

Control of HPAI by Vaccination: Opportunities and Challenges

Santanu Bandyopadhyay

FAO, Vietnam

This presentation has been prepared by selectively copying from presentations on related subjects by Experts such as Ken Inui, David Swayne, Les Sims and a few others

The big question today is that for the control of HPAI in an endemic situation, whether poultry are....

“...to be or not to be.....”

Vaccinated

The general principles of control of HPAI in Poultry

- ❑ Early detection/stamping out
- ❑ Efficient surveillance and reporting with adequate compensation policy
- ❑ Risk reduction throughout the production/supply chain
 - Farm biosecurity standards
 - Improving traders/markets/slaughterhouse hygiene and biosecurity practices
 - Farm inputs (hatcheries, feed)
- ❑ Major cities banning live poultry
Moving to Quality Assured poultry supply
AND
- ❑ **Vaccination**

HPAI Vaccination

Why, When, Who and Where ???

Why include vaccination?

- ❑ Reduce losses to poultry production and ensure supply of poultry products
- ❑ Reduce human exposure to virus (reduce pandemic risk)
- ❑ Well vaccinated poultry have higher resistance to infection and generally excrete far less virus than unvaccinated counterparts
- ❑ Amount of virus circulating should be reduced by reducing the size of the susceptible population
- ❑ Short term silent shedding is possible (but also possible in unvaccinated older ducks)
- ❑ Well managed avian influenza vaccination programs have been shown to be effective
- ❑ Short-live poultry and rapid population turnover can make vaccination difficult

When to vaccinate

- ❑ High incidence of human cases
- ❑ High incidence of poultry outbreaks
- ❑ Too many un-controlled risk factors
 - Free grazing ducks
 - Complex production/marketing supply chains with little biosecurity
 - Poor identification of outbreaks
 - Limited 'industry' commitment to improved biosecurity and disease eradication



Who to vaccinate

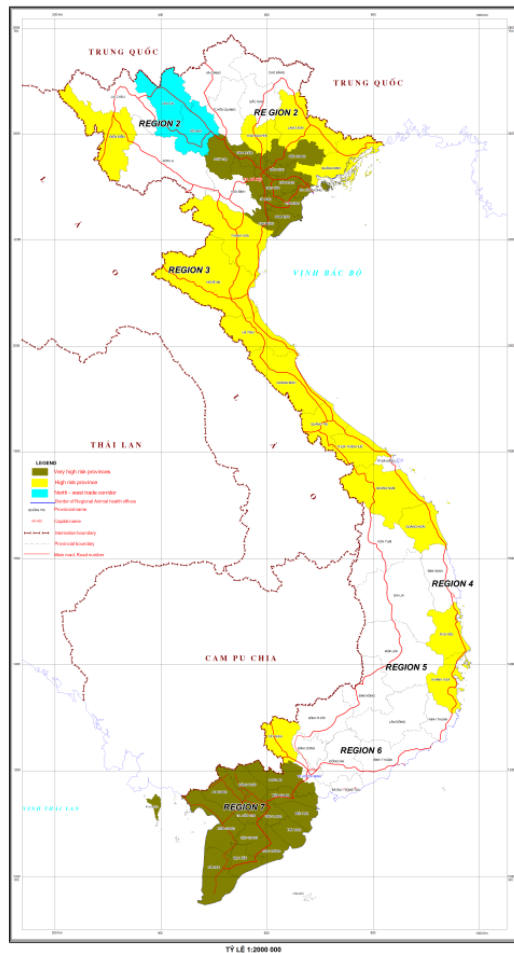
This is solely situation dependent and requires identification of risk groups, e.g.,

- Mass or risk-based(targeted)*
- layer birds or broilers*
- chickens or ducks*
- Free-grazing or confined*
- Small farms or large farms*

Where to vaccinate

- Needs meticulous risk-mapping
- Needs complete understanding of the value chain
- Mass vaccination and targeted vaccination
- Ring vaccination
- Cross-border area vaccination

A regional risk-map of Vietnam



- High risk
- Moderate risk
- Low risk
- Trade corridor

The criteria adopted for risk mapping include poultry density, human population density, poultry movement, poultry species, nature and location of markets, production practices, scale of operation, proximity to border etc.

Which Vaccine

Licensing of vaccines:

- Which national challenge strain(s)?
- Which host species?
- Licensed for how long?
- Was a challenge test completed for licensing?

Sufficient and consistent potency (antigenic mass) of vaccine batches:

Only release batches that meet the minimum serological standard or antigen content

Proper seed strain: Can and should these change based on field viruses?

- Antigenic drift in field viruses may require continual development of vaccine seed strains for optimal protection
- Virological surveillance for variant strains

Proper adjuvants for inactivated vaccine

- Inactivated vaccines optimized for chickens and turkeys but..
- Need adjuvants specific for waterfowl?

Advantages of vaccination

- ❑ Reduced replication of virus in respiratory and intestinal tracts (Minimum, 10^2 EID₅₀ -Typical, 10^{3-5} EID₅₀)
- ❑ Prevents HPAIV infection of meat and blood
- ❑ Best vaccines protect from high challenge doses (10^{6-8} EID₅₀)

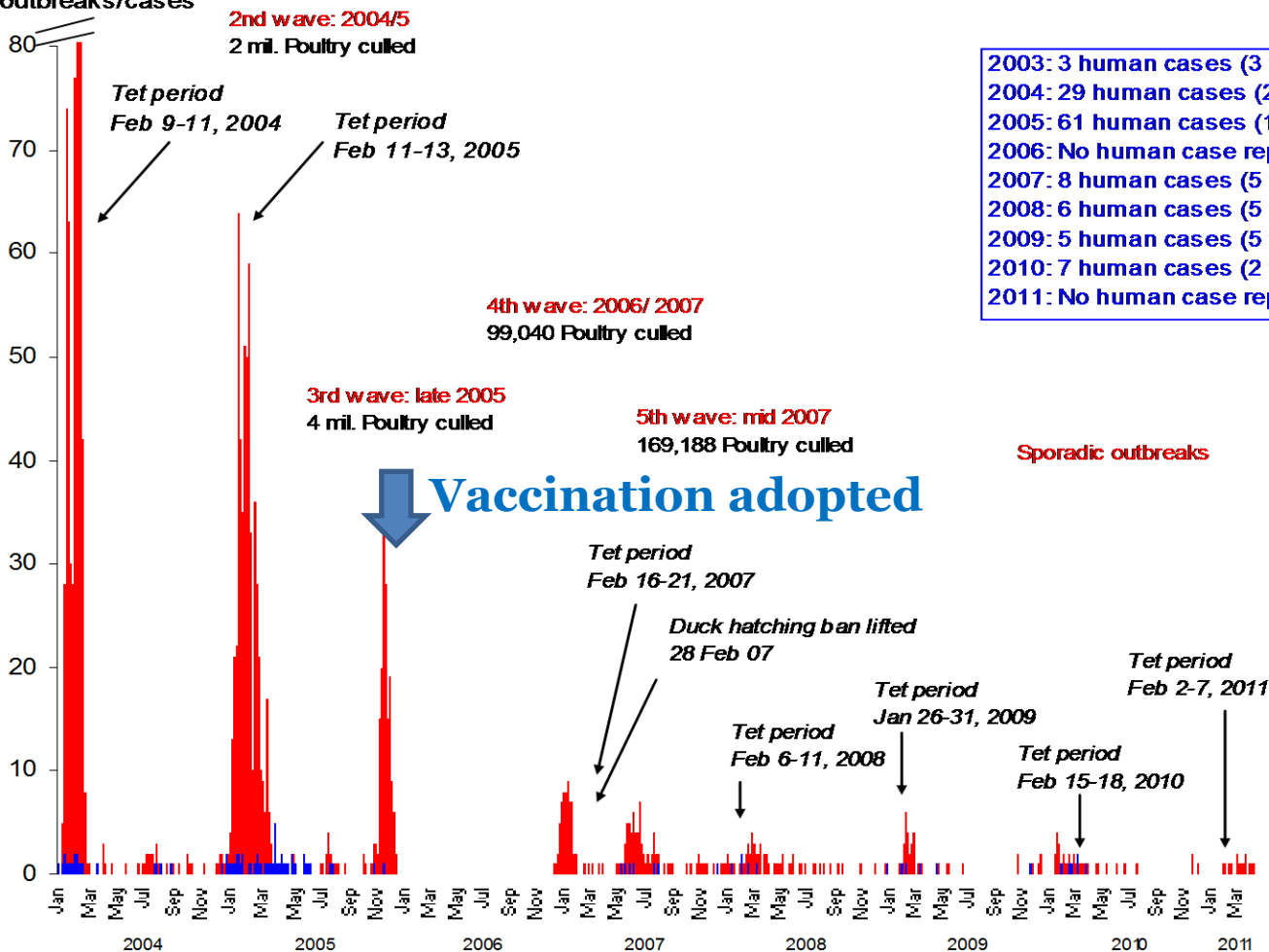
Results:

- Resistance of poultry to infections – enhanced food security and maintenance of livelihoods
- Reduced environmental contamination
- Reduced transmission
- Reduced human infections

1st wave: 2003/4
45 mil. Poultry culled

Timeline of HPAI H5N1 in Vietnam: 2004-2011

No. outbreaks/cases



2003: 3 human cases (3 fatal)
2004: 29 human cases (20 fatal)
2005: 61 human cases (19 fatal) ←
2006: No human case reported
2007: 8 human cases (5 fatal)
2008: 6 human cases (5 fatal)
2009: 5 human cases (5 fatal)
2010: 7 human cases (2 fatal)
2011: No human case reported so far



Data source: DAH and WHO
Update 21 April 2011



Challenges of vaccination

❑ Inactivated vaccine

- Two shots required for sustained immunity (~6 months)
- Age at vaccination (maternal antibody versus holding time)
- Cold chain maintenance

❑ High turnover of poultry population

- Short lived meat chickens and ducks

❑ Ducks

- Many 'grazing' ducks, difficult to vaccinate

❑ Field protection less than in laboratory

- Layer-breeds have best immunity, but immunity drops at peak of lay
- Broilers are more difficult to get good antibody titers

❑ No "Sterilizing Immunity" in the field

❑ Induces complacency among producers and authorities

❑ Silent transmission possible in spite of vaccination

Vaccination Logistic Challenges

- Cost of vaccine and vaccination
- Deployment of manpower
- Fatigue due to burn-out
- Maintenance of cold chain at field level
- Farmers reluctance to cooperate
- Obtaining optimum herd immunity
- Trade Embargo

A successful Vaccination campaign should have...

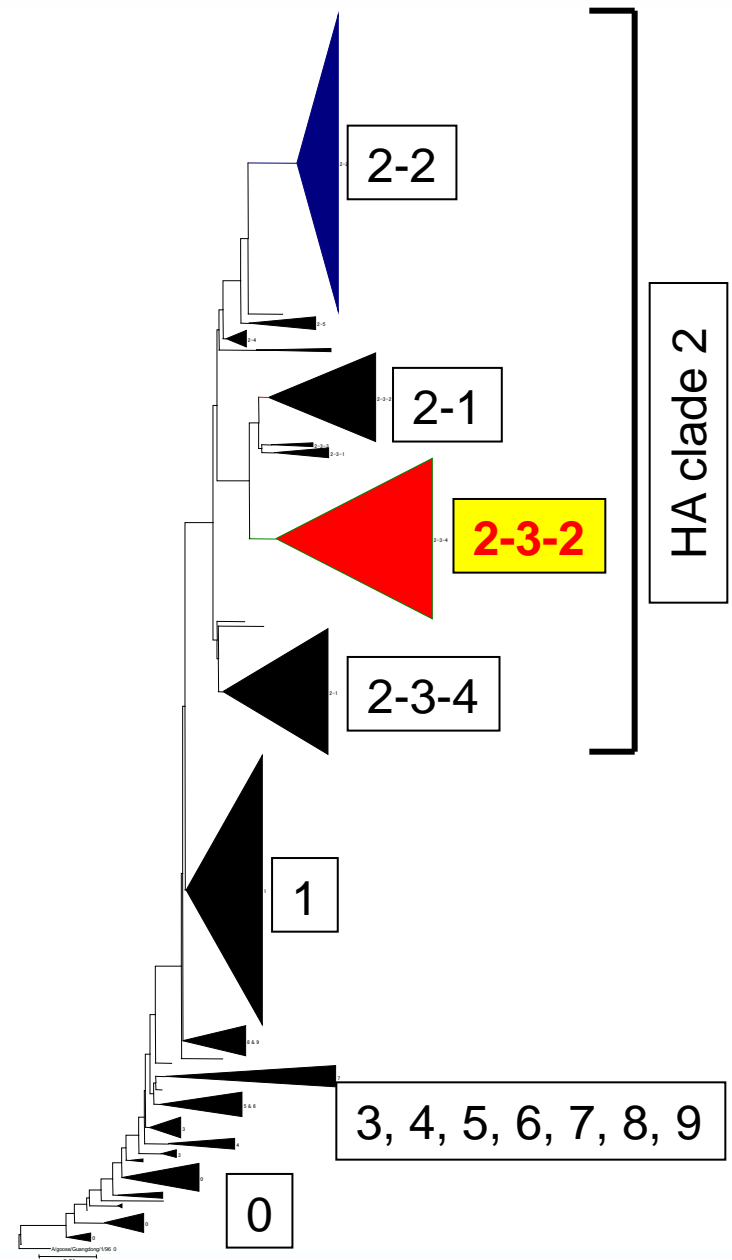
- A vaccination strategy with clearly defined goals
- A firm financial and administrative commitments on a long-term basis
- Adequate infra-structure and human resources in place
- A risk profile of the disease
- Adequate epidemiological information of the disease
- A projected cost benefit analysis
- A robust post-vaccination monitoring programme
- A close virus surveillance including genetic and antigenic mapping
- A clear exit strategy with a road-map with milestones
- A strong will to succeed

How important it is to select appropriate vaccine strain and monitoring circulating virus for regular efficacy testing ?

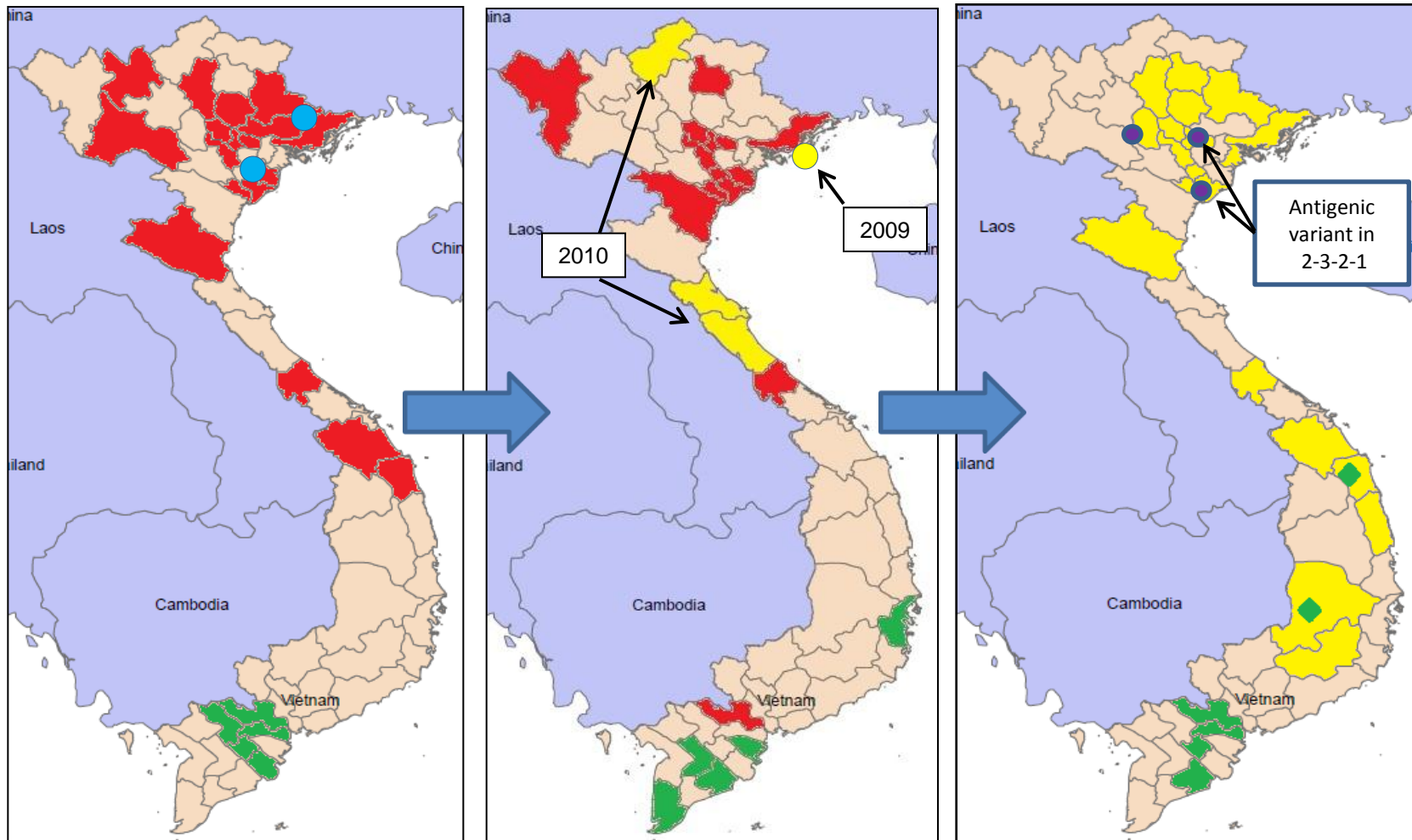
What is HA clade ?

- H5N1 virus has been evolving.
- H5N1 viruses are now **divided into 10 groups** based on HA gene sequences
- **Each group is numbered from 0 to 9.**
= HA clade 0 to 9
- Large clade (such as 2) are divided into sub-clade, and sub-sub-clade. And we now talking about sub-sub-sub-clade (2.3.2.1)

Phylogenetic relationship of 1500 H5N1 viruses based on HA gene sequences



Change of HA Clade in the North Vietnam during 2008-2011

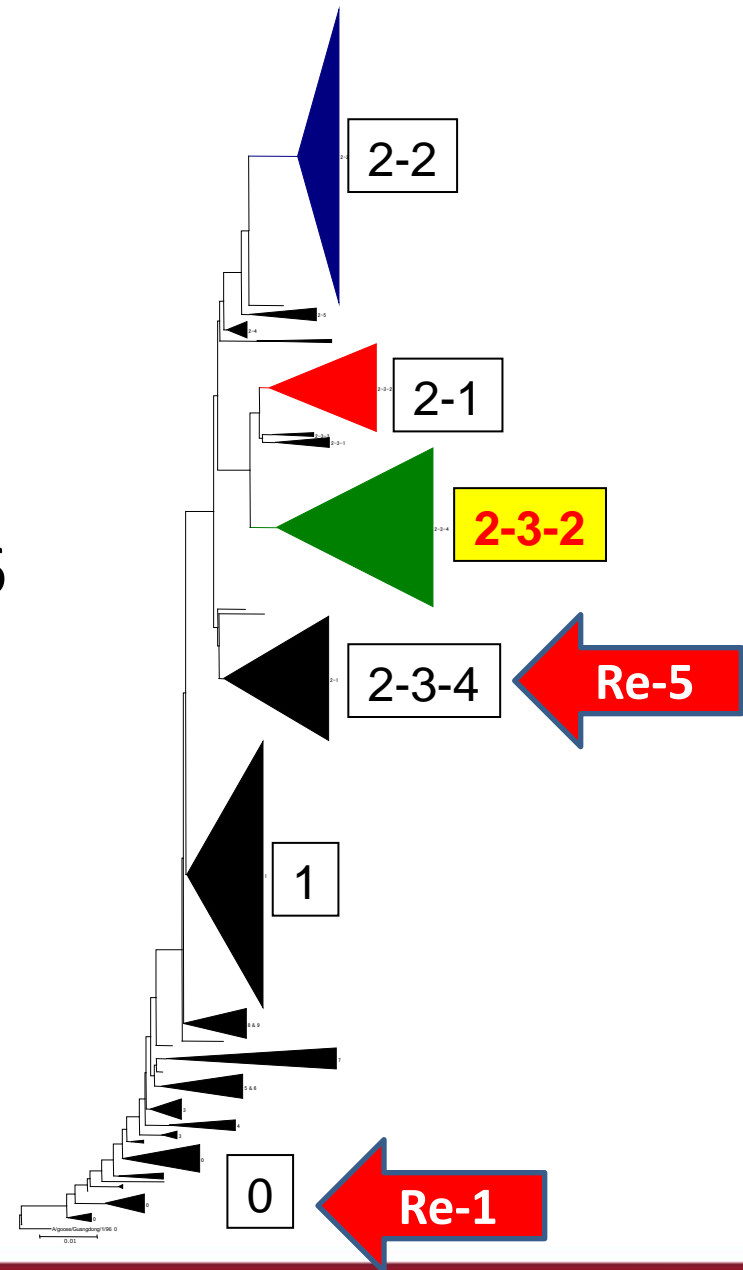


- Clade 7**
- Clade 2-3-4**
- Clade 2-3-2-1**
- Clade 1**

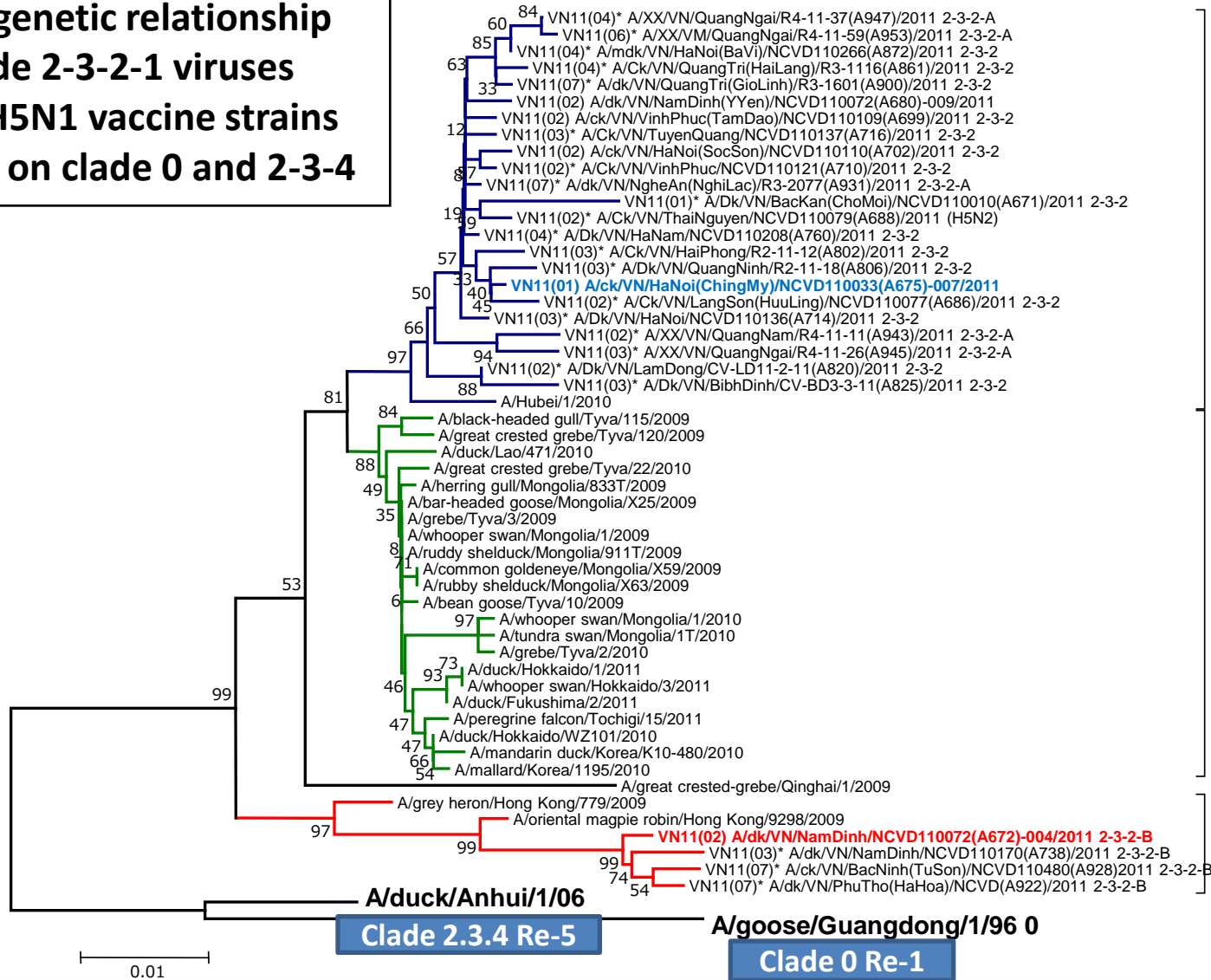
Month	Jan - Dec	Jan - June	July - Dec	Jan - June	July - Dec	Jan - August
Year	2008	2009		2010		2011

H5N1 vaccines most used in Vietnam

- **Re-1:**
 - clade 0
 - A/goose/Guangdong/1/1996
 - Used in China till 2008
- **Re-5:**
 - clade 2-3-4
 - A/duck/Anhui/1/2006
 - Used in China since 2009 (?)



**Phylogenetic relationship
of clade 2-3-2-1 viruses
with H5N1 vaccine strains
based on clade 0 and 2-3-4**



Routine testing of newly isolated viruses for antigenicity against antiserum to vaccines

HI test of antiserum to Re-5 vaccine with different clade of viruses

HI antigen		Serum dilution (log2)										
		1	2	3	4	5	6	7	8	9	10	11
Clade	Virus											
	VN1203											
2-3-4	Anhui/1/05											
	T15											
2-3-2-1	A668											
	A675											
2-3-2-1 variant	A672											
	A738											

Vaccine efficacy test in chicken against H5N1 viruses **2010-2011**

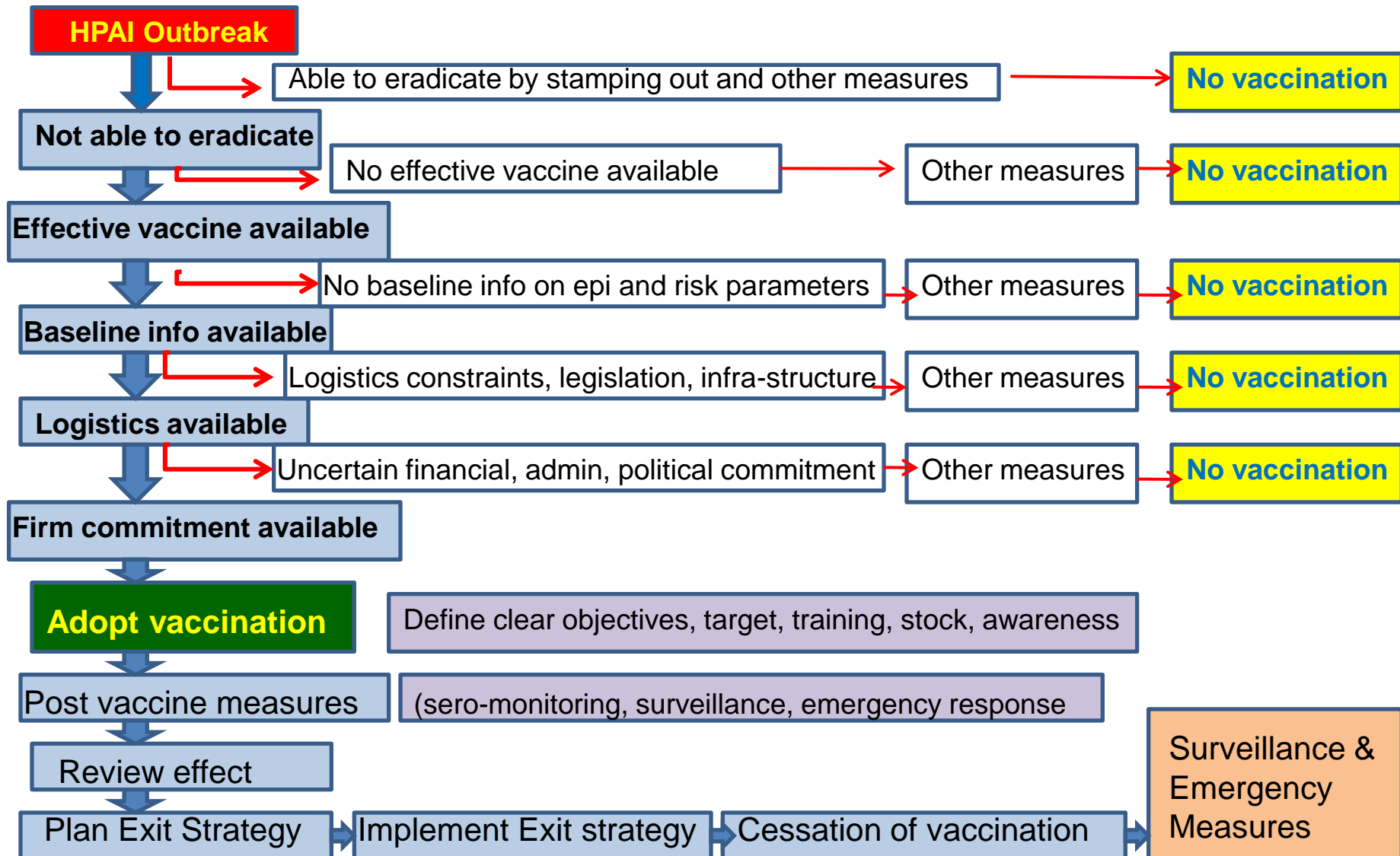
Vaccines		Re-1				Re-5			
Challenge virus (HA clade)		1	2.3.4	2.3.2	2.3.2	1	2.3.4	2.3.2	2.3.2
				A	B			A	B
Mortality of vaccinated birds after challenge		0%	0%	0%	50%	10%	10%	0%	80%
HI antibody titer before challenge (log2)	HI antigen= Vaccine-like virus	7.4	7.9	6.5	6.9	7.4	8.1	7.7	8.0
	HI antigen= Challenge virus							6.8	2.8
Virus excretion in dead birds		NA	NA	NA	+++	+++	+++	NA	+++
Virus excretion in survived birds		+	+	+	+	+	+	+	+

For each experiment 5 non-vaccinated control were included for challenge, and 100% of them died in all experiments.

To pursue a vaccination campaign, it is important to:

- 1. Select the most appropriate vaccine virus strain**
- 2. Closely monitor the circulating viruses from clinical and sub-clinical infections**
- 3. Regularly carry out vaccine efficacy test using recently circulating AI viruses as challenge virus**
- 4. If needed, collaborate with a reference laboratory for quick genetic analysis of circulating viruses**

Logical Vaccination Decision Making Tree



Conclusion

- ❑ Vaccination to be implemented when all other control measures did not help eradicate or control
- ❑ Vaccination is not the final solution to the problem of HPAI
- ❑ Vaccination can be viewed only as a tool to reduce loss of livelihood, food and nutrition crisis, reduce risk of exposure of virus to human
- ❑ There is no example of eradication of HPAI by vaccination in any country