



GSK's Pandemic Vaccine Development

From 1st to 2nd Generation Candidate Vaccines

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GSK's pandemic vaccine development

From 1st to 2nd generation candidate vaccine

- Search for antigen sparing approach to address global pandemic vaccination needs
- 1st candidate vaccine developed
 - Whole virus
 - Alum adjuvanted
- Program initiated in 1997 (1st H5N1 outbreak)
- Registration submitted to EMEA in December 2005
- Positive CHMP opinion in December 2006
- 2nd generation vaccine development started in 2005
- Clinical development continued with H5N1 candidate vaccines in 2006 (1st and 2nd generation)

Whole virus vaccine development

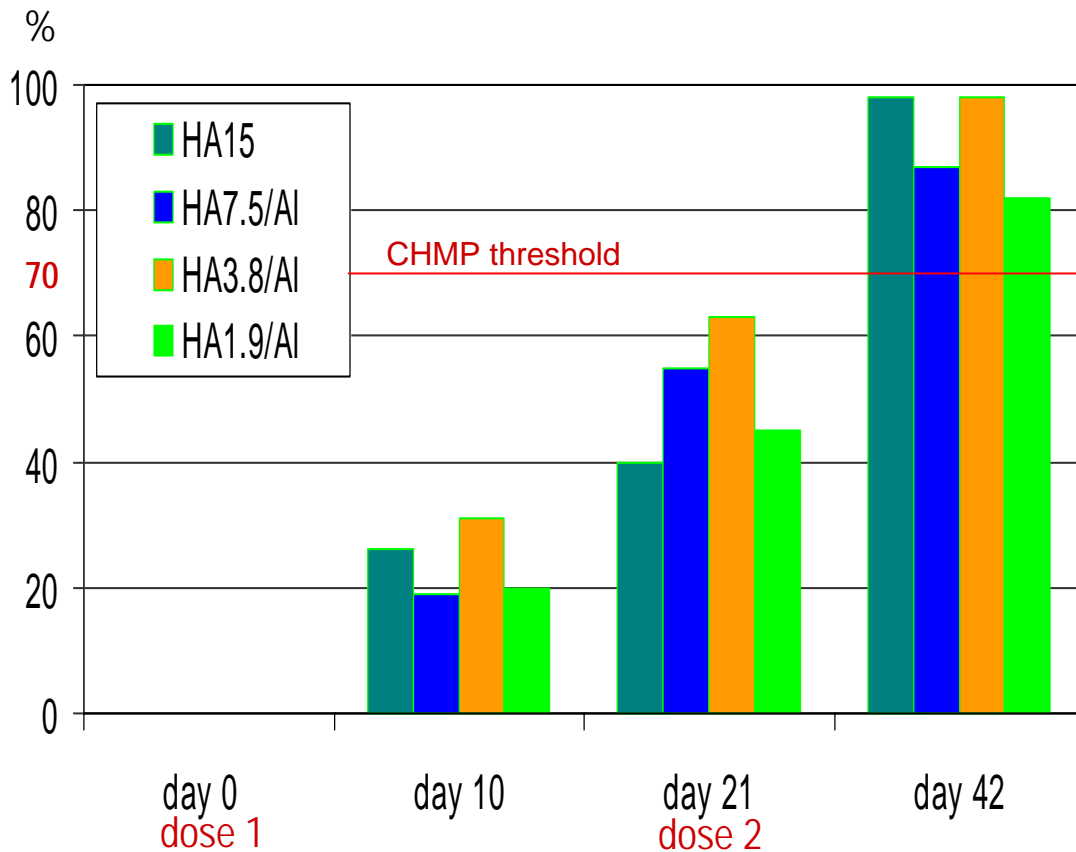
History of clinical trials

Study ID	Objective	N immuno	N safety	N compar.
<i>Flu 033</i>	<i>exploratory (primed pop.)</i>	400	400	100
Flu 037	reacto (whole v. + AI)	-	200	50
Flu 038	immuno H2N2	200 + 200	400	50 + 50
Flu 041	immuno H9N2	200	200	50
Flu 045	immuno H9N2	50	50	-
Flu 059	immuno H9N2	375	375	55

Whole virus vaccine development

H2N2 vaccine data

H2N2: Seroprotection rates in adults aged 18 – 30 years



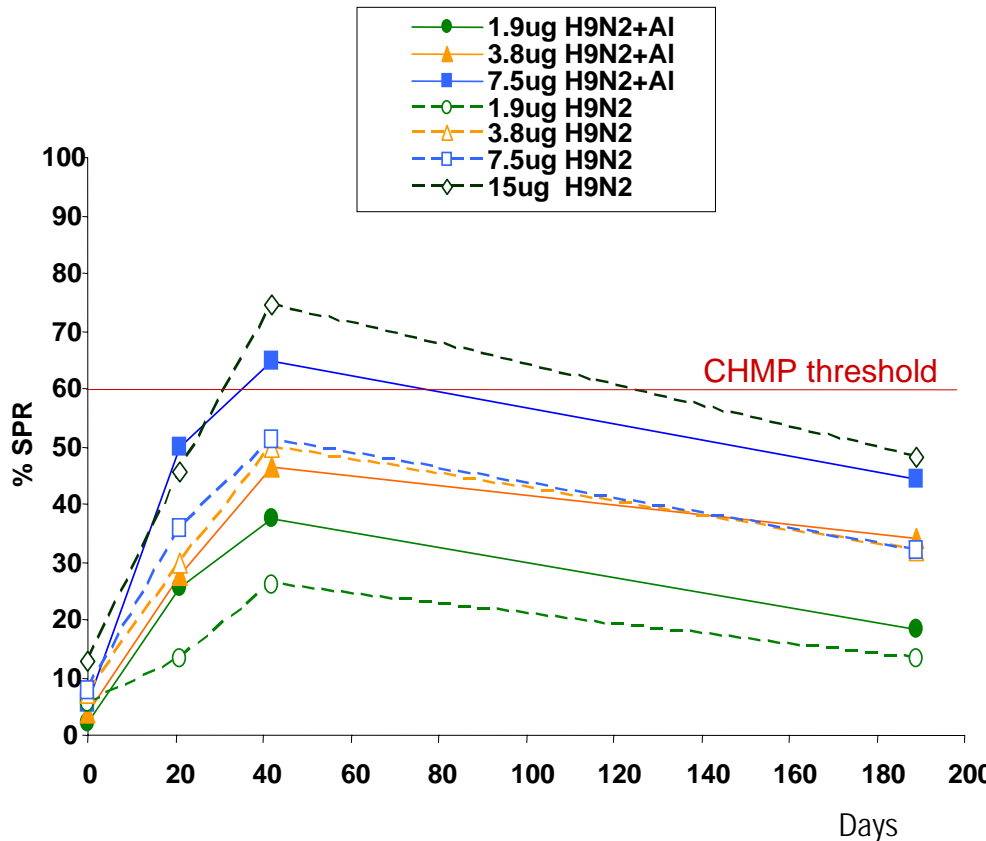
- Protective titers were reached after two doses
- Seroprotective **HIT** levels were met by alum adjuvanted whole virus vaccines with **4 to 8 fold reduced HA** content in adults
- Supported by **neutralizing Ab** results

Source: Hehme N et al.: Virus Res. 2004; 103:163-71, Hehme N et al.: Med Microbiol Immunol. 2002; 191:203-8

Whole virus vaccine development

H9N2 vaccine data

H9N2: Seroprotection rates in elderly aged >60 years



- Protective titers were reached after two doses
- Seroprotective HIT levels were met by alum adjuvanted whole virus vaccines with 4 to 8 fold reduced HA content in adults
- Supported by neutralizing Ab results (H2N2 study)
- Avian viruses and elderly target populations might require **higher HA contents** (H9N2 studies)

Whole virus vaccine development H5N1 trial

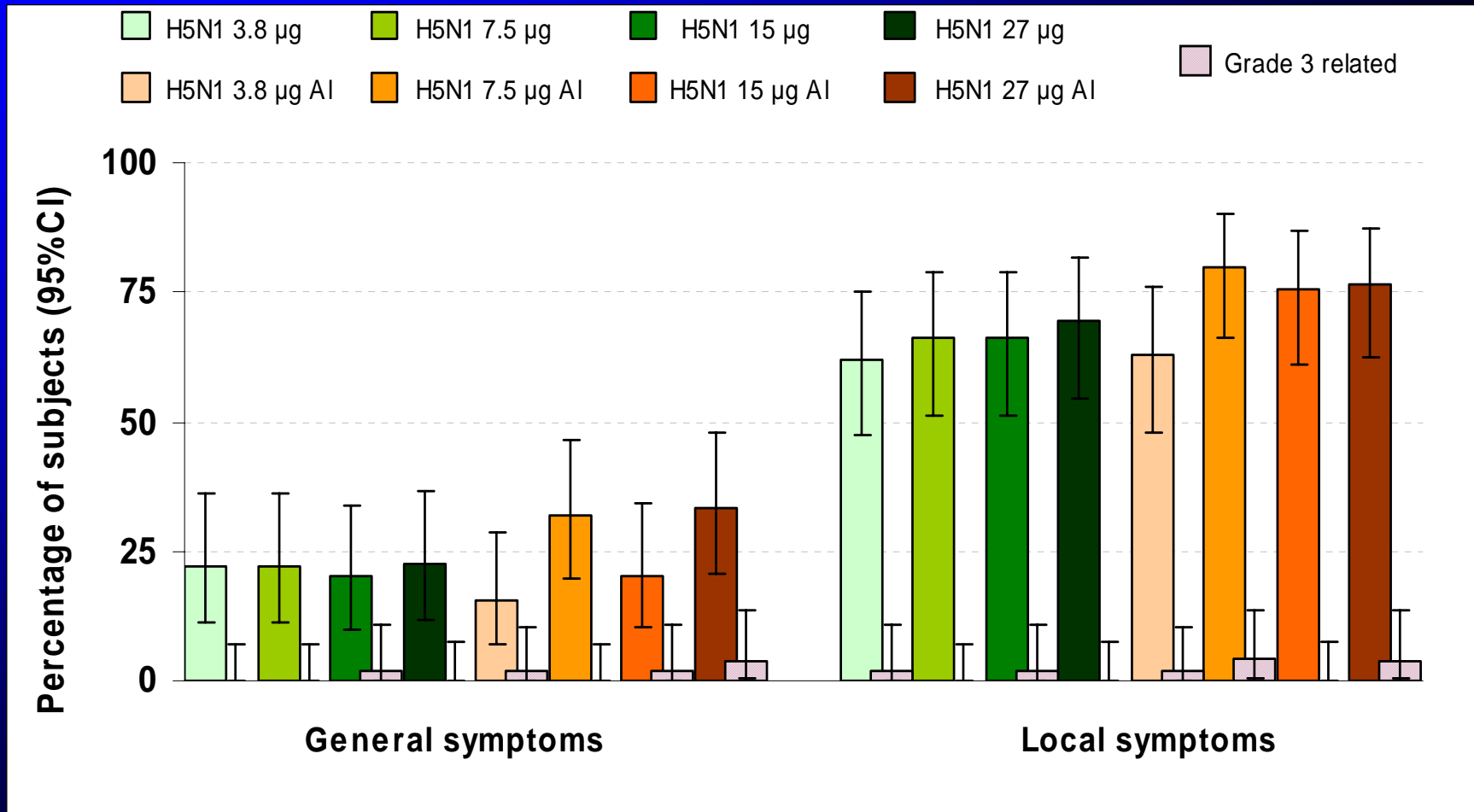
- Observer-blind, randomized, multi-center study (Germany)
- Study population: 400 adults aged 18 – 60 years
- Study vaccine: A/Vietnam/1194/2004 (H5N1) – NIBRG-14

Study groups								
Subjects (n)	50	50	50	50	50	50	50	50
HA (µg)	3.8	7.5	15	27	3.8	7.5	15	27
Adjuvant	-	-	-	-	alum	alum	alum	alum



H5N1 whole virus vaccine

Reactogenicity results



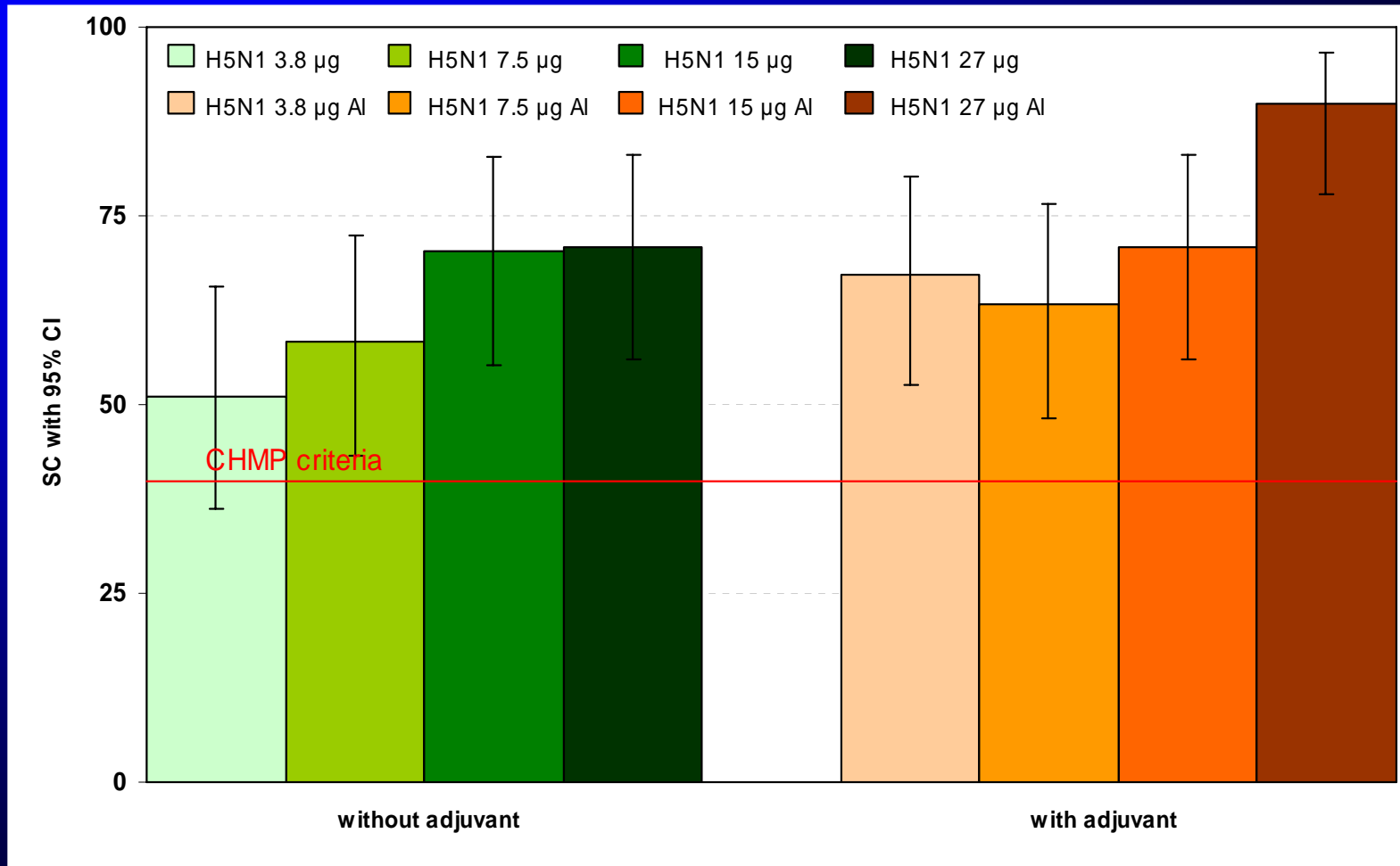
H5N1 whole virus vaccine

Safety & reactogenicity

- No SAE was reported
- Rates of local and general symptoms tended to be higher in subjects with alum adjuvanted vaccines
- No statistically significant differences
- By far most symptoms were mild and transient

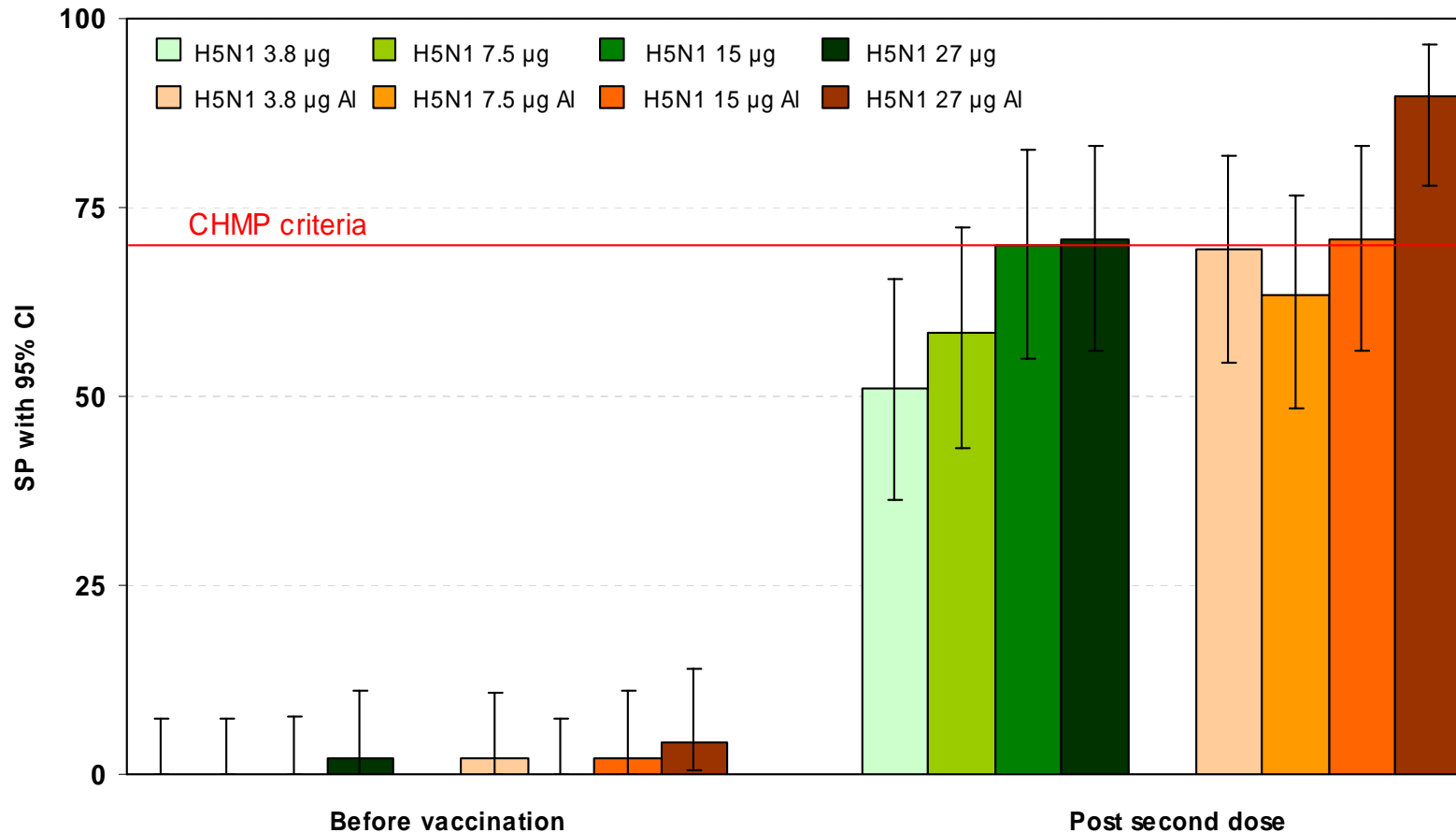
H5N1 whole virus vaccine

Immunogenicity: SC rate (HI)



H5N1 whole virus vaccine

Immunogenicity: SP rate (HI)



H5N1 whole virus vaccine

Immunogenicity: Summary CHMP criteria

Day 42	N	Seroconversion Rate ≥40 %	Seroprotection Rate ≥70 %	Geometric Mean-fold GMR ≥2.5
H5N1 - 27µg	46	71.7	71.7	14.7
H5N1 - 15µg	46	69.6	69.6	10.7
H5N1 - 7.5µg	47	57.4	57.4	7.9
H5N1 - 3.8µg	49	51.0	51.0	5.7
H5N1 - 27µg+Al	47	91.9	91.9	30.5
H5N1 - 15µg+Al	46	71.7	71.7	14.3
H5N1 - 7.5µg+Al	45	62.2	62.2	10.2
H5N1 - 3.8µg+Al	45	68.9	68.9	12.2

- Non adjuvanted vaccines: **27 µg HA/dose** fulfilled all CHMP criteria
- Alum adjuvanted vaccines: **15 µg HA/dose** fulfilled all CHMP criteria

Split virus vaccine development H5N1 trial

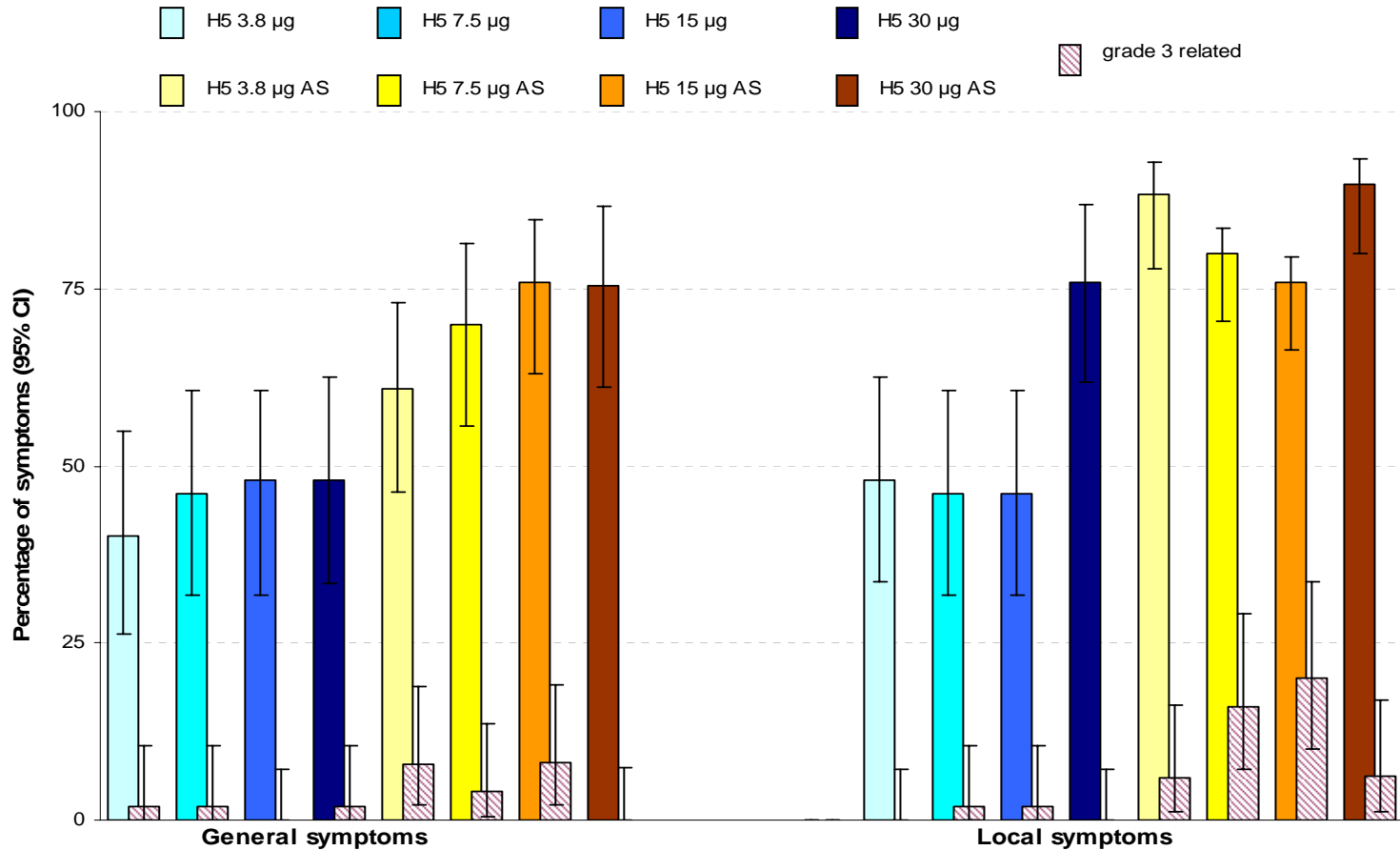
- Observer-blind, randomized, mono-center study (Belgium)
- Study population: 400 adults aged 18 – 60 years
- Study vaccine: A/Vietnam/1194/2004 (H5N1) – NIBRG-14

Study groups								
Subjects (n)	50	50	50	50	50	50	50	50
HA (µg)	3.8	7.5	15	27	3.8	7.5	15	27
Adjuvant	-	-	-	-	AS	AS	AS	AS



H5N1 split virus vaccine

Reactogenicity results



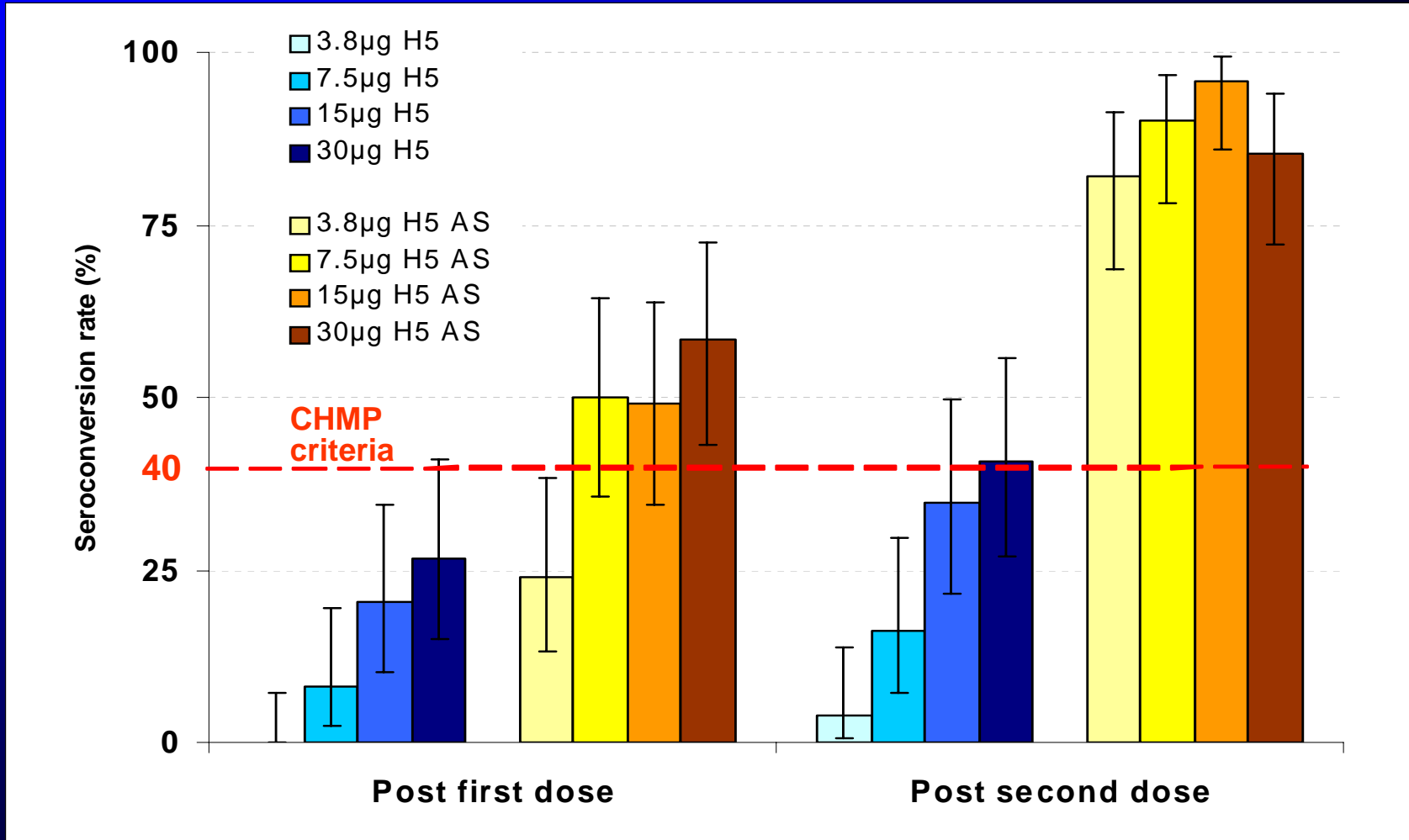
H5N1 split virus vaccine

Safety & reactogenicity

- No SAE was reported
- The AS-adjuvanted pandemic prototype vaccine induced more local and general symptoms
- Most symptoms were mild or moderate and transient
- The safety profile of all four adjuvanted groups was clinically acceptable

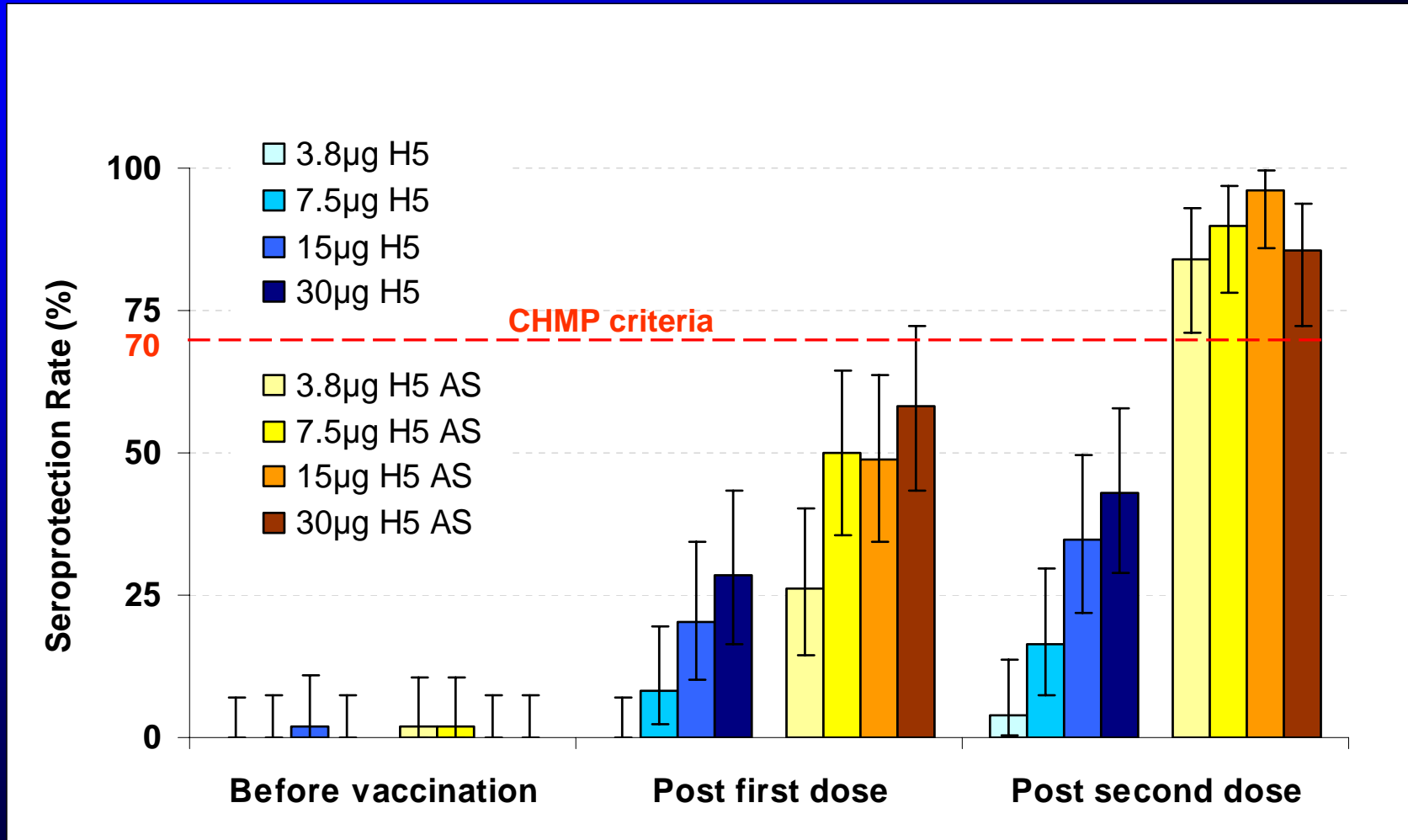
H5N1 split virus vaccine

Immunogenicity: SC rate (HI)



H5N1 split virus vaccine

Immunogenicity: SP rate (HI)



H5N1 split virus vaccine

Immunogenicity: Summary CHMP criteria

Day 42	N	Seroconversion Rate ≥40 %	Seroprotection Rate ≥70 %	Geometric Mean-fold GMR ≥2.5
H5N1 - 30µg	49	40.8	42.9	3.9
H5N1 - 15µg	49	34.7	34.7	2.8
H5N1 - 7.5µg	49	16.3	16.3	1.7
H5N1 - 3.8µg	50	4.0	4.0	1.2
H5N1 - 30µg+AS	48	85.4	85.4	36.4
H5N1 - 15µg+AS	49	95.9	95.9	60.5
H5N1 - 7.5µg+AS	50	90.0	90.0	38.1
H5N1 - 3.8µg+AS	50	82.0	84.0	27.9

- All AS adjuvanted groups met CHMP criteria after 2nd dose
- None of the non-adjuvanted groups fulfilled all 3 CHMP criteria
- 83...100% of subjects in adjuvanted groups seroconverted (neutralization assay)

GSK's pandemic vaccine development

Next data releases

Key data further supporting GSK split / AS vaccine candidate selection will be communicated at upcoming scientific meetings

- Cross-protection in animal model
- Cross-reactivity of immune response

- Large-scale safety trial

IX International
Symposium on
Respiratory Viral
Infections
HongKong, March 2007

Options for the
Control of Influenza
VI
Toronto, June 2007

GSK's pandemic vaccine development Summary

- Both H5N1 alum adjuvanted whole virus and AS adjuvanted split virus candidate vaccines provided acceptable safety and reactogenicity profiles
- Clinical data of GSK's 2nd generation candidate vaccine support a 4-fold better antigen-sparing potential
- Additional data supporting selection of the split AS candidate vaccine will be disclosed at upcoming scientific meetings
- Split / AS vaccine developed both as pre-pandemic and pandemic vaccine; registration files submitted at EMEA