracing of poultry in outbreak areas, enhanced biosecurity measures, farmer and public education on AI, monitoring, eliminating positive poultry, disinfection of facilities and equipment, decontamination and disposal of infectious materials, and compensation. Although the components were similar between countries, the variability in the number of outbreaks and time until eradication suggest that individual countries varied significantly in the quantitative implementation and practice of each component.

The first vaccine usage for HPAI control occurred during 1995 in Mexico (H5N2) and Pakistan (H7N3), but widespread use was not seen until 2004, with the H5N1 HPAI panzootic of Asia, Europe and Africa. Major conclusions from the survey covering 2002 to 2010 included the following.

– The majority of countries had an option for AI vaccination in their HPAI control plans, but fewer countries had an AI vaccination option in their H5 and H7 LPNAI control plans.

– Over half of the countries had written vaccination plans, but only a small number had completed simulation exercises or worked out the logistics of implementing a vaccination programme and/or an exit strategy.

– One-third of the countries had used vaccines for HPAI control, while only one-sixth had used vaccines to control H5 and H7 LPNAI or non-H5/H7 LPAI (mainly H9N2 LPAI).

– To provide vaccine for emergency use, only 13 countries had developed H5 and/or H7 national AI vaccine banks, with eight countries receiving help from donors through international and national donor organisations.

– The most common reasons for not using AI vaccines included:

i) traditional control measures, including stamping out, were effective in eradication campaigns *ii)* AI vaccines and vaccination were perceived to have certain negative consequences, such as the potential for silent infections and subclinical shedding of AI virus, and the imposition of trade restrictions on poultry products by importing countries.

– The most common reasons for using AI vaccines included:

i) traditional control methods failed to control or eradicate the infection

ii) the outbreaks were large with a high risk of spread

iii) AI vaccination was perceived to have certain positive consequences, such as a decrease in susceptibility to infection, a decrease in virus shedding and the prevention of clinical disease and mortality.

– The majority of countries used AI vaccine as an emergency measure, with half of these using AI vaccine as preventive or routine measure.

– More than 113 billion doses of AI vaccine were used in the at-risk poultry population of >131 billion birds in 15 countries, to protect against HPAI, from 2002 to 2010.

– Most countries did not achieve a 100% AI vaccine coverage rate in their poultry population because of the limited availability of the vaccine and the complex logistics of vaccination, especially in countries with large poultry populations in the village/household and small farm sectors. This suggests that a more targeted vaccination approach would be more realistic and successful.

– The majority of AI vaccine was used in four countries with enzootic H5N1 HPAI virus infections and mass vaccination programmes: China (90.99%), Egypt (4.65%), Indonesia (2.32%) and Vietnam (1.43%). The remaining 11 countries used a more targeted vaccination approach with minimal usage; i.e. accounting for less than 1% of the total AI vaccine use.

– More countries used AI vaccine in non-poultry birds in zoos and other collections than in poultry species, but the overall number of doses used in non-poultry species was very low, representing less than 0.000003% of the total.

– Employing the AI vaccine did not lead to enzootic HPAI virus infections, since:

i) three countries used H5 or H7 AI vaccine and did not have HPAI in their poultry

ii) eight countries used AI vaccines and eradicated HPAI virus infections

iii) China, Egypt, Indonesia and Vietnam had enzootic or recurring H5N1 HPAI before vaccination commenced

iv) Bangladesh and eastern India have not used AI vaccine and have enzootic or recurring H5N1 HPAI.

– The total vaccine use against H5/H7 LPNAI was low: 8.1% of total vaccine usage (compared to more than 91.9% against HPAI). Most of the vaccine against LPNAI was used in Central America and Italy. Vaccine usage in Italy against LPNAI has been eliminated as improvements have been made in managing and rearing poultry.

– The most consistent vaccination protocols used two vaccinations for meat birds and three to four vaccinations for breeder and layer birds. The use of a single vaccination for short-lived broilers and meat ducks did not provide consistent immunity and protection, especially in the presence of maternal antibodies.

– The HI test was most commonly used for field assessment of post-vaccination immunity, with the minimum protective titre being 1:16 to 1:128.

– Infected birds in the vaccinated population were identified using a variety of test methods, including:

i) clinical, serological and virological assessment of non-vaccinated sentinels (88%)

ii) heterologous neuraminidase vaccines and serological testing for anti-neuraminidase antibodies against the field virus in vaccinated birds (50%)

iii) examination of vaccinated birds for the field virus (80%).

– Twenty countries have licensed AI vaccines, including six countries which have licensed live recombinant vaccines. In all 20 countries a challenge test is required to demonstrate efficacy. Some licences were issued for as little as one year and others had no expiration date. The manufacturing base for AI vaccines was small with only eight countries manufacturing vaccines, while the other countries relied on importation.

– Most countries had an exit strategy for ending the use of AI vaccine. Some countries have a projected cessation date, such as 2011 (Pakistan), 2013 (Mexico) or 2015 (Vietnam); other countries use risk assessment data and only stop vaccinating when surveillance indicates that infection has been absent for a certain period, e.g. three to six months. In countries with enzootic HPAI and LPNAI, developing and implementing exit strategies has proved difficult.

– Problems in vaccine and vaccination control strategies have involved both vaccine efficacy and vaccination effectiveness. Vaccine quality and efficacy have improved tremendously over the past seven years. There is evidence of antigenic drift of H5N1 HPAI viruses in the field, and some evidence of failure to protect by classic H5 vaccines, but recent designer, reverse genetic vaccines have provided optimal protection against emerging variant field strains. Most field vaccination failures have been the result of improper or suboptimal application of vaccines.

Recommendations

Several recommendations for more effective HPAI and LPNAI control programmes can be made:

– Stamping-out programmes are preferred for HPAI and LPNAI control and eradication.

– Vaccination can be an effective adjunct component under defined conditions:

i) as a preventive measure when there is a high risk of the introduction of HPAI and/or LPNAI into a country

ii) as an emergency measure following the introduction of HPAI or LPNAI, when stamping-out programmes are not effective in getting ahead of the spread

iii) as a routine measure when enzootic infection exists.

– Emergency AI vaccination programmes need advanced planning, plans and logistics should be practised in the field, and vaccine banks should be developed and used effectively.

– Preventive AI vaccination can be improved with advanced planning, but is not as time-sensitive as emergency AI vaccination programmes.

– Routine AI vaccination programmes can be used to maintain rural livelihoods and food security, and to reduce human exposure and infections, but they are logistically difficult to implement, unlikely to successfully vaccinate all poultry, and expensive to sustain, with low potential for effective HPAI elimination.

– AI vaccines can be used in preventive or emergency programmes to protect zoo birds, endangered species and other valuable, non-poultry species to maintain biodiversity, and such vaccine use should not prevent trade in poultry and poultry products.

– All vaccination programmes should include statistically valid, post-vaccination immunity studies at the flock and within-flock levels to assess the success of the programme.

– As the AI outbreak matures, and epidemiological data become available, routine vaccination programmes should be updated to become risk-based, with resources being focused on the populations and reservoirs at highest risk.

– An exit strategy is crucial in any country using AI vaccination and should be developed based on specific field conditions, while resources should be redirected to high-risk conditions/populations, with a risk-based, phase-out strategy.

– There is no one AI control solution for all countries; each AI strategy must be specific to the country and production sectors concerned.

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– OIE staff in Headquarters and Regional and Sub-Regional Representations for technical, logistic and other support.

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Évaluation des stratégies nationales de lutte contre l'influenza aviaire hautement pathogène et l'influenza aviaire faiblement pathogène à déclaration obligatoire chez les volailles, et plus particulièrement du recours aux vaccins et à la vaccination

D.E. Swayne, G. Pavade, K. Hamilton, B. Vallat & K. Miyagishima

Résumé

Depuis 1959, le monde a connu 29 épizooties distinctes d'influenza aviaire hautement pathogène (IAHP). Parmi elles, la plus importante a été la panzootie d'IAHP due au virus H5N1 et survenue en Asie, en Afrique et en Europe de l'Est, qui a affecté les volailles et/ou l'avifaune de 63 pays. Si les programmes d'abattage sanitaire ont réussi à éradiquer 24 de ces épizooties (et sont en voie d'éradiquer l'épizootie actuelle due au virus H5N2 chez les autruches en Afrique du Sud), pour quatre autres épizooties l'abattage sanitaire s'est avéré inefficace appliqué seul et il a été décidé d'introduire la vaccination dans les programmes de lutte. Plus de 113 milliards de doses de vaccin contre l'influenza aviaire ont été administrées entre 2002 et 2010 aux populations de volailles jugées à risque, lesquelles comptaient plus de 131 milliards d'individus. À raison de deux à trois doses par volatile dans les 15 pays pratiquant la vaccination, la couverture vaccinale nationale moyenne s'est élevée à 41,9 %, portant à 10,9 % la couverture vaccinale mondiale des populations de volailles contre l'influenza aviaire. Le taux le plus élevé de couverture vaccinale, se rapprochant de 100 % des volailles, a été enregistré à Hong Kong, tandis que le taux national le plus bas, inférieur à 0,01 % des volailles, a été enregistré en Israël et aux Pays-Bas. Les vaccins utilisés étaient pour 95,5 % d'entre eux des vaccins à virus inactivé, tandis que les vaccins à virus recombinant représentaient 4,5 % du total. Ces vaccins ont été majoritairement utilisés lors de la panzootie d'IAHP à H5N1, et plus de 99 % d'entre eux ont été utilisés en Chine, en Égypte, en Indonésie et au Vietnam. L'introduction de la vaccination dans ces quatre pays a eu lieu après que l'IAHP à H5N1 ait pris une dimension enzootique chez les volailles domestiques et n'a pas été à l'origine des infections enzootiques. Le recours aux vaccins a permis de prévenir la maladie clinique ainsi que la mortalité chez les poulets, tout en préservant les moyens de subsistance et la sécurité alimentaire des sociétés rurales affectées par les foyers d'IAHP. L'influenza aviaire faiblement pathogène (IAFP) due aux virus de type H5 et H7 est devenue une maladie à déclaration obligatoire auprès de l'Organisation mondiale de la santé animale en 2006, lorsqu'il est apparu que certains de ces virus pouvaient subir une mutation les rendant hautement pathogènes. Les notifications de foyers d'IAFP à déclaration obligatoire ont été moins nombreuses que celles de foyers d'IAHP et six pays seulement ont introduit la vaccination dans leurs programmes de lutte, ce qui porte à 8,1 % le pourcentage des vaccins utilisés contre l'influenza aviaire due aux virus H5/H7, par opposition au pourcentage de vaccins utilisés contre l'IAHP qui s'élève à plus de 91,9 % du total. Six pays ont choisi de vacciner pour lutter contre l'IAFP à déclaration obligatoire, la majorité des vaccins ayant été utilisée au Mexique, au Guatemala, au Salvador et en Italie. Dans les pays où l'IAHP et l'IAFP à déclaration obligatoire sévissent à l'état enzootique, la conception et la mise en œuvre des stratégies de sortie se sont avérées difficiles.

Mots-clés

Banque de vaccins – Immunité – Influenza aviaire – Influenza aviaire faiblement pathogène – Influenza aviaire faiblement pathogène à déclaration obligatoire – Influenza aviaire hautement pathogène – Maladie animale – Maladie aviaire – Vaccin – Vaccination – Virus de l'influenza aviaire – Volailles.

■

Evaluación de estrategias nacionales de lucha contra la influenza aviar altamente patógena y la influenza aviar levemente patógena de declaración obligatoria en aves de corral, haciendo hincapié en las vacunas y la vacunación

D.E. Swayne, G. Pavade, K. Hamilton, B. Vallat & K. Miyagishima

Resumen

Desde 1959 ha habido veintinueve epizootias distintas de influenza aviar altamente patógena (IAAP). La mayor de todas ellas fue la panzootia por el virus H5N1 que golpeó Asia, África y Europa Oriental y afectó a la población avícola de corral o salvaje de 63 países. La aplicación de programas de sacrificio sanitario se saldó con la erradicación de 24 de esas epizootias (y está cerca de llevar a idéntico desenlace la epizootia por el virus H5N2 que afecta actualmente a avestruces en Sudáfrica), pero en cuatro casos en que esa política no resultaba por sí sola lo bastante eficaz se practicaron vacunaciones para completar los programas de lucha. Entre 2002 y 2010 se administraron más de 113.000 millones de dosis de vacuna contra la influenza aviar (IA), para una población de aves de corral en situación de riesgo que, en el conjunto de los países, suponía en total más de 131.000 millones de ejemplares. A razón de dos o tres dosis por ejemplar en los 15 países vacunadores, la tasa de cobertura nacional de vacunación fue en promedio del 41,9% y la de cobertura mundial del 10,9% de toda la población de aves de corral. Los índices más elevados de cobertura nacional, de casi un 100%, se dieron en Hong Kong, y los más bajos, de alrededor del 0,01%, en Israel y los Países Bajos. De todas las vacunas contra la IA administradas, un 95,5% fueron vacunas inactivadas, y un 4,5% vacunas vivas de virus recombinantes. La mayoría de ellas se utilizaron durante la panzootia de IAAP por H5N1, concentradas, en más del 99%, en la República Popular de China, Egipto, Indonesia y Vietnam. En estos cuatro países se instituyó la vacunación después de que la IAAP por H5N1 cobrara carácter enzoótico en las aves domésticas, y la vacunación no resultó en infecciones enzoóticas. El uso de vacunas previno la infección clínica y mortalidad de pollos y en las zonas rurales protegió los medios de subsistencia y la seguridad alimentaria durante los brotes de IAAP. En 2006 la Organización Mundial de Sanidad Animal (OIE) decidió imponer la obligatoriedad de notificar la influenza aviar levemente patógena (IALP) porque ciertos virus H5 y H7 causantes de esa afección tenían la capacidad de mutar y provocar la IAAP. Se han comunicado menos brotes de IALP que de IAAP, y solamente seis países han recurrido a vacunaciones como parte de los programas de lucha, lo que significa que un 8,1% del total de vacunas fueron utilizadas contra las cepas H5 o H7, en comparación con un porcentaje de más del 91,9% de vacunas empleadas contra la IAAP. Hay seis países que han recurrido a la vacuna para controlar la IALP de declaración obligatoria, pero el grueso de las vacunaciones se ha concentrado en México, Guatemala, El Salvador e Italia. En países donde había IAAP y IALP de declaración obligatoria de carácter enzoótico, la elaboración y aplicación de estrategias de salida ha sido un proceso difícil.

Palabras clave

Aves de corral – Banco de vacunas – Enfermedad animal – Enfermedad aviar – Influenza aviar – Influenza aviar altamente patógena – Influenza aviar levemente patógena – Influenza aviar levemente patógena de declaración obligatoria – Inmunidad – Vacuna – Vacunación – Virus de la influenza aviar.

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References

1. Aly M.M., Arafa A. & Hassan M.K. (2008). – Epidemiological findings of outbreaks of disease caused by highly pathogenic H5N1 avian influenza virus in poultry in Egypt during 2006. *Avian Dis.*, **52** (2), 269–277.

2. Bertelsen M.F., Klausen J., Holm E., Grondahl C. & Jorgensen P.H. (2007). – Serological response to vaccination against avian influenza in zoo-birds using an inactivated H5N9 vaccine. *Vaccine*, **25** (22), 4345–4349.

3. Capua I., Marangon S., Dalla P. & Santucci U. (2000). – Vaccination for avian influenza in Italy. *Vet. Rec.*, **147** (26), 751.

4. Capua I., Schmitz A., Jestin V., Koch G. & Marangon S. (2009). – Vaccination as a tool to combat introductions of notifiable avian influenza viruses in Europe, 2000 to 2006. *In* Avian influenza (T. Mettenleiter, ed.). *Rev. sci. tech. Off. int. Epiz.*, **28** (1), 245–259.

5. Capua I., Terregino C., Cattoli G. & Toffan A. (2004). – Increased resistance of vaccinated turkeys to experimental infection with an H7N3 low-pathogenicity avian influenza virus. *Avian Pathol.*, **33** (2), 158–163.

6. Capua I., Terregino C., Cattoli G., Mutinelli F. & Rodriguez J.F. (2003). – Development of a DIVA (differentiating infected from vaccinated animals) strategy using a vaccine containing a heterologous neuraminidase for the control of avian influenza. *Avian Pathol.*, **32** (1), 47–55.

7. Castellan D. (2006). – FAO Mission in support of avian influenza prevention and control in Egypt. Food and Agriculture Organization of the United Nations (FAO), Cairo, Egypt, 1–30.

8. Cecchinato M., Comin A., Bonfanti L., Terregino C., Monne I., Lorenzetto M. & Marangon S. (2011). – Epidemiology and control of low pathogenicity avian influenza infections in rural poultry in Italy. *Avian Dis.*, **55** (1), 13–20.

9. Chen H. (2004). – H5N1 avian influenza in China. *Science in China (Series C)*, **52** (5), 419–427.

10. Chen H. (2009). – Avian influenza vaccination: the experience in China. *In* Avian influenza (T. Mettenleiter, ed.). *Rev. sci. tech. Off. int. Epiz.*, **28** (1), 267–274.

11. Chen H., Deng G., Li Z., Tian G., Li Y., Jiao P., Zhang L., Liu Z., Webster R.G. & Yu K. (2004). – The evolution of H5N1 influenza viruses in ducks in southern China. *Proc. natl Acad. Sci. USA*, **101** (28), 10452–10457.

12. Chen J., Fang F., Yang Z., Liu X., Zhang H., Zhang Z., Zhang X. & Chen Z. (2009). – Characterization of highly pathogenic H5N1 avian influenza viruses isolated from poultry markets in central China. *Virus Res.*, **146** (1–2), 19–28.

13. European Food Safety Authority (EFSA) (2007). – Opinion of the Scientific Panel on Animal Health and Welfare (AHAW) on a request from the Commission related with the vaccination against avian influenza of H5 and H7 subtypes as a preventive measure carried out in Member States in birds kept in zoos under Community approved programmes. Available at: www.efsa.europa.eu/en/efsajournal/pub/450.htm (accessed on 19 July 2011).

14. European Union Commission (2011). – Avian influenza – vaccination. Vaccination in zoos. Available at: ec.europa.eu/food/animal/diseases/controlmeasures/avian/eu_resp_vaccination_en.htm (accessed on 19 May 2011).

15. Food and Agriculture Organization of the United Nations (FAO) (2011). – FAOSTAT. Available at: faostat.fao.org/site/339/default.aspx (accessed on 19 June 2011).

16. Food and Agriculture Organization of the United Nations (FAO) (2011). – Highly pathogenic avian influenza. *Transboundary Anim. Dis. Bull.*, **37**, 21–29.

17. Frame D.D., McCluskey B.J., Buckner R.E. & Halls F.D. (1996). – Results of an H7N3 avian influenza vaccination program in commercial meat turkeys. *In* Proc. 46th Western Poultry Disease Conference, University of California, Davis, California, 32.

18. Freiji M. (2006). – Lessons learnt from avian influenza H5N1 epidemic in Egypt. *In* Proc. Conference on Co-ordinated Response Strategy to Avian Influenza, 29 May 2006, International Financial Corporation, World Bank Group, Cairo, Egypt.

19. Furger M., Hoop R., Steinmetz H., Eulenberger U. & Hatt J. (2008). – Humoral immune response to avian influenza vaccination over a six-month period in different species of captive wild birds. *Avian Dis.*, **52** (2), 222–228.

20. Gilbert M., Xiao X., Pfeiffer D.U., Epprecht M., Boles S., Czarnecki C., Chaitaweesub P., Kalpravidh W., Minh P.Q., Otte M.J., Martin V. & Slingenbergh J. (2008). – Mapping H5N1 highly pathogenic avian influenza risk in Southeast Asia. *Proc. natl Acad. Sci. USA*, **105** (12), 4769–4774.

21. Government of Egypt (2010). – Integrated National Plan for avian and human influenza. Animal health and livelihood sustainability strategy. Ministry of Agriculture and Land Reclamation, Cairo, Egypt, 1–27.

22. Guan Y., Peiris M., Kong K.F., Dyrting K.C., Ellis T.M., Sit T., Zhang L.J. & Shortridge K.F. (2002). – H5N1 influenza viruses isolated from geese in southeastern China: evidence for genetic reassortment and interspecies transmission to ducks. *Virology*, **292** (1), 16–23.

23. Guan Y., Smith G.J.D., Webby R. & Webster R.G. (2009). – Molecular epidemiology of H5N1 avian influenza. *In* Avian influenza (T. Mettenleiter, ed.). *Rev. sci. tech. Off. int. Epiz.*, **28** (1), 39–47.

24. Halvorson D.A. (2002). – Twenty-five years of avian influenza in Minnesota. *In* Proc. 53rd North Central Avian Disease Conference, 6–8 October, Minneapolis, Minnesota, 65–69.

25. Halvorson D.A. (2008). – Control of low pathogenicity avian influenza. *In* Avian influenza (D.E. Swayne, ed.). Blackwell, Ames, Iowa, 513–536.

26. Hesterberg U., Harris K., Stroud D., Guberti V., Busani L., Pittman M., Piazza V., Cook A. & Brown I. (2009). – Avian influenza surveillance in wild birds in the European Union in 2006. *Influenza & Other Respir. Viruses*, **3** (1), 1–14.

27. Lécu A., De Langhe C., Petit T., Bernard F. & Swam H. (2009). – Serologic response and safety to vaccination against avian influenza using inactivated H5N2 vaccine in zoo birds. *J. Zoo Wildl. Med.*, **40** (4), 731–743.

28. Lee C., Suarez D.L., Tumpey T.M., Sung H., Kwon Y., Lee Y., Choi J., Joh S., Kim M., Lee E., Park J., Lu X., Katz J.M., Spackman E., Swayne D.E. & Kim J. (2005). – Characterization of highly pathogenic H5N1 avian influenza A viruses isolated from South Korea. *J. Virol.*, **79** (6), 3692–3702.

29. Li K.S., Guan Y., Wang J., Smith G.J.D., Xu K.M., Duan L., Rahardjo A.P., Puthavathana P., Buranathai C., Nguyen T.D., Estoepangestie A.T.S., Chaisingh A., Auewarakul P., Long H.T., Hanh N.T.H., Webby R.J., Poon L.L.M., Chen H., Shortridge K.F., Yuen K.Y., Webster R.G. & Peiris J.S.M. (2004). – Genesis of a highly pathogenic and potentially pandemic H5N1 influenza virus in eastern Asia. *Nature*, **430** (6996), 209–213.

30. Marangon S., Busani L. & Capua I. (2007). – Practicalities of the implementation of a vaccination campaign for avian influenza. *Avian Dis.*, **51**, 297–303.

31. Marangon S., Capua I., Pozza G. & Santucci U. (2004). – Field experiences in the control of avian influenza outbreaks in densely populated poultry areas. *Dev. Biol. (Basel)*, **119**, 155–164.

32. Marangon S., Cristalli A. & Busani L. (2007). – Planning and executing a vaccination campaign against avian influenza. *Dev. Biol. (Basel)*, **130**, 99–108.

33. Mariner J. (2011). – Final report: operational research in Indonesia for more effective control of highly pathogenic avian influenza. International Livestock Research Institute, Nairobi, Kenya, 1–154.

34. Ministry of Agriculture of China (2011). – Feasibility of production of human AI vaccine in AI vaccine manufacturers in China. Available at: https://docs.google.com/viewer?a=v&q=cache:uUO0-Lh8buwJ:www.who.int/entity/csr/disease/influenza/MoA_China.pdf+doses+H5N1+vaccine+China+poultry&hl=en&gl=uk&pid=bl&srcid=ADGEEShIePfcLg60zi-mBdj3ydbTzvlP1XUUGXlnX372bXmhdIAeYu310LwdVVoGMuXjdnFBIPXb_WyIs0tSloGI_IroLS1bWIDF5PTuWtJK11t6WWcYr3Bj6b2h5zdLqJXUoOyFe3mi&sig=AHIEtbTECX3XNlHTbeKs9aSVOclhVA0MHw (accessed on 20 September 2011).

35. Naeem K. & Siddique N. (2006). – Use of strategic vaccination for the control of avian influenza in Pakistan. *Dev. Biol. (Basel)*, **124**, 145–150.

36. Nguyen D.C., Uyeki T.M., Jadhao S., Maines T., Shaw M., Matsuoka Y., Smith C., Rowe T., Lu X., Hall H., Xu X., Balish A., Klimov A., Tumpey T.M., Swayne D.E., Huynh Lien P.T., Nghiem H.K., Nguyen Hanh H.T., Hoang L.T., Cox N.J. & Katz J.M. (2005). – Isolation and characterization of avian influenza viruses, including highly pathogenic H5N1, from poultry in live bird markets in Hanoi, Vietnam, in 2001. *J. Virol.*, **79** (7), 4201–4212.

37. Obon E., Bailey T.A., O'Donovan D., McKeown S., Kent J., Joseph S. & Wernery U. (2007). – Humoral response to H5N2 vaccination in exotic birds in the United Arab Emirates. *Vet. Rec.*, **161** (25), 860–861.

38. Oh S., Martelli P., Hock O.S., Luz S., Furley C., Chiek E.J., Wee L.C. & Keun N.M. (2005). – Field study on the use of inactivated H5N2 vaccine in avian species. *Vet. Rec.*, **157** (10), 299–300.

39. Pavade G., Awada L., Hamilton K. & Swayne D.E. (2011). – The influence of economic indicators, poultry density and the performance of Veterinary Services on the control of high pathogenicity avian influenza in poultry. *Rev. sci. tech. Off. int. Epiz.*, **30** (3), 661-671.

40. Philippa J., Baas C., Beyer W., Bestebroer T., Fouchier R., Smith D., Schaftenaar W. & Osterhaus A. (2007). – Vaccination against highly pathogenic avian influenza H5N1 virus in zoos using an adjuvanted inactivated H5N2 vaccine. *Vaccine*, **25** (19), 3800–3808.

41. Philippa J.D., Munster V.J., Bolhuis H., Bestebroer T.M., Schaftenaar W., Beyer W.E., Fouchier R.A., Kuiken T. & Osterhaus A.D. (2005). – Highly pathogenic avian influenza (H7N7): vaccination of zoo birds and transmission to non-poultry species. *Vaccine*, **23** (50), 5743–5750.

42. Pittman M. & Laddomada A. (2008). – Legislation for the control of avian influenza in the European Union. *Zoonoses public Hlth*, **55** (1), 29–36.

43. Sawitri S.E., Darminto, Weaver J. & Bouma A. (2007). – The vaccination programme in Indonesia. *Dev. Biol. (Basel)*, **130**, 151–158.

44. Sims L.D. & Brown I.H. (2008). – Multi-continental epidemic of H5N1 high pathogenicity avian influenza (1996–2007). *In* Avian influenza (D.E. Swayne, ed.). Blackwell, Ames, Iowa, 251–286.

45. Suarez D.L., Spackman E. & Senne D.A. (2003). – Update on molecular epidemiology of H1, H5, and H7 influenza virus infections in poultry in North America. *Avian Dis.*, **47** (3 Suppl.), 888–897.

46. Swayne D.E. (2008). – The global nature of avian influenza. *In* Avian influenza (D.E. Swayne, ed.). Blackwell, Ames, Iowa, 123–143.

47. Swayne D.E. & Halvorson D.A. (2008). – Influenza. *In* Diseases of poultry (Y.M. Saif, J.R. Glisson, A.M. Fadly, L.R. McDougald & L. Nolan, eds). Blackwell, Ames, Iowa, 153–184.

48. Swayne D.E. & Kapczynski D.R. (2008). – Vaccines, vaccination and immunology for avian influenza viruses in poultry. *In* Avian influenza (D.E. Swayne, ed.). Blackwell, Ames, Iowa, 407–451.

49. Swayne D.E. & Slemons R.D. (2008). – Using mean infectious dose of high- and low-pathogenicity avian influenza viruses originating from wild duck and poultry as one measure of infectivity and adaptation to poultry. *Avian Dis.*, **52** (3), 455–460.

50. Swayne D.E. & Suarez D.L. (2000). – Highly pathogenic avian influenza. *In* Diseases of poultry: world trade and public health implications (C.W. Beard & M.S. McNulty, eds). *Rev. sci. tech. Off. int. Epiz.*, **19** (2), 463–482.

51. Tumpey T.M., Kapczynski D.R. & Swayne D.E. (2004). – Comparative susceptibility of chickens and turkeys to avian influenza A H7N2 virus infection and protective efficacy of a commercial avian influenza H7N2 virus vaccine. *Avian Dis.*, **48** (1), 167–176.

52. Turner J., Clothier H.J. & Kaye M. (2005). – Influenza surveillance in Victoria, 2004. *Commun. Dis. Intell.*, **29** (1), 71–76.

53. Villarreal C. (2007). – Experience in control of avian influenza in the Americas. *Dev. Biol. (Basel)*, **130**, 53–60.

54. Webster R.G., Guan Y., Peiris M., Walker D., Krauss S., Zhou N.N., Govorkova E.A., Ellis T.M., Dyrting K.C., Sit T., Perez D.R. & Shortridge K.F. (2002). – Characterization of H5N1 influenza viruses that continue to circulate in geese in southeastern China. *J. Virol.*, **76** (1), 118–126.

55. World Organisation for Animal Health (OIE) (2010). – Chapter 10.4. Avian influenza. *In* Terrestrial Animal Health Code. OIE, Paris. Available at: www.oie.int/index.php?id=169&L=0&htmfile=chapitre_1.10.4.htm (accessed on 19 June 2011).

56. World Organisation for Animal Health (OIE) (2010). – Terrestrial Animal Health Code. OIE, Paris. Available at: www.oie.int/en/international-standard-setting/terrestrial-code/access-online/ (accessed on 19 May 2011).

57. World Organisation for Animal Health (OIE) (2011). – Animal health data (prior to 2005). *In* Handistatus II. OIE, Paris. Available at: web.oie.int/wahis/public.php?page=home (accessed on 27 July 2011).

58. World Organisation for Animal Health (OIE) (2011). – Vaccine bank. OIE, Paris. Available at: www.oie.int/en/support-to-oie-members/vaccine-bank/ (accessed on 19 June 2011).

59. World Organisation for Animal Health (OIE) (2011). – World Animal Health Information System. OIE, Paris. Available at: web.oie.int/wahis/public.php?page=home (accessed on 19 May 2011).

60. Xu X., Subbarao K., Cox N.J. & Guo Y. (1999). – Genetic characterization of the pathogenic influenza A/goose/Guangdong/1/96 (H5N1) virus: similarity of its hemagglutinin gene to those of H5N1 viruses from the 1997 outbreaks in Hong Kong. *Virology*, **261** (1), 15–19.

Appendix

World Organisation for Animal Health avian influenza vaccines and vaccination survey

English or French language versions were sent to the 80 countries that reported outbreaks of high-pathogenicity avian influenza or low-pathogenicity notifiable avian influenza between 2002 and 2010

I. General avian influenza (AI) vaccine use (short and long questionnaire)

1. Do you have an option in your national response plan to use vaccine for H5 or H7 low-pathogenicity AI (LPAI)?

Yes □ No □

2. Do you have an option for vaccine use in your high-pathogenicity AI (HPAI) control programme?

Yes □ No □

3. Do you have written plans on vaccine usage including specific criteria to decide on when to use vaccine?

Yes □ No □

Have you conducted simulations or table-top exercises of these vaccination plans?

Yes □ No □

If yes, when and how often have you done simulations or table-top exercises for vaccination?

....

4. What other components do you have in your national control strategy such as quarantine, enhanced biosecurity, education, surveillance, monitoring, rapid diagnostics, compensation, etc.?

....

II. AI vaccine and vaccination questions for 2002–2010

5. Has your country used vaccines to control HPAI?

Yes □ No □

6. Has your country used vaccines to control H5 or H7 LPAI?

Yes □ No □

7. Has your country conducted field trials with H5 or H7 AI vaccines?

H5	LPAI □	HPAI □	Both □
H7	LPAI □	HPAI □	Both □

8. Has your country used vaccines to control non-H5 or non-H7 low pathogenic avian influenza?

Yes □ No □

If yes, what subtypes?

....

9. Additional comments:

....

III. Vaccine bank questions

10. Do you have an H5 and/or H7 AI national (or regional) vaccine bank?

Yes □ No □

11. How many doses of each subtype?

Date vaccines acquired?

Expiration date?

What specific seed strain(s) are in the vaccine?

12. Who will cover the cost of the vaccine?

13. Who will cover the cost of the vaccination campaign?

14. Is the vaccine held by:

□ the government □ poultry association □ private company

15. Are vaccines stored as:

□ frozen virus □ process antigen □ final emulsified product

16. Under what circumstances would you use this vaccine?

17. What would be your main reasons for not using H5 or H7 AI vaccines in a control programme?

	LPAI	HPAI	Both
H5			
H7			

18. What would be your main reasons for using H5 or H7 vaccine in an AI control programme?

	LPAI	HPAI	Both
H5			
H7			

19. Are you aware of the OIE H5 Vaccine Bank?

Yes □ No □

If yes, have you acquired H5 AI vaccine from the OIE Vaccine Bank?

Yes □ No □

If yes, have you used your doses of the vaccine in the field?

Yes □ No □

20. Have you used any compensation mechanisms for farmers in your country (in case of stamping out linked with an AI outbreak)?

Yes □ No □

If yes, the source of funds is:

□ public □ private □ both

IV. Vaccine usage (long questionnaire only)

If you are currently using AI vaccines for HPAI control or have used AI vaccines in the past eight years (2002–2010), please answer the following questions:

21. Your use of H5/H7 AI vaccine has been as:

Preventive vaccination before AI entered your country's poultry?

Yes □ No □

Emergency vaccination after appearance of AI in your country's poultry?

Yes □ No □

Routine vaccination after AI was endemic in your country's poultry?

Yes □ No □

22. What type of birds have been vaccinated and how many doses per year for each type by thousand (k) or million (m) of doses?

	2002	2003	2004	2005	2006	2007	2008	2009
Meat chickens								
Broiler breeders								
Egg chickens								
Layer breeders								
Meat turkeys								
Turkey breeders								
Meat ducks								
Breeder ducks								
Meat geese								
Breeder geese								
Zoo, hunting (falcons), pet, conservation (rare and endangered species or breeds) and special collection birds								
Other Galliformes such as quail, guinea fowl, pheasants, peacocks, grouse, etc.								
Total doses								

23. What distinct production sectors has AI vaccination been used in (sectors 1–4)?

Sector 1 (Industrial, vertically integrated production)

Yes □ No □

Doses:

Proportion of farms with vaccination:

Sector 2 (Commercial poultry, non-vertically integrated, using slaughterhouses and live markets)

Yes □ No □

Doses:

Proportion of farms with vaccination:

Sector 3 (Smallholder commercial, including waterfowl, and sold mainly through live markets)

Yes □ No □

Doses:

Proportion of farms with vaccination:

Sector 4 (Village and backyard production)

Yes □ No □

Doses:

Proportion of farms with vaccination:

24. What is the typical vaccination protocol for the birds in terms of age and number of doses per bird?

25. Is any surveillance conducted to determine the antibody protection level in vaccinated flocks?

Yes □ No □

If yes, what tests are used and what is the minimal protective titre?

V. Vaccination strategy (long questionnaire only)

26. Do you have a strategy to identify infected animals within a vaccinated population (i.e. DIVA strategy)?

Yes □ No □

If so, do you use non-vaccinated sentinel birds for clinical, serological and/or virological surveillance?

Yes □ No □

If yes, how often and by what tests?

....

If so, do you use heterologous neuraminidase vaccine using the neuraminidase differentiation test in vaccinated birds?

Yes □ No □

If yes, how often and by what tests?

....

If so, do you use virological surveillance on sick and dead vaccinated birds?

Yes □ No □

If yes, how often and by what tests?

....

VI. Vaccine licensing (long questionnaire only)

27. Do you manufacture AI vaccine in your country?

Yes □ No □

28. Do you import AI vaccines?

Yes □ No □

29. Are the AI vaccines licensed or registered in your country?

Yes □ No □

30. Is a challenge test required in the licensure or registration procedure?

Yes □ No □

31. After an AI vaccine is licensed/registered, for how many years is the vaccine licensed or registered?

....

32. Do you have a regulatory method to update AI inactivated vaccine seed strains?

Yes □ No □

33. What do you require as a test to pass each vaccine batch for use?

....

34. Do you have a regulatory method to license or register live recombinant (vectored) vaccines for AI?

Yes □ No □

If so, have you licensed or registered recombinant AI vaccines in your country?

Yes □ No □

VII. Concluding questions (long questionnaire only)

35. Do you have criteria to stop AI vaccination (exit strategy)?

Yes □ No □

What are the criteria?

....

36. If you are using H5/H7 AI vaccine, when is your projected time to end AI vaccination?

	LPAI	HPAI	Both
H5			
H7			

VIII. Comments (long questionnaire only)

37. Provide additional comments or attach additional information files: