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**Meeting on Options for increasing the access of  
developing countries to H5N1 and other potential  
pandemic vaccines**

**Industrialized country perspectives  
on increasing access to potential  
pandemic influenza vaccines**

**Presentation by Dr. Gaudenz Silberschmidt**

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## Situation 2005/2006

- Insufficient production capacity
- Hardly any cross-protection → excluding the scope for stockpiling
- Most of the capacity used for seasonal flu vaccine production



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## Current situation: industry

- Companies are increasing capacity for antigen production (industrial plants) from 300 Mio. Trivalent 15µg towards doubling over the next few years on egg based technology (+ cell culture technology)
- Limited spare capacity is available now (window between northern and southern hemisphere production periods, some plants produce only for one hemisphere)



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## Current situation: industry

- Two companies bring novel adjuvants to the market
- Decrease of antigen dosage necessary through adjuvants → increase of number of doses available
- Necessity to follow closely and confirm by independent testing these recent developments

## H5N1 heterologous challenge

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### ■ Protection data on Day 5 post-challenge

	<b>Dead**</b>	<b>Alive</b>	<b>% survival</b>
<b>AS alone</b>	6	0	<b>0</b>
<b>Unadjuvanted H5N1 (15 µg)</b>	6	0	<b>0</b>
<b>H5N1 – AS (1.7 µg)</b>	1	5	<b>83</b>
<b>H5N1 – AS (3.8 µg)</b>	0	6	<b>100</b>
<b>H5N1 – AS (7.5µg)*</b>	0	5	<b>100</b>
<b>H5N1 – AS (15 µg)</b>	0	6	<b>100</b>

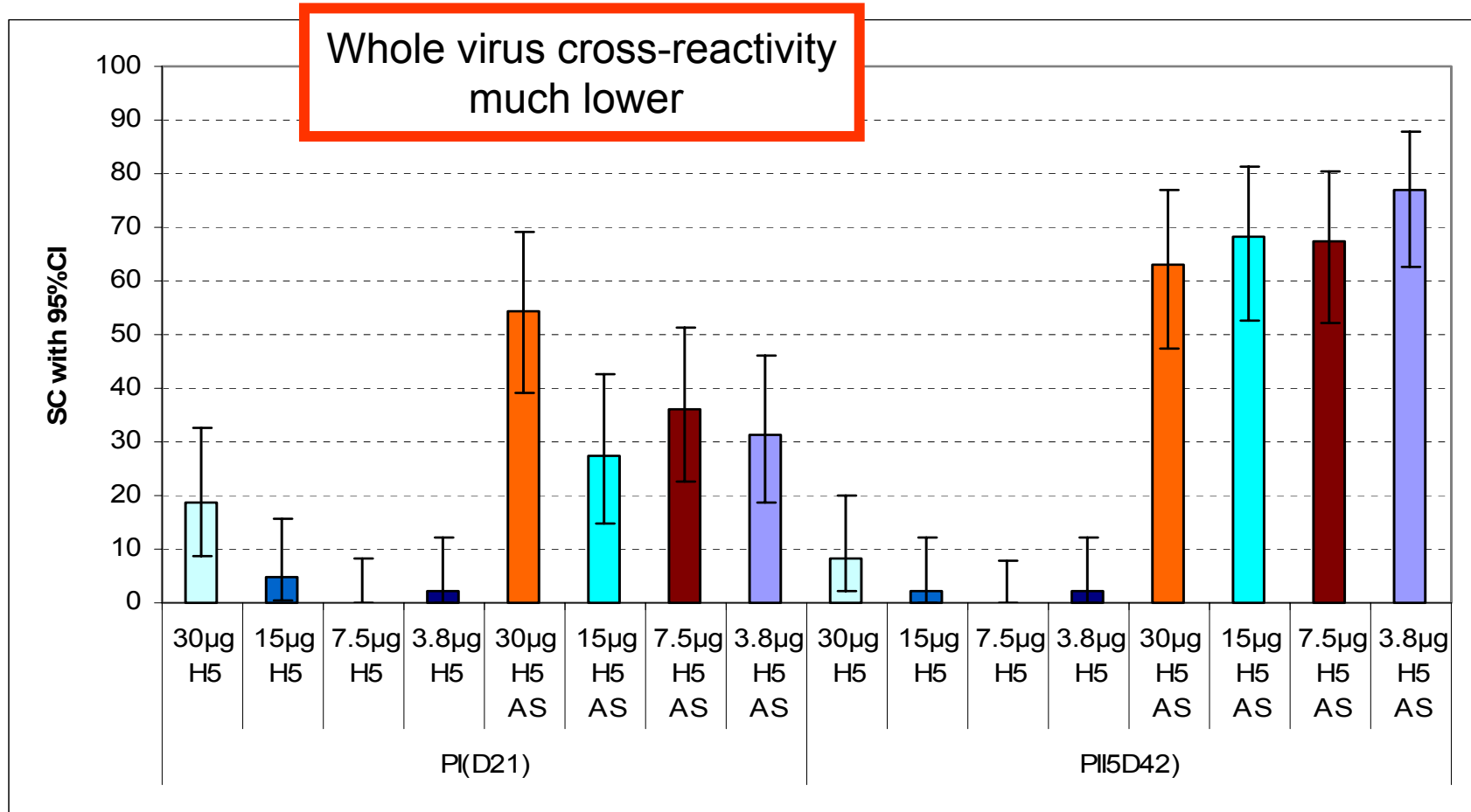
\* The challenge of one animal from the 7.5 µg vaccinated group was not compliant to protocol guidelines and was excluded from the data recording process

\*\* Ferrets died or were euthanized (moribund sacrifice) on day 3 or 4 post-challenge

**Full cross-protection with AS-split vaccine  $\geq$  3.8 µg**



## Neutralization assay: Seroconversion rates against A/Indonesia/5/05 heterologous strain





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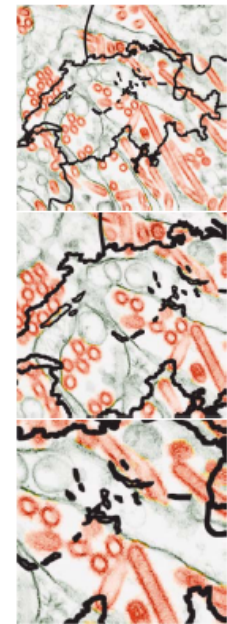
## Swiss strategy

National pandemic plan with 4 pillars:

- society preparedness (contingency planning)
- public health measures
- Antivirals
- Vaccines

### Swiss Influenza Pandemic Plan 2006

Strategies and measures in preparation for an influenza pandemic



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## Current situation: globally

- Countries and WHO have to develop their strategy while technology is advancing
- Different situations according to countries, also amongst industrialized countries
- National circumstances matter (host or not to production plants, budget, national strategy, priorities, etc.)



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## Swiss strategy

- Stockpiling of one dose of H5N1 pre-pandemic vaccine for the entire population
- Advanced purchasing contract for pandemic vaccine (one dose) for the entire population
- Testing of actual cross-reactivity in pandemic phase 4
- Voluntary vaccination with pre-pandemic vaccine from level 4/5 of WHO pandemic phases



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## Swiss strategy

### Description of product:

- two components stored separately (antigen and oil in water adjuvant)
- good results for cross-protection H5N1 clade 1 (Vietnam) to clade 2 (Indonesia) with
- 2 doses monovalent 3.75 µg antigen + novel adjuvant give good cross-protection
- no guarantee for protection against future pandemic strain



## Difficulties encountered implementing the strategy

- Complexity of purchasing process and logistics
- Needed to change the law on epidemics to give a legal basis for the purchase
- High costs (overall contract volume of 150 millions USD)
- Need to find a way to negotiate the purchase of a not yet registered product
- Risk of investing without using the product (no pandemic during shelf live or insufficient cross-protection)



## Context

- Such a strategy is always a compromise;  
we chose 1dose prepandemic+1 dose pandemic vaccin for the whole population  
others might take 2+0 or 2+1 or 1+1 for medical personnel and risk groups; we have multidose vials, others might stock bulk
- Strategy is dependent on national circumstances: Switzerland has no local production, readiness to invest in preparedness
- Swiss purchase contribute to increase of global production capacity
- Key to pandemic preparedness is a national plan with hygiene measures complemented as appropriate by antivirals and/or vaccine



## Towards internationally coordinated strategies: technical work needed

- Independent tests of the available products
- Test shelf live of adjuvant and antigen
- Testing of combinations of adjuvant from one and antigen of other producers
- Need to determine precisely the minimum effective dosage to maximize production capacity (currently 3.75 or 7.5 µg might go lower)
- Rapid registration and WHO pre-qualification while respecting all quality standards



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## Towards internationally coordinated strategies: policy work needed

- Explore option for WHO stockpile (donation and/or international financing)
- Elaborating strategy for use of a potential international stockpile (indications, logistics, etc.)
- Need for engagement of producing countries to honor export commitments
- Study liability issues
- Allow differential pricing



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## Towards coordinated strategies : learn from experience with oseltamivir

- Donation from industry to WHO
- Increase of production capacity
- Joint ventures with voluntary sublicenses
- Differential pricing
- Higher announcement of demand than actual orders
- Revolving articles and fears of side-effects, etc.



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## Conclusion

- Global production capacity is increasing dramatically (>20x over a few years)
- Limited international stockpiling in addition to national preparedness of pre-pandemic vaccine could quickly become an option
- Technical details need to be worked out before taking a decision
- Engage in a constructive dialogue with industry
- We are happy to work with WHO on the follow up