



World Health
Organization

Update on AI vaccines and their potential use in pandemic settings

Dr Jean-Marc Olivé

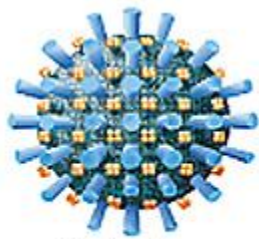
WHO Representative to Viet Nam

Presentation Outline

- | Update on H5N1 human vaccines
- | Global Action Plan on Pandemic vaccine supply
- | WHO grant activities in six developing countries
- | WHO H5N1 vaccine stockpile and possible use



Current Influenza Vaccines



Whole virus



Split virus



Subunit
(surface antigen)



Live attenuated

(Source: IFPMA)



H5N1 'pandemic' influenza vaccine trials

- 16 manufacturers from more than 10 countries developing prototype pandemic H5N1 vaccines.
- Aluminum adjuvanted split vaccines have shown modest increase in immunogenicity over unadjuvanted vaccines, but not sufficient to allow significant dose sparing.
- Some split and subunit vaccines formulated with proprietary adjuvants (such as MF59 and AS) show encouraging increase in immunogenicity.
- Some studies suggest that vaccination with currently available H5N1 prototype vaccines can also induce some cross-protection against antigenically drifted H5N1 viruses, similar to what is seen with seasonal influenza viruses.



H5N1 'pandemic' influenza vaccine

– **H5N1 vaccines are a relatively new development, so limited information on:**

- Safety
- Efficacy
- Degree and duration of protective effect



Immunogenicity (HI*) of H5N1 Vaccines

US-Study; A/Vietnam/1203/H5N1 (NEJM 354 1343-51)

Vaccine dose (ug)	GMT at baseline	28 days after 1 st dose of vaccine		28 days after 2 nd dose of vaccine		GMT after 2 nd dose
		No. tested	% with Ab	No. tested	% with Ab	
90	10.4	102	28%	99	57	46
45	10.8	98	23%	93	41	32.9
15	10.3	101	10%	100	24	18.3
7.5	11.4	100	5%	95	13	14.2
Placebo	10.6	48	0%	48	0	10.3



EU H5N1 Vaccine 'Mock-Ups'

- | GSK Daronrix H5N1 Mock-up vaccine March 2007
 - Whole virus, inactivated, alum-adjuvanted.
 - Derived from A/Viet Nam/1194/2004 (H5N1) virus. 2 dose.

- | Novartis 'Focetria' H5N1 Mock-up vaccine May 2007
 - Derived from A/Viet Nam/1194/2004 (H5N1).
 - Adjuvanted (MF95) - 2 dose schedule, low Ag

- | Only for use during a declared pandemic
 - Still require inclusion of the matching pandemic influenza vaccine strain into the vaccine but **faster approval**.
 - Need to give protective Ab levels in at least 70% of people



Global Action Plan on Influenza Vaccine

- | In order to strengthen pandemic-influenza preparedness and response, WHA 58.5 requested to WHO secretariat to seek solutions *with international and national partners, including the private sector*, to reduce the potential global shortage of influenza vaccines for both epidemics and pandemics, including vaccination strategies that economize on the use of antigens, and development and licensing of antigen-sparing vaccine formulations.



Global Pandemic Influenza Action Plan to Increase Vaccine Supply (GAP)

Objective:

To increase the supply of a pandemic vaccine and thereby reduce the gap between the potential vaccine demand and supply anticipated during an influenza pandemic .

- | **Increase in seasonal vaccine use**
- | **Increase in vaccine production capacity**
- | **Further research and development**



Increase in Vaccine Production Capacity

- | Improving production yields and immunogenicity for vaccines based on H5N1 influenza strains
- | Building new production plants in both developing and industrialized countries
- | Focusing on further development of adjuvanted vaccines with adjuvants widely used in licensed vaccines
- | Evaluating the potential for delivering vaccines by alternative routes – for example, the intradermal route, using needle-free delivery devices such as jet injectors



Country List of Awardees

- | Brazil (Instituto Butantan)
- | India (Serum Institute of India)
- | Indonesia (BioFarma)
- | Mexico (BIRMEX)
- | **Thailand (GPO)**
- | **Vietnam (IVAC)**



“Projected supply of pandemic influenza vaccine sharply increases”

23 OCTOBER 2007 | GENEVA –

Recent scientific advances and increased vaccine manufacturing capacity have prompted experts to increase their projections of how many pandemic influenza vaccine courses can be made available in the coming years.

Last spring, the World Health Organization (WHO) and vaccine manufacturers said that about 100 million courses of pandemic influenza vaccine based on the H5N1 avian influenza strain could be produced immediately with standard technology.

Experts now anticipate that global production capacity will rise to **4.5billion** pandemic immunization courses per year in 2010.



Rationale for WHO H5N1 vaccine stockpile

- Resource poor countries considered that HPAI H5N1 virus to be a national security and public health threat (especially those with human cases due to H5N1 infections)
- These countries also perceived that they **do not** have access to this vaccine:
 - Timely access
 - Quantities required
 - At an affordable price



WHO Global Stockpile

- | Currently no doses in WHO hands but promise from one manufacturer (GSK) of 1M doses
 - Likely to make more available
 - Also making tiered pricing system for developing countries
- | Other manufacturers have also expressed an interest
 - Estimating 6 M within next years.
- | How much is needed for developing countries?
 - Estimate 30 M doses
 - Rough estimate assuming coverage for 1% of the 3B people in countries with average per capita income <\$1000



Possible Uses of Stockpile

- | Many questions to answer, often with little evidence base to make decisions
- | Is there a role for pre-pandemic vaccination?
- | Is there a role in pandemic containment operations?
- | How would pandemic vaccine stockpile be distributed during a pandemic?



Role for Pre-Pandemic Vaccination?

- | Priming dose for general population?
 - Part of a two-dose strategy
 - Second dose given after pandemic strain is available
 - People given the two doses of vaccine necessary to provoke immunity in a naïve individual.
 - Public acceptance?

- | Protection for people in H5N1 affected countries?
 - Not enough to immunise everyone, especially with 2 doses
 - Prioritize by high-risk? How do you define high-risk? Most vulnerable, protect essential functions?
 - Public acceptance – may be higher if risk perception higher



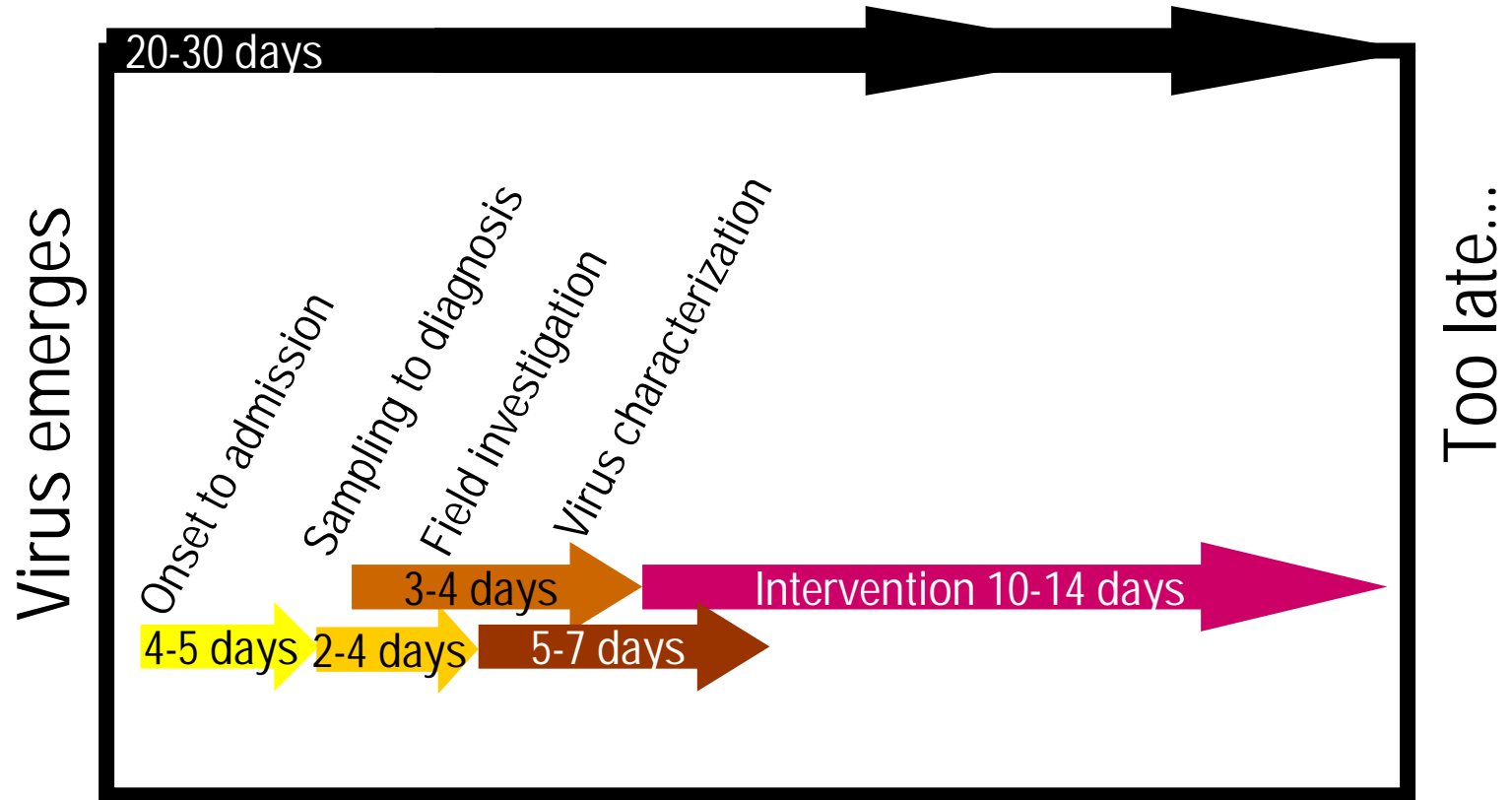
Role in Pandemic Containment?

- | That is, controlling an H5N1 outbreak where the virus shows high pandemic potential

- | Modelling says Yes....maybe
 - Should increase your chance of control of discrete outbreaks **IF** used in addition to other measures.
(e.g. anti-virals, social distancing, movement restrictions)
 - Assumes reasonably close match with vaccine
 - Requires very wide vaccination belt around the outbreak
e.g. 1-2M vaccinees in a semi-urban setting.
 - Risk of distracting resources from other containment activities?
 - Is timely delivery feasible?



Timely Rapid Response and Containment RRC



Role in a Declared Pandemic?

- | Assumes reasonably close match with stockpile vaccine. i.e. H5N1 or very close.
- | Distribution in the setting of a major influenza pandemic a major challenge
- | Equitable distribution a much greater challenge.
 - Which countries?
 - Who first in the country?
 - Whom to vaccinate
- | One or two dose strategy?
 - More people/less protection Vs Less people /more protection?



WHO H5N1 Vaccine Review Process

- | WHO Scientific Mtg on H5N1 Vaccines 1-3 Oct 2007
 - Technical considerations for developing options for use of human H5N1 influenza vaccines and a WHO H5N1 vaccine stockpile

- | WHO SAGE Committee on H5N1 Vaccines 6-11 Nov
 - To review technical considerations from scientific mtg and make recommendations on how the H5N1 vaccines and the WHO H5N1 vaccine stockpile should be used.

- | WHO Intergovernmental Meeting on Pandemic Influenza Preparedness (20-23 Nov) Geneva

