



## GATHERING EVIDENCE FOR A TRANSITIONAL STRATEGY (GETS) FOR HPAI H5N1 VACCINATION IN VIET NAM

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### WHAT WERE THE MAIN GOALS OF GETS?

The main goal of the GETS program was to gather evidence to support government decisions on future vaccination programs for poultry, shifting from a large scale, broad campaign to a more targeted cost effective program. This was achieved through a multi-faceted program covering not only trials on different vaccination strategies but also studies on policy development, surveys of farm practices and on cost effectiveness. The program was launched effectively from April, 2009 to June, 2011 in five pilot provinces of Viet Nam.



### WHAT RECOMMENDATIONS WERE MADE ABOUT FUTURE VACCINATION PROGRAMS FROM GETS?

GETS provided additional evidence for broader application of a targeted vaccination program focusing on ducks with vaccine delivered to these birds at the recommended ages for vaccination. GETS recommended that this age-based vaccination program should replace the current campaign conducted twice per year. It recommended that where this program is used, vaccination of other poultry should be gradually withdrawn, starting with scavenging chickens, then meat chickens and finally layer chickens.

A regional program should be applied in the Mekong Delta where mobile duck flocks pose a particular hazard and many of these birds are not vaccinated. The reasons for the poor uptake were discussed in the policy analysis document and the factors that inhibit vaccination uptake will need to be addressed including the fact that the birds have moved from their



home base before the second dose of vaccine is due. Vaccination of short lived meat ducks is not recommended if only a single dose of vaccine can be delivered to these birds.

The HPAI viruses circulating in the south of the country differ from those in the north. One strain of virus has persisted in the south since it first appeared in 2003/4 (these were initially called Clade 1 viruses but have now evolved over time and are now called Clade 1.1 viruses). In the north there has been a regular procession of new viruses introduced with earlier strains disappearing and new ones appearing.

For example in a 12 month period in 2010-11 in Nam Dinh two outbreaks detected in the GETS project in the same commune were caused by different strains of H5N1 virus (first Clade 2.3.4 then Clade 2.3.2.1). Testing for virus in ducks at market in Nam Dinh did not reveal any positive ducks suggesting that prolonged shedding of this variant virus in flocks was not occurring. GETS has again confirmed that winter is the period with the highest probability of clinical cases in poultry and this period was also the period when more viruses were detected in unvaccinated sentinel birds.

GETS also recommended that market surveillance is 10 times more sensitive and is also more cost effective means of virus detection than sentinel studies and this has been adopted subsequently by the Government of Vietnam by expanding the live bird (duck) market surveillance in 30 high risk provinces in 2011-12.

### WHAT METHODS DID GETS USE TO HELP FIND NEW VACCINATION STRATEGIES?

The studies in GETS were based around the reasonable assumption that ducks were the most important target species for vaccination because they can be infected silently and infected ducks can shed virus for a few days to a few weeks. It was argued that if the virus could be contained in ducks then there should be a lower likelihood of spillover to other poultry and subsequent spillover to humans.

In 5 pilot provinces of the GETS study, ducks were vaccinated according to a standard vaccination schedule involving two shots as juveniles and then at regular intervals of every six months.

Farmers who still wanted to vaccinate their other poultry (apart from ducks) were given the option of doing so but had to pay for the vaccine. In some provinces (notably Soc Trang) some farmers took up this option. Large commercial farms were already required to fund their own vaccination programs.

In one part of one pilot province in what was considered a lower risk area in Central Vietnam, vaccination was removed altogether in all poultry species.

### WHY WAS VACCINATION INTRODUCED TO VIETNAM IN THE FIRST PLACE?

The primary reason vaccination was introduced in 2005 was to reduce the likelihood of human exposure to H5N1 viruses (and therefore human cases) by reducing the amount of virus circulating in poultry, keeping in mind that HPAI was already endemic in the country. At that time Vietnam was the country with the most human cases of any country and fears of a global pandemic with a highly lethal virus were very high.

When mass vaccination programs were first introduced to Vietnam it was never expected that it would eliminate the viruses or prevent their circulation because it was never going to be possible in a mass campaign to get sustained high level immunity in all poultry, especially in ducks.

It was also recognized that it was going to be difficult to sustain such a large scale program delivered by government not only because of the cost but because of waning enthusiasm for such a massive task that took resources away from other animal health problems.

### IS VACCINATION STILL VALID?

GETS has demonstrated that H5N1 viruses are still circulating and this means that measures are still needed to protect humans and poultry from these viruses. Vaccination remains one of the tools worth considering to reduce the likelihood of infection and to reduce shedding of virus especially for free running ducks given there are few alternative strategies available to reduce the level of infection in these birds. But current vaccines are not the full answer.

Virus is circulating in places where clinical disease in poultry is not apparent and in places where vaccination is being used, both of which were expected findings. This was demonstrated using unvaccinated sentinel ducks in a large number of flocks across all districts in the five provinces covered by GETS. This work involved the testing of tens of thousands of blood samples and swabs. Other ducks were also tested for evidence of infection when they arrive at local markets by collection of swabs.

Only a small number of swabs from sentinel ducks were positive for virus. However, many more duck flocks had evidence from blood tests that they had been exposed to H5 virus. In many districts at certain times of the year 20% or more of the ducks had apparent evidence of exposure to virus.



Fortunately Vietnam did not have any reported human cases in 2011 (although 4 new cases were reported in the first two months of 2012) but it is not clear why given H5N1 viruses were still circulating in the duck population and occasionally spilling over into the chicken population. At the same time, across the border in Cambodia eight fatal human cases occurred with viruses virtually identical to the ones in southern Vietnam, demonstrating the potential for these viruses to cause severe disease.

Ducks will continue to play a very important role in the persistence of H5N1 viruses even when vaccination is used and targeted at duck populations. This does not mean that duck vaccination is a failure as it may be reducing the levels of shedding by ducks that subsequently get exposed to virus and it may be making some well vaccinated ducks resistant to infection, as occurs in experimental studies under controlled conditions. What the results from GETS show is that we can't rely on current vaccines to prevent all virus circulation in duck populations but it might still be playing a role in reducing viral shedding and transmission. It also demonstrated that through appropriate mass vaccination of ducks, it is possible to move out of vaccination among chickens without any added risks.

**DID GETS DEMONSTRATE THAT VACCINES AS APPLIED IN THE GETS PROVINCES ARE HELPING TO PREVENT INFECTION?**

The results from GETS strongly suggest (but do not prove) that vaccination is helping. The main evidence collected to support this view is as follows:



In some districts there was a mismatch between the number of doses of vaccine delivered and the population of ducks in the districts which correlated with an increase in the number of outbreaks and virus circulation in those districts.

Of the two Mekong Delta provinces studied, one had a much higher percent of unvaccinated mobile duck flocks entering the province (as detected by the CAHW) and a higher occurrence of outbreaks and virus circulation than the other suggesting that unvaccinated mobile duck flocks were playing a role in the transmission of H5N1 viruses.

The results have to be treated with some caution because in a project of this size compliance with the requirements for the study varied between districts. In addition it was not possible to conduct this study as a typical research trial with a 'treatment' group and a 'control' group. Nevertheless the findings provide justification for continuing vaccination of ducks if the costs of running the program can be sustained.

**ARE THERE SITUATIONS WHERE VACCINE SHOULD NOT BE USED?**

Based on results from the centre of Vietnam obtained in GETS (and supported by recent laboratory studies elsewhere) a single dose of vaccine for meat ducks is probably of little or no value. It does not generate sufficient immunity to prevent virus shedding and may even leave the birds susceptible to disease.

The results of the study suggest that it is possible to stop vaccinating small flocks of chickens without greatly increasing the risk but the caveat here is that in the high risk GETS provinces where this was done and the results were monitored, duck vaccination was still being conducted. If duck vaccination is removed the risk to small flocks may increase in those provinces with a large population of ducks.

**WERE MORE OR LESS OUTBREAKS OF DISEASE ASSOCIATED WITH H5N1 IN OTHER UNVACCINATED POULTRY AFTER GETS INTERVENTIONS?**

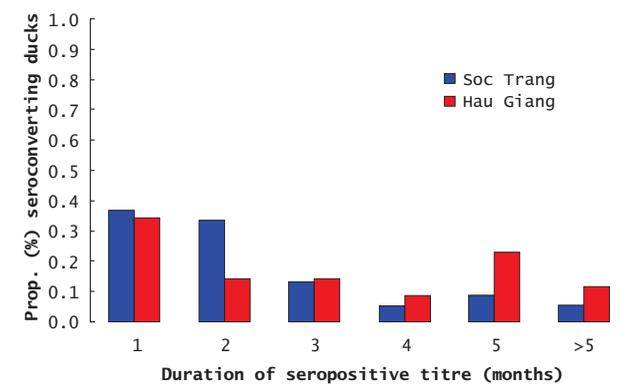
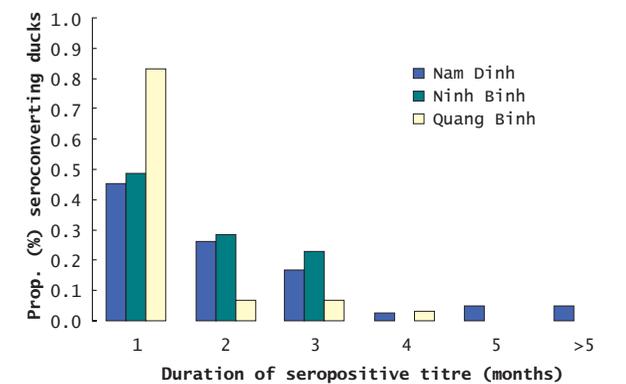
More samples from suspected outbreaks were received during GETS than in the period preceding GETS but less of these were positive for H5N1 virus. The percentage of suspect samples that were found positive with HPAI was 17.4% in the pre-GETS period compared to only 4.6% in the GETS period. In the GETS period, 66% of samples from suspected outbreaks were sent to the laboratory for analysis to confirm HPAI infection whereas only 24% were sent in the pre-GETS period. These findings demonstrated improvements in reporting that were made as a part of training of community animal health workers conducted under GETS and that the GETS modifications did not increase the risk of outbreaks in the unvaccinated poultry, at least in the short term.

It was noted during this project that samples were not submitted from a significant number of dead sentinel ducks in southern provinces demonstrating that some outbreaks of disease go undetected or undiagnosed. The reluctance of farmers to report disease in poultry was also confirmed in the survey of small to medium sized producers. The message that dead poultry should be submitted for testing has been repeated many times over the past few years and yet it is still not changing behavior. Ways need to be found to increase reporting of disease (a problem that occurs in many countries in the region). It also needs to be remembered that much of the infection in ducks (even if not vaccinated) is silent so even if all clinical cases were reported it would not mean all cases of infection are found. To do this targeted active surveillance to detect infection in ducks is also required.



**WHAT OTHER OBSERVATIONS WERE MADE ON LABORATORY TESTS ON BLOOD?**

One of the most striking results was the short time that antibodies could be detected in ducks once they became positive. As the figure below shows a high percentage of ducks that became seropositive were no longer seropositive one or two months later. This effect was less marked in the southern provinces and perhaps reflects repeated exposure of these birds to H5 virus.



The rapid fall in titers was even confirmed in one batch of infected sentinels in which virus was isolated and multiple birds died.

Despite the fact that viruses tend to come and go in the north there is apparent evidence of seroconversion throughout the year in some districts. Further examination of this phenomenon is warranted examining a smaller number of flocks and perhaps using a range of tests and test variations to understand the immune response in ducks.

This finding has implications for post-vaccination monitoring of response to vaccination. It is backed by experimental studies elsewhere that demonstrated some vaccinated ducks that do not have detectable antibody are still protected from challenge. In other words antibody levels as measured in blood tests are not an accurate indicator of protection.

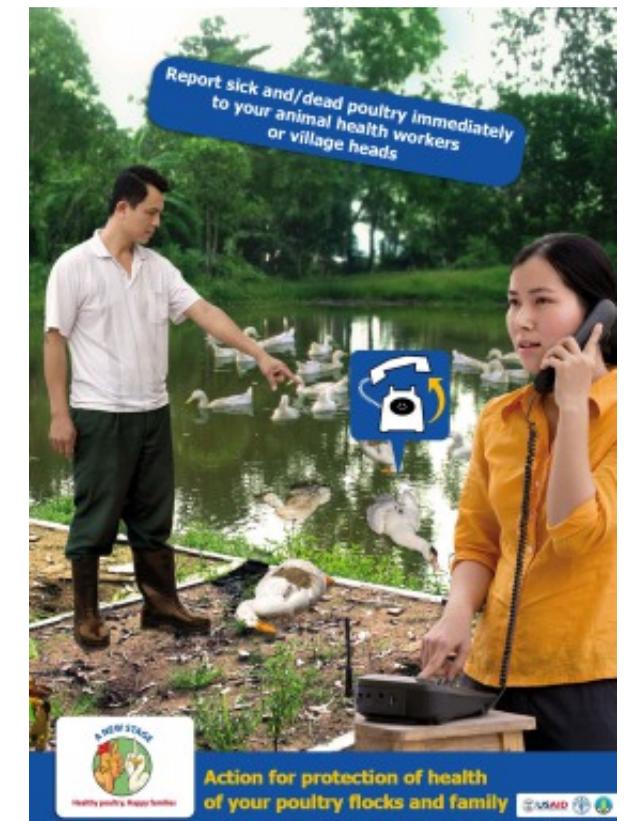
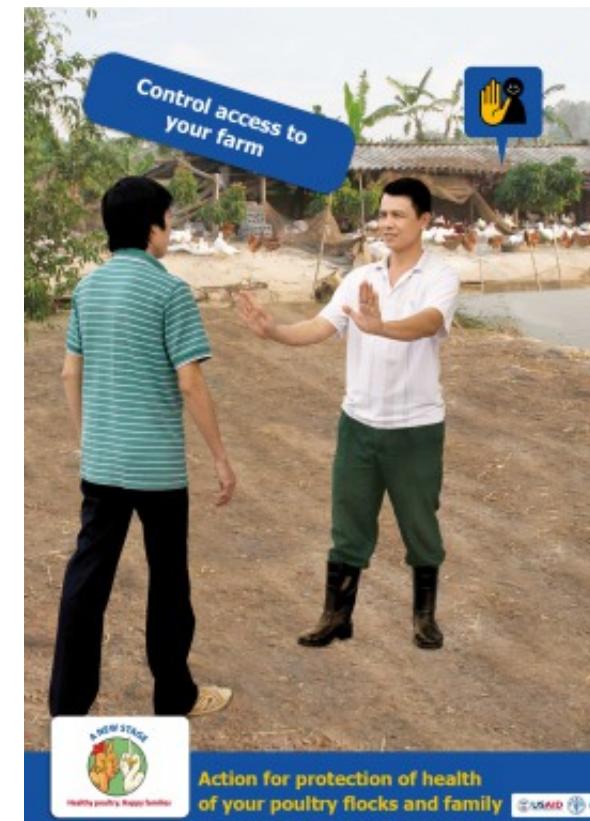
#### IS VACCINATION COST EFFECTIVE?

In assessing costs it needs to be remembered that the main reason for vaccinating at present is to reduce the likelihood of human exposure. This means that it is not possible to do a standard cost-benefit analysis based on costs of poultry outbreaks prevented versus the cost of vaccination.

Instead in this study the cost of vaccination was considered. In most provinces the cost of vaccination fell when it was applied to ducks only. Further cost reductions could be made by reducing sentinel surveillance in favour of live market surveillance.

#### WHAT OTHER IMPORTANT FINDINGS CAME OUT OF THE STUDIES ON FARM PRACTICES?

A survey conducted on farms rearing up to 1000 head of poultry provided an excellent snap shot of the state of the industry. The study found that most of the farmers surveyed did not keep their poultry confined and that ducks in particular were more likely to spend time outside the farm including grazing on paddy fields. Most farmers did not report dead poultry, they considered H5N1 HPAI the most important disease to control and had received information on the disease. The main reason they used H5 vaccine was that it was free. Some farmers received the vaccine but did not use it because it was not compulsory to do so and because the farmer wanted to time the vaccination. Information on the dangers posed by visitors, especially traders was weak. This information was converted to a series of billboards to raise awareness.



#### WAS THERE A POLICY ADVISORY ON VACCINATION FOLLOWING THE STUDY?

This study pointed out that in the long term the best way to prevent avian influenza is through improvements in farm biosecurity but that there are many factors that inhibit uptake of biosecurity measures, including availability of specific information (rather than generic information), the cost, enforcement provisions and capacity to ensure farmers meet certain standards. This paper reviewed the various measures that had been used to control avian influenza and confirmed the need for the GETS program in that the current broad scale campaign needed to be modified toward targeted vaccination because of the cost burden on government and the reduced enthusiasm for implementation at the provincial level. This study also provided useful information on management arrangements for poultry including the shift towards large integrated operations and away from contract growers as a result of earlier outbreaks of AI.