OFFLU avian influenza virus characterisation meeting
29 – 30 March 2017
FAO Headquarters, Rome, Italy

An overview of issues from day 1

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Asia Pacific Veterinary Information Services

Why needed?

- Gs/GD H5Nx, H9N2 not eradicable at present (various well documented reasons) but local elimination possible (zones, compartment, country). Chinese H7N9 is still in terrestrial poultry so theoretical possibility of virus eradication
- Vaccination is still needed to assist in control and prevention of (potential) zoonotic avian influenza at source and (for farmers) to prevent disease – other measures, as applied, are not (always) working
- Currently H5, H7, H9 but need to keep a watch on others widespread in poultry (e.g. H6)
- Continuing emergence of novel strains/clades - a feature of production systems (markets, ducks at interface with wild birds etc), …. and antigenic variation in existing strains

Who needs it?

- All countries that use vaccine or are considering using vaccine need up-to-date information on antigenic characteristics of circulating strains in country and for strains likely to invade and cause disease in poultry – part of recommendations on vaccination
- Some countries already have systems in place that result in vaccine updates (e.g. China, Indonesia – no need to reinvent the wheel but how can OFFLU capture this information) – time lags
- Information must be timely but often little time to get that information (e.g. ensuring supply of appropriate emergency vaccine for intercontinental invasions)
- Need to be sure an antigenic variant is important (Clade 2.3.2.1b)

The process – deciding to deploy vaccine

- Two key initial steps
- Is vaccine likely to be of some benefit in control or prevention of avian influenza
- Objectives of vaccination program – what is/are the goals

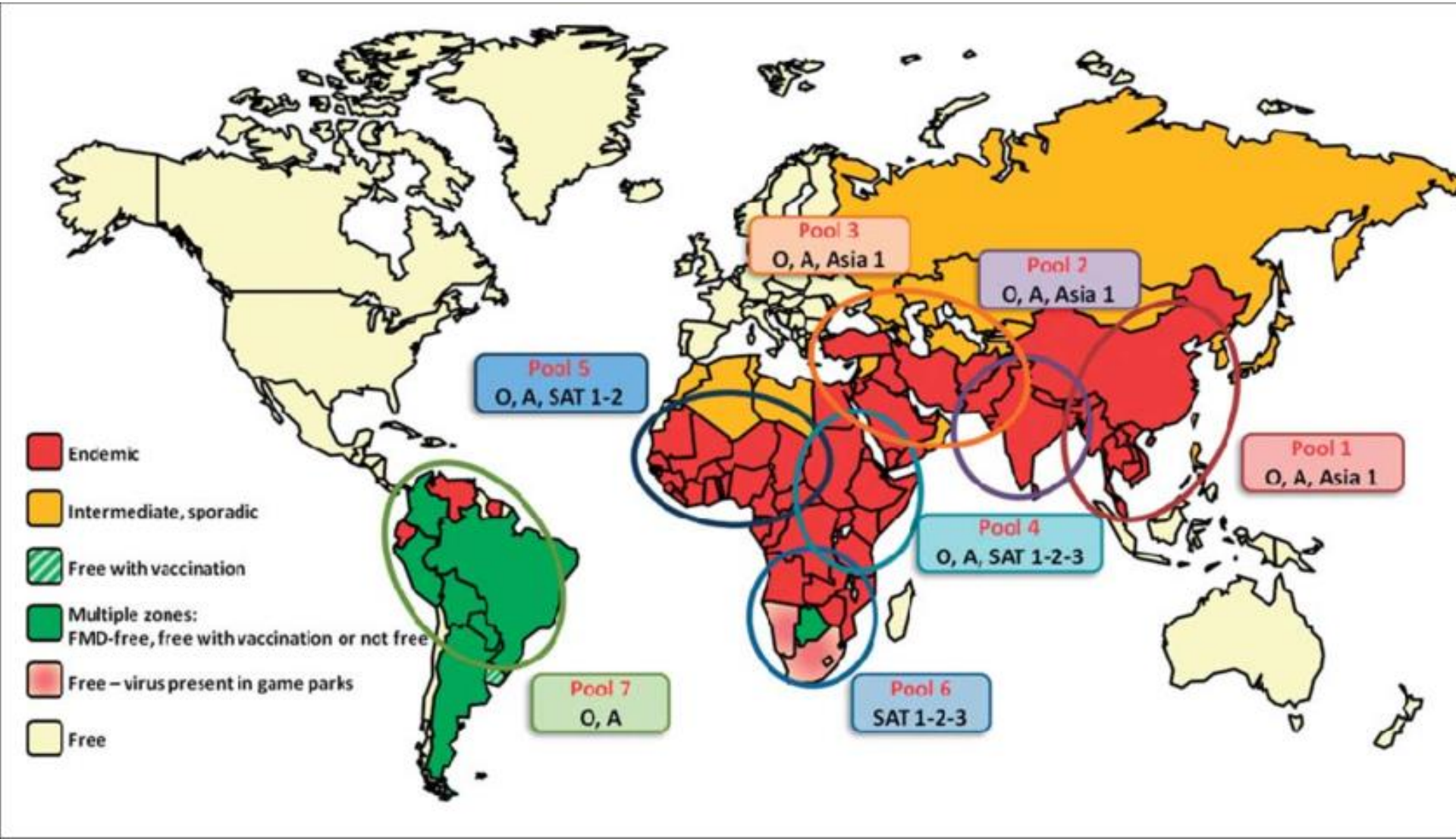
Main question asked by countries considering vaccination?

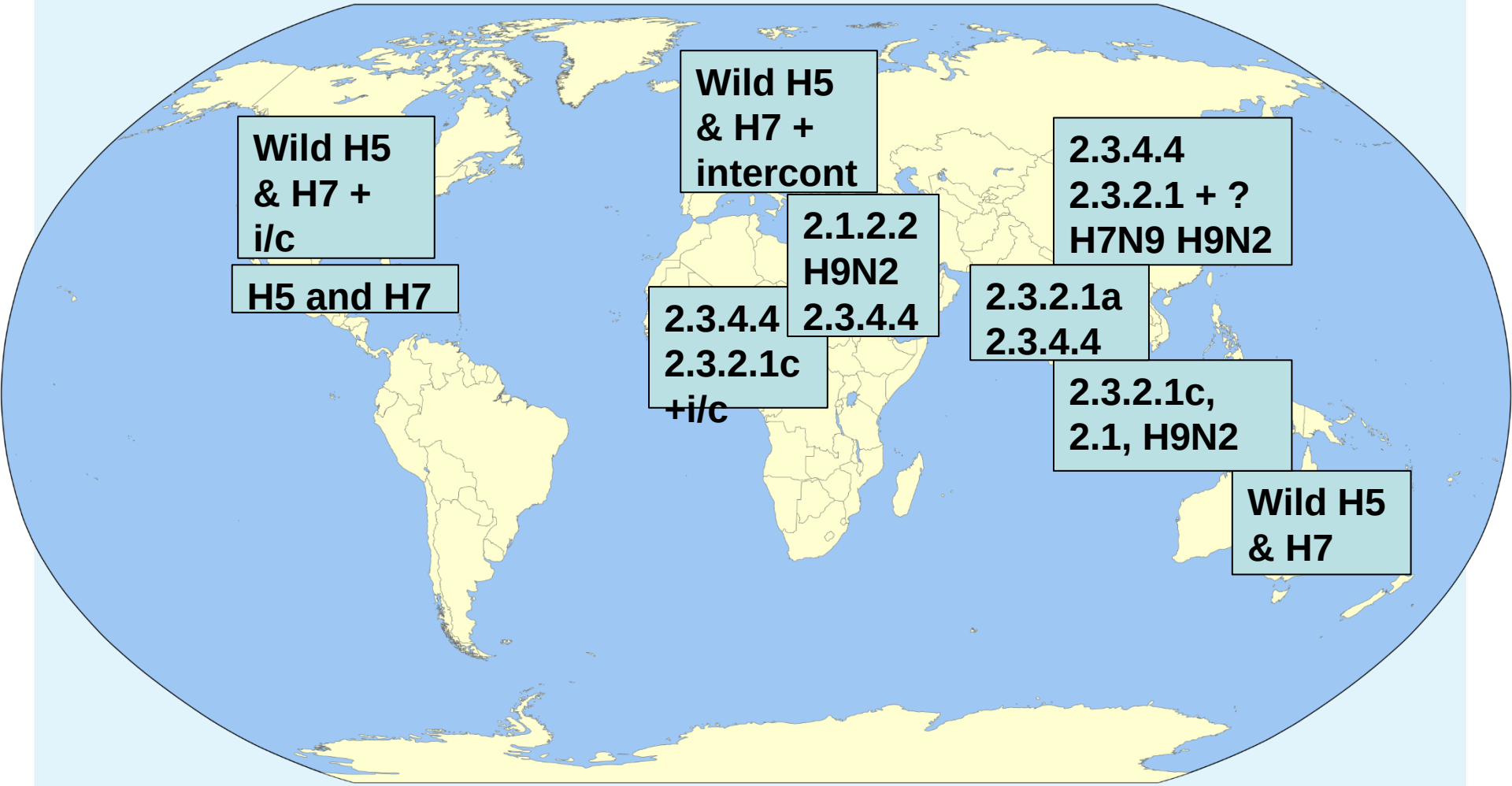
- Which vaccine should I use?
- OFFLU can't and shouldn't provide that information
- But can provide information on available antigens that are reasonably matched antigenically (define), and,
- If available, results of well conducted challenge studies against relevant strain(s) with particular vaccines
- Note issues of vaccine availability even if a suitable vaccine is on the market it may not be immediately available

Other systems in the animal world

- Equine influenza – can utitlise many of the techniques but better data available for horses given value of individual animals and degree of monitoring (especially high performance horses)
- Foot and mouth disease
- Seven virus pools with different recommendations – but limited range of vaccines available

FMD Pools


Pool 3
O, A, Asia 1
Pool 2
O, A, Asia 1
Pool 5
O, A, SAT 1-2
Pool 1
O, A, Asia 1
Pool 4
O, A, SAT 1-2-3
Pool 7
O, A
Pool 6
SAT 1-2-3
Endemic
Intermediate, sporadic
Free with vaccination
Multiple zones:
FMD-free, free with vaccination or not free
Free – virus present in game parks
Free


Wild H5 & H7 + i/c
H5 and H7
Wild H5 & H7 + intercont
2.1.2.2 H9N2
2.3.4.4
2.3.4.4 2.3.2.1c +i/c
2.3.4.4 2.3.2.1 + ? H7N9 H9N2
2.3.2.1a 2.3.4.4
2.3.2.1c, 2.1, H9N2
Wild H5 & H7

Some examples

- West Africa – endemic infection, “illegal” vaccination, previous methods not working, two strains of virus
- South Korea – massive cost of outbreaks and repeated incursions even after successful stamping out (at huge cost) – egg industry wants vaccination – selecting antigen
- North America - local H5 and H7 versus intercontinental H5 strains (so far only once) – stockpiles and emergency vaccination if allowed
- Hong Kong – vaccination for all poultry – needs early warning of antigenic variants (e.g. 2008) – want to use vaccine for H7
- China – how to improve H5 vaccination and whether to use vaccination for H7N9

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What information is already available?

- Material collected for WHO meeting (strains available – both human and avian, and assessed using ferret antisera)
- On-going process of characterisation in countries using vaccination based on genetic and antigenic characterisation of viruses and outbreaks (e.g Clade 7 outbreak in 2006) and in some cases challenge trials (e.g. Viet Nam)
- Published information on vaccine trials and field experiences but quality variable – a lot of unpublished observations
- Various lab tools available and potential for development of improved information

Table 3. Haemagglutination inhibition assays of influenza A(H7N9) viruses.

REFERENCE ANTIGENS	Epidemic wave / lineage	An/1	An/1-RG	Sh/2	Hu/2650-RG
A/Anhui/1/2013	1st	**160**	80	320	320
A/Anhui/1/2013-RG	1st	320	**160**	640	640
A/Shanghai/2/2013	1st	320	160	**640**	640
A/Shanghai/2/2013-RG	1st	320	160	**640**	640
A/Hunan/2650/2016-RG	4th/YRD#	80	40	80	**640**
A/Hunan/2650/2016	4th/YRD	160	40	160	**640**
TEST ANTIGENS					
A/Fujian/2152/2017	5th/YRD	160	40	160	640
A/Fujian/54840/2016	5th/YRD	160	40	160	640
A/Jiangsu/6463/2017	5th/YRD	320	80	160	1280
A/Jiangsu/6454/2017	5th/YRD	80	40	160	320
A/Anhui/60936/2016	5th/YRD	80	40	80	320
A/Jiangsu/60460/2016	5th/YRD	80	40	80	320
A/Hunan/2287/2017	5th/YRD	160	40	80	640
A/Hunan/6948/2017	5th/YRD	40	<†	80	320
A/Anhui/60933/2016	5th/YRD	<	<	<	<
A/Guangdong/60060/2016	5th/PRD‡	320	160	640	320
A/Guangdong/17SF004/2017	5th/PRD	320	160	640	640
A/Guangdong/60061/2016	5th/PRD	160	80	320	320
A/Guangdong/17SF003/2016§	5th/ YRD	<	<	<	80
A/Guangdong/17SF006/2017§	5th/ YRD	40	<	40	160

Yangtze River Delta lineage; † represents a haemagglutination inhibition titre of <40; ‡ Pearl River Delta lineage; § HPAI viruses

Many factors determine efficacy and effectiveness of vaccine/vaccination

- Not just the antigen but clearly getting that wrong makes it harder to generate a good immune response to circulating strains (US experiences with H5N2 outbreak and vaccines)
- Lab versus field
- Species differences
- Introduction of new strains (e.g. Indonesia with 2.3.2.1c)

Ideal system

- Would have early information on all emerging strains
.
- Would be able to advise countries on which vaccines are able to provide good protection for the relevant strain(s) from existing and new studies
- Would have the capacity to conduct rapid standardised vaccine efficacy studies or obtain this information from elsewhere
- Would have valid scientific information on vaccine effectiveness in places where it is used including information on vaccine breakdowns
- Costs and resources prohibitive

First steps

- Inventory of vaccines – provides information on available antigens and formulation (invite vaccine manufacturers to provide) – not a form of endorsement by OFFLU
- Access to vaccine antigens for production of antisera
- Collection of “reference” strains (use WHO candidate vaccine strains as a baseline?) – but keep list up to date – e.g. no need today for Clade 0, 1, some clade 2 derivatives and clades 3 to 9) – use WHO process as a flag for possible antigenic variants
- Able to provide information on antigenic characteristics against a relevant antigens
- Strong disease intelligence for strains on the move and rapid access to isolates (not always possible) – e.g. recent example of Uvs-Nuhr virus – prepublication of antigenic characterisation

Two pillars - related but separate issues

- 1. Evidence of antigenic variation that has the capacity to affect vaccine efficacy/effectiveness
- 2. Standardised protocol for challenge studies to measure vaccine efficacy
- Many unresolved issues with this (OIE standard only a starting point)
- Need more nuanced approach than just % survival - e.g. failure to prevent systemic infection in the face of antibody
- Percent reduction in shedding very important in birds with immune response to vaccine
- Existing SEPRL model seems to have delivered useful results but transmission not included

Nimble system needed

- Gs/GD H5 - Don't always get a lot of warning
- Europe/Middle East/Africa - virus in southern Russia/Tibetan plateau
- North America – virus in East Asia in wild birds in Autumn or in NE Russia
- .Not necessarily consistent with an "annual" meeting
- Short annual report likely useful but will be demands for information at other times

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Gaps

- Limited number of suitable vaccines
- Ideal world – each new antigenic variant would be tested against vaccines in use (or those being considered) with a standardised protocol
- Pre-emptive vaccination for countries at high risk – difficulty in choosing antigen
- Serological DIVA complicated in areas with multiple subtypes circulating (e.g. Indonesia – before and after H9N2) – not the main concern in places where virus is endemic
- Vaccines for mass administration in the face of outbreaks
- Better vaccines for ducks (killed vaccines as applied protecting from disease but probably having limited effect on shedding)

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Other issues

- Continue promoting responsible use of vaccines (see e.g. FAO guide – aiming for high level immunity in the vaccinated population and vaccination programs with clear objectives)
- Vaccines do have a role to play for endemic diseases while developing capacity for elimination
- Antigenic variants arise when there are opportunities for virus to multiply
- If vaccines are used there will be a need for regular updates but frequency varies (e.g. Clade 1 in Viet Nam)
- Vaccine is being used as a response to endemic infection not the primary cause (H5, H9)