

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

<b>Study No.:</b> 113462 (FLU D-PAN H1N1-009)
<b>Title:</b> Safety and immunogenicity study of GSK Biologicals' pandemic influenza candidate vaccine (GSK2340272A) in children aged 6 to 35 months. GSK2340272A (Flu 1): GlaxoSmithKline (GSK) Biologicals' Pandemic influenza vaccine comprising 1.9 µg haemagglutinin (HA) from the A/California/7/2009 (H1N1)v-like strain combined with AS03 <sub>B</sub> adjuvant. GSK2340272A (Flu 2): GSK Biologicals' Pandemic influenza vaccine comprising 3.75 µg HA from the A/California/7/2009 (H1N1)v-like strain combined with AS03 <sub>A</sub> adjuvant.
<b>Rationale:</b> The aim of the study was to assess the safety and immunogenicity of a 2 doses schedule of Flu 1 or Flu 2 vaccines in children aged between 6 and 35 months. Note: This summary presents results up to Day 42 and will be updated when additional data become available. The Company has decided not to move forward with the booster dose as was previously planned in the protocol. Therefore, the protocol has been amended to cancel the booster phase. The step 3 of the enrolment schedule has been cancelled too. As a consequence several sections of this summary were updated.
<b>Phase:</b> II
<b>Study Period:</b> 10 September 2009 to 19 January 2010 (Data Lock Point Day 42)
<b>Study Design:</b> Randomised, open-label study with two parallel groups. The enrolment was divided in 2 steps: - Step 1: Open enrolment of subjects into Flu 1 Group. - Step 2: Open-label, randomised enrolment of subjects in a 1:1 randomisation ratio between Flu 1 Group (completion of enrolment) and Flu 2 Group Note: Following amendment of the study Protocol, the enrolment schedule has been modified.
<b>Centres:</b> 5 centres in Spain
<b>Indication:</b> Immunization against A/California/7/2009 (H1N1)v-like influenza of healthy children aged 6 to 35 months.
<b>Treatment:</b> Study groups were as follows: <ul style="list-style-type: none"> <li>Flu 1 Group: subjects received two doses of Flu 1 vaccine according to a 0, 21-day schedule.</li> <li>Flu 2 Group: subjects received two doses of Flu 2 vaccine according to a 0, 21-day schedule.</li> </ul> The vaccine was administered intramuscularly in the deltoid region of the arm or in the anterolateral part of the thigh if the subject was < 12 months at the entry of the study. Note: Following amendment of the study Protocol, the planned number of doses to administer has been modified.
<b>Objectives:</b> <ul style="list-style-type: none"> <li>To evaluate whether the haemagglutination-inhibition (HI) immune response to the vaccine-homologous virus of Flu 1 vaccine meets or exceeds the EMEA (CHMP) criteria* 21 days post dose 2 vaccination.</li> </ul> <i>*The CHMP criteria are fulfilled if the point estimate for seroconversion rate (SCR) is &gt; 40%, the point estimate for seroprotection rate (SPR) is &gt; 70% and the point estimate for seroconversion factor (SCF) is &gt; 2.5.</i>  Note: Following amendment of the study Protocol, the objectives have been modified to be consistent with the updated vaccination schedule.
<b>Primary Outcome/Efficacy Variable:</b> <i>Immunogenicity</i> <ul style="list-style-type: none"> <li>For the humoral immune response in terms of HI antibodies (in subjects receiving two doses of Flu 1 vaccine), the following parameters were calculated with 95% CIs: Observed variable: <ul style="list-style-type: none"> <li>H1N1 HI antibodies on Day 0 and on Day 42.</li> </ul> Derived variable: <ul style="list-style-type: none"> <li>Geometric mean titres (GMTs) and seropositivity rates of H1N1 HI antibodies on Days 0 and 42;</li> <li>SCR* on Day 42</li> <li>SPR** on Day 42</li> <li>SCF*** on Day 42</li> </ul> </li> </ul> <i>*SCR was defined as the percentage of vaccinees that have either a pre-vaccination titre &lt; 1:10 and a postvaccination titre ≥ 1:40, or a pre-vaccination titre ≥ 1:10 and at least a 4-fold increase in post-vaccination titre. The Committee for Medicinal Products for Human Use (CHMP) criterion was fulfilled if the point estimate for SCR was &gt; 40% in subjects 18 to 60 years of age. The same CHMP criterion was used for this paediatric study.</i>

\*\*SPR was defined as the percentage of vaccinees with a serum HI titre  $\geq$  1:40 that usually is accepted as indicating protection. The CHMP criterion was fulfilled if the post-vaccination time point estimate for SPR was  $>$  70% in subjects 18 to 60 years of age. The same CHMP criterion was used for this paediatric study.

\*\*\*SCF was defined as the fold increase in serum HI GMTs post-vaccination compared to pre-vaccination. The criterion was fulfilled if the point estimate for SCF was  $>$  2.5 in subjects 18 to 60 years of age. The same CHMP criterion was used for this paediatric study.

Note: Following amendment of the study Protocol, the Primary Outcomes have been modified to be consistent with the updated vaccination schedule.

#### **Secondary Outcome/Efficacy Variable(s):**

##### *Immunogenicity*

- For the humoral immune response in terms of HI antibodies (for all subjects), the following parameters were calculated with 95% CIs:

Observed variable:

- H1N1 HI antibodies on Day 0, Day 21, Day 42 and at Month 11-12#.

Derived variables:

- GMTs and seropositivity rates on Days 0, 21, 42 and at Month 11-12#;
- SCRs on Days 21, 42 and at Month 11-12#;
- SPRs on Days 0, 21, 42 and at Month 11-12#;
- SCFs on Days 21, 42 and at Month 11-12#.

The same analyses as above were performed in each age stratum (6 to 11 months, 12 to 23 months, and 24 to 35 months).

- For the humoral immune response in terms of neutralising antibodies (in all subjects aged 6 to 11 months and in a subset of subjects randomly selected), the following parameters<sup>§</sup> were calculated with 95% CIs:

Observed variable:

- Serum neutralising antibody titres on Day 0, Day 21, Day 42 and Month 11-12#.

Derived variables:

- GMTs of serum neutralising antibody titres;
- SCRs;

##### *Safety:*

- Percentage, intensity and relationship to vaccination of solicited local and general signs and symptoms during a 7-day follow-up period, i.e., day of vaccination and six subsequent days after each vaccination up to Day 21.
- Percentage, intensity and relationship to vaccination of unsolicited adverse events (AEs) during the 21-day follow-up period after the first vaccination and during the 62-day follow-up period after the second vaccination#.
- Occurrence of medically-attended events (MAEs), adverse events of specific interest (AESIs)/potential immune-mediated disease (pIMDs), serious adverse events (SAEs) and relationship to vaccination during the entire study period#.
- The number and percentage of subjects with normal or abnormal values of biochemical parameters on Day 0, Day 21 and Day 42.

# At the time of writing this summary, data were available up to Day 42 only. This summary will be updated when additional results become available.

§ Not available at the time of writing this summary.

Note: Following amendment of the study Protocol, the Secondary Outcomes have been modified to be consistent with the updated vaccination schedule

#### **Statistical Methods:**

Analyses were performed on the Total Vaccinated cohort and the According-To-Protocol (ATP) cohort for immunogenicity.

- The Total Vaccinated cohort included all vaccinated subjects.
- The ATP cohort for immunogenicity included all evaluable subjects (i.e., those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study) for whom two doses were taken and assay results were available for antibodies against H1N1 antigen for the blood sample taken twenty one days after the second dose for all subjects.

##### *Analysis of immunogenicity:*

The analysis was done on the ATP cohort for immunogenicity. The analysis of immunogenicity was done as a descriptive analysis of the humoral immune response in children 6 to 35 months of age and also within age sub-strata: 6 to 11 months, 12 to 23 months, and 24 to 35 months.

For the humoral immune response in terms of H1N1 HI antibodies (with 95% CIs):

- Seropositivity rates and GMTs of H1N1 HI antibody titres at Day 0, Day 21 and Day 42.

- SCR at Day 21 and Day 42.
- SCF at Day 21 and Day 42.
- SPR at Day 0, Day 21 and Day 42.

**Analysis of safety:**

The analysis was done on the Total Vaccinated cohort.

The percentage of subjects reporting each individual solicited local and general symptom during the solicited follow-up period, i.e., day of vaccination and six subsequent days after each primary vaccination dose was tabulated with exact 95% CI. The same tabulation was performed for grade 3 symptoms and for general symptoms assessed by the investigator as related to vaccination.

The proportion of subjects with at least one report of unsolicited AE classified by the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms up to Day 42 was tabulated. The same tabulation was performed for grade 3 unsolicited AEs and for unsolicited AEs assessed by the investigator as related to vaccination.

The proportion of subjects with MAEs, and with AESIs/pIMDs reported after each primary vaccination was tabulated up to Day 42.

SAEs reported up to Day 42 and classified by the MedDRA preferred terms were tabulated.

Selected serum biochemistry safety parameters were tabulated on Day 0, Day 21 and Day 42.

**Study Population:** Healthy children, male or female, aged between 6 and 35 months at the time of first study vaccination.

A written informed consent was obtained from the parent(s) or legally acceptable representative(s) of the subject prior to study entry.

<b>Number of subjects</b>					<b>Flu 2 Group</b>			<b>Flu 1 Group</b>			
Planned, N					51			102			
Randomised, N (Total Vaccinated cohort)					53			104			
Completed to Day 42, n (%)					53 (100)			104 (100)			
Total Number Subjects Withdrawn, n (%)					0 (0.0)			0 (0.0)			
Withdrawn due to Adverse Events, n (%)					0 (0.0)			0 (0.0)			
Withdrawn due to Lack of Efficacy, n (%)					Not applicable			Not applicable			
Withdrawn for other reasons, n (%)					0 (0.0)			0 (0.0)			
<b>Demographics</b>					<b>Flu 2 Group</b>			<b>Flu 1 Group</b>			
N (Total Vaccinated cohort)					53			104			
Females: Males					26:27			43:61			
Mean Age, months (SD)					19.7 (8.81)			19.3 (9.33)			
White - Caucasian / European heritage, n (%)					46 (86.8)			96 (92.3)			
<b>Primary Efficacy Results:</b> Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity)											
					<b>≥ 1:10</b>				<b>GMT</b>		
							<b>95% CI</b>		<b>value</b>	<b>95% CI</b>	
<b>Antibody against</b>	<b>Group</b>	<b>Sub-group</b>	<b>Timing</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>	<b>value</b>	<b>LL</b>	<b>UL</b>
Flu A/CAL/7/2009	Flu 2 Group	6-11M	PRE	15	1	6.7	0.2	31.9	6.02	4.05	8.94
			PI(D21)	15	15	100	78.2	100	278.44	205.01	378.18
			PII(D42)	15	15	100	78.2	100	2228.48	1627.09	3052.16
		12-23M	PRE	17	1	5.9	0.1	28.7	5.31	4.67	6.04
			PI(D21)	17	17	100	80.5	100	354.43	236.00	532.30
			PII(D42)	18	18	100	81.5	100	2660.38	2043.87	3462.84
		24-35M	PRE	16	4	25.0	7.3	52.4	9.99	4.82	20.72
			PI(D21)	16	16	100	79.4	100	334.16	237.10	470.96
			PII(D42)	17	17	100	80.5	100	1924.29	1530.14	2419.97
	Overall	PRE	48	6	12.5	4.7	25.2	6.82	5.22	8.91	
		PI(D21)	48	48	100	92.6	100	322.30	265.43	391.35	
		PII(D42)	50	50	100	92.9	100	2259.61	1947.61	2621.59	
	Flu 1 Group	6-11M	PRE	34	4	11.8	3.3	27.5	7.37	4.85	11.18
			PI(D21)	34	34	100	89.7	100	354.39	267.01	470.37
PII(D42)			32	32	100	89.1	100	2083.73	1737.12	2499.50	
12-23M		PRE	34	1	2.9	0.1	15.3	5.15	4.85	5.48	
		PI(D21)	34	34	100	89.7	100	326.58	252.37	422.61	

		PII(D42)	32	32	100	89.1	100	1995.41	1623.51	2452.50
	24-35M	PRE	33	0	0.0	0.0	10.6	5.00	5.00	5.00
		PI(D21)	33	33	100	89.4	100	264.86	210.41	333.40
		PII(D42)	33	33	100	89.4	100	1948.18	1621.24	2341.06
	Overall	PRE*	101	5	5.0	1.6	11.2	5.75	5.00	6.63
		PI(D21)	101	101	100	96.4	100	313.48	270.89	362.77
		PII(D42)*	97	97	100	96.3	100	2007.70	1805.24	2232.87

6-11M = Subjects aged between and including 6 to 11 months old  
12-23M = Subjects aged between and including 12 to 23 months old  
24-35M =Subjects aged between and including 24 to 35 months old  
Overall = All subjects aged between and including 6 to 35 months old  
GMT = geometric mean antibody titre calculated on all subjects  
N = number of subjects with available results  
n/% = number/percentage of subjects with titre within the specified range  
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit  
PRE = Pre-vaccination (Day 0)  
PI (D21) = Post-dose 1 (Day 21)  
PII(D42)= Post-dose 2 (Day 42)  
\* Primary Outcome variable

**Primary Efficacy Results: SCR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity)**

					SCR			
					95% CI			
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/2009	Flu 2 Group	6-11M	PI(D21)	15	15	100	78.2	100
			PII(D42)	15	15	100	78.2	100
		12-23M	PI(D21)	16	16	100	79.4	100
			PII(D42)	17	17	100	80.5	100
		24-35M	PI(D21)	16	15	93.8	69.8	99.8
			PII(D42)	16	16	100	79.4	100
	Overall	PI(D21)	47	46	97.9	88.7	99.9	
		PII(D42)	48	48	100	92.6	100	
	Flu 1 Group	6-11M	PI(D21)	34	33	97.1	84.7	99.9
			PII(D42)	32	32	100	89.1	100
		12-23M	PI(D21)	34	34	100	89.7	100
			PII(D42)	32	32	100	89.1	100
		24-35M	PI(D21)	33	33	100	89.4	100
			PII(D42)	33	33	100	89.4	100
Overall		PI(D21)	101	100	99.0	94.6	100	
		PII(D42)*	97	97	100	96.3	100	

6-11M = Subjects aged between and including 6 to 11 months old  
12-23M = Subjects aged between and including 12 to 23 months old  
24-35M =Subjects aged between and including 24 to 35 months old  
Overall = All subjects aged between and including 6 to 35 months old  
Seroconversion defined as:  
For initially seronegative subjects, antibody titre  $\geq$  1:40 after vaccination  
For initially seropositive subjects, antibody titre after vaccination  $\geq$  4 fold the pre-vaccination antibody titre  
N = Number of subjects with pre- and post-vaccination results available  
n/% = Number/percentage of seroconverted subjects  
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  
PI (D21) = Post-dose 1 (Day 21)  
PII(D42)= Post-dose 2 (Day 42)  
\* Primary outcome variable

**Primary Efficacy Results: SPR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity)**

					SPR			
					95% CI			

Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/2009	Flu 2 Group	6-11M	PRE	15	1	6.7	0.2	31.9
			PI(D21)	15	15	100	78.2	100
			PII(D42)	15	15	100	78.2	100
		12-23M	PRE	17	0	0.0	0.0	19.5
			PI(D21)	17	17	100	80.5	100
			PII(D42)	18	18	100	81.5	100
		24-35M	PRE	16	3	18.8	4.0	45.6
			PI(D21)	16	16	100	79.4	100
			PII(D42)	17	17	100	80.5	100
		Overall	PRE	48	4	8.3	2.3	20.0
			PI(D21)	48	48	100	92.6	100
			PII(D42)	50	50	100	92.9	100
	Flu 1 Group	6-11M	PRE	34	3	8.8	1.9	23.7
			PI(D21)	34	34	100	89.7	100
			PII(D42)	32	32	100	89.1	100
		12-23M	PRE	34	0	0.0	0.0	10.3
			PI(D21)	34	34	100	89.7	100
			PII(D42)	32	32	100	89.1	100
		24-35M	PRE	33	0	0.0	0.0	10.6
			PI(D21)	33	33	100	89.4	100
			PII(D42)	33	33	100	89.4	100
		Overall	PRE	101	3	3.0	0.6	8.4
			PI(D21)	101	101	100	96.4	100
			PII(D42)*	97	97	100	96.3	100

6-11M = Subjects aged between and including 6 to 11 months old  
12-23M = Subjects aged between and including 12 to 23 months old  
24-35M = Subjects aged between and including 24 to 35 months old  
Overall = All subjects aged between and including 6 to 35 months old  
N = Number of subjects with available results  
n/% = Number/percentage of seroprotected subjects (HI titre  $\geq$  1:40)  
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  
PRE= pre-vaccination (Day 0)  
PI (D21) = Post-dose 1 (Day 21)  
PII(D42)= Post-dose 2 (Day 42)  
\* Primary outcome variable

**Primary Efficacy Results:** SCF for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity)

Antibodies against	Group	Sub-group	Timing	N	SCF			
					Value	95% CI		
						LL	UL	
Flu A/CAL/7/09	Flu 2 Group	6-11M	PI(D21)	15	46.29	35.83	59.80	
			PII(D42)	15	370.48	217.97	629.69	
		12-23M	PI(D21)	16	64.06	38.55	106.44	
			PII(D42)	17	472.16	343.74	648.57	
		24-35M	PI(D21)	16	33.44	18.59	60.16	
			PII(D42)	16	189.16	83.80	427.01	
		Overall	PI(D21)	47	46.29	35.42	60.49	
			PII(D42)	48	322.67	231.61	449.52	
		Flu 1 Group	6-11M	PI(D21)	34	48.12	34.34	67.42
				PII(D42)	32	276.14	167.23	455.99
			12-23M	PI(D21)	34	63.37	48.13	83.43
				PII(D42)	32	386.45	308.54	484.02
	24-35M		PI(D21)	33	52.97	42.08	66.68	
			PII(D42)	33	389.64	324.25	468.21	
	Overall	PI(D21)	101	54.47	46.39	63.96		

					PII(D42)*	97	346.86	287.54	418.42		
6-11M = Subjects aged between and including 6 to 11 months old 12-23M = Subjects aged between and including 12 to 23 months old 24-35M =Subjects aged between and including 24 to 35 months old Overall = All subjects aged between and including 6 to 35 months old N = Number of subjects with pre- and post-vaccination results available SCF = Fold increase in serum HI GMTs post-vaccination 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI (D21) = Post-dose 1 (Day 21) PII(D42)= Post-dose 2 (Day 42) * Primary outcome variable											
<b>Secondary Outcome Variable(s):</b> Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)											
		<b>Flu 2 Group</b>					<b>Flu 1 Group</b>				
		<b>95 % CI</b>					<b>95 % CI</b>				
<b>Symptom</b>	<b>Intensity</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>
<b>Dose 1</b>											
Pain	Any	53	31	58.5	44.1	71.9	104	37	35.6	26.4	45.6
	Grade 3	53	0	0.0	0.0	6.7	104	1	1.0	0.0	5.2
Redness	Any	53	17	32.1	19.9	46.3	104	19	18.3	11.4	27.1
	> 50 mm	53	2	3.8	0.5	13.0	104	0	0.0	0.0	3.5
Swelling	Any	53	11	20.8	10.8	34.1	104	12	11.5	6.1	19.3
	> 50 mm	53	1	1.9	0.0	10.1	104	0	0.0	0.0	3.5
<b>Dose 2</b>											
Pain	Any	52	27	51.9	37.6	66.0	104	43	41.3	31.8	51.4
	Grade 3	52	2	3.8	0.5	13.2	104	3	2.9	0.6	8.2
Redness	Any	52	23	44.2	30.5	58.7	104	34	32.7	23.8	42.6
	> 50 mm	52	6	11.5	4.4	23.4	104	1	1.0	0.0	5.2
Swelling	Any	52	17	32.7	20.3	47.1	104	30	28.8	20.4	38.6
	> 50 mm	52	4	7.7	2.1	18.5	104	1	1.0	0.0	5.2
<b>Across doses</b>											
Pain	Any	53	37	69.8	55.7	81.7	104	54	51.9	41.9	61.8
	Grade 3	53	2	3.8	0.5	13.0	104	4	3.8	1.1	9.6
Redness	Any	53	27	50.9	36.8	64.9	104	41	39.4	30.0	49.5
	> 50 mm	53	6	11.3	4.3	23.0	104	1	1.0	0.0	5.2
Swelling	Any	53	21	39.6	26.5	54.0	104	38	36.5	27.3	46.6
	> 50 mm	53	5	9.4	3.1	20.7	104	1	1.0	0.0	5.2
N= number of subjects with the administered dose n (%)= number (percentage) of subjects reporting at least once the symptom 95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit Any= occurrence of any local symptom regardless of intensity grade Grade 3 pain= cried when limb was moved/spontaneously painful											
<b>Secondary Outcome Variable(s):</b> Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)											
		<b>Flu 2 Group</b>					<b>Flu 1 Group</b>				
		<b>95 % CI</b>					<b>95 % CI</b>				
<b>Symptom</b>	<b>Intensity/ Relationship</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>
<b>Dose 1</b>											
Drowsiness	Any	53	14	26.4	15.3	40.3	104	24	23.1	15.4	32.4
	Grade 3	53	2	3.8	0.5	13.0	104	0	0.0	0.0	3.5
	Related	53	11	20.8	10.8	34.1	104	17	16.3	9.8	24.9
Irritability	Any	53	17	32.1	19.9	46.3	104	33	31.7	22.9	41.6
	Grade 3	53	5	9.4	3.1	20.7	104	2	1.9	0.2	6.8
	Related	53	12	22.6	12.3	36.2	104	28	26.9	18.7	36.5

Loss of appetite	Any	53	17	32.1	19.9	46.3	104	25	24.0	16.2	33.4
	Grade 3	53	1	1.9	0.0	10.1	104	1	1.0	0.0	5.2
	Related	53	11	20.8	10.8	34.1	104	18	17.3	10.6	26.0
Temperature (Axillary)	≥ 37.5 °C	53	13	24.5	13.8	38.3	104	21	20.2	13.0	29.2
	> 39 °C	53	1	1.9	0.0	10.1	104	1	1.0	0.0	5.2
	Related	53	10	18.9	9.4	32.0	104	16	15.4	9.1	23.8
<b>Dose 2</b>											
Drowsiness	Any	52	25	48.1	34.0	62.4	104	36	34.6	25.6	44.6
	Grade 3	52	2	3.8	0.5	13.2	104	0	0.0	0.0	3.5
	Related	52	22	42.3	28.7	56.8	104	35	33.7	24.7	43.6
Irritability	Any	52	31	59.6	45.1	73.0	104	48	46.2	36.3	56.2
	Grade 3	52	4	7.7	2.1	18.5	104	3	2.9	0.6	8.2
	Related	52	27	51.9	37.6	66.0	104	45	43.3	33.6	53.3
Loss of appetite	Any	52	30	57.7	43.2	71.3	104	44	42.3	32.7	52.4
	Grade 3	52	4	7.7	2.1	18.5	104	4	3.8	1.1	9.6
	Related	52	26	50.0	35.8	64.2	104	41	39.4	30.0	49.5
Temperature (Axillary)	≥ 37.5 °C	52	37	71.2	56.9	82.9	104	70	67.3	57.4	76.2
	> 39 °C	52	9	17.3	8.2	30.3	104	4	3.8	1.1	9.6
	Related	52	34	65.4	50.9	78.0	104	64	61.5	51.5	70.9
<b>Across doses</b>											
Drowsiness	Any	53	31	58.5	44.1	71.9	104	47	45.2	35.4	55.3
	Grade 3	53	3	5.7	1.2	15.7	104	0	0.0	0.0	3.5
	Related	53	26	49.1	35.1	63.2	104	43	41.3	31.8	51.4
Irritability	Any	53	38	71.7	57.7	83.2	104	60	57.7	47.6	67.3
	Grade 3	53	8	15.1	6.7	27.6	104	5	4.8	1.6	10.9
	Related	53	31	58.5	44.1	71.9	104	54	51.9	41.9	61.8
Loss of appetite	Any	53	35	66.0	51.7	78.5	104	54	51.9	41.9	61.8
	Grade 3	53	5	9.4	3.1	20.7	104	5	4.8	1.6	10.9
	Related	53	29	54.7	40.4	68.4	104	49	47.1	37.2	57.2
Temperature (Axillary)	≥ 37.5 °C	53	41	77.4	63.8	87.7	104	79	76.0	66.6	83.8
	> 39 °C	53	10	18.9	9.4	32.0	104	5	4.8	1.6	10.9
	Related	53	37	69.8	55.7	81.7	104	70	67.3	57.4	76.2

N= number of subjects with the administered dose

n (%)= number (percentage) of subjects reporting at least once the symptom

95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Any= occurrence of any general symptom regardless of intensity grade

Grade 3= general symptom that prevented normal activity

Grade 3 Loss of appetite: not eating at all

Related= general symptom assessed by the investigator as causally related to the study vaccination

**Secondary Outcome Variable(s):** Percentage of subjects reporting medically-attended events (MAEs) up to Day 42 (Total Vaccinated cohort)

<b>Most frequent MAEs occurring within the 42-day (Days 0-41) post-vaccination period</b>	<b>Flu 2 Group N = 53</b>	<b>Flu 1 Group N = 104</b>
Subjects with any MAEs, n (%)	31 (58.5)	69 (66.3)
Ear pain	1 (1.9)	-
Conjunctival hyperaemia	1 (1.9)	-
Diarrhoea	-	3 (2.9)
Stomatitis	1 (1.9)	-
Vomiting	5 (9.4)	-
Pyrexia	-	3 (2.9)
Bronchitis	-	4 (3.8)
Ear infection	1 (1.9)	-
Gastroenteritis	4 (7.5)	7 (6.7)
Herpangina	2 (3.8)	-

Laryngitis	1 (1.9)	6 (5.8)
Otitis media	-	5 (4.8)
Otitis media acute	1 (1.9)	5 (4.8)
Pharyngitis	2 (3.8)	5 (4.8)
Respiratory tract infection	2 (3.8)	5 (4.8)
Tonsillitis	1 (1.9)	-
Upper respiratory tract infection	15 (28.3)	32 (30.8)
Traumatic brain injury	1 (1.9)	-
Blood creatinine increased	1 (1.9)	-
Asthma	4 (7.5)	4 (3.8)
Dermatitis allergic	1 (1.9)	-
Prurigo	2 (3.8)	-
Rash	-	3 (2.9)
Urticaria	1 (1.9)	-

-. event absent or not meeting the selected rule: If more than 30 subjects per group and ≤ 3 groups, then only the 10 most frequent adverse events in each group are to be listed.

**Secondary Outcome Variable(s):** Occurrence of AE of Specific Interest (AESI) / potential Immune-Mediated Diseases (pIMDs) up to Day 42 (Total Vaccinated cohort)

<b>Most frequent AESI/pIMDs occurring within the 42-day (Days 0-41) post-vaccination period</b>	<b>Flu 2 Group N = 53</b>	<b>Flu 1 Group N = 104</b>
Subjects with any AESI(s)/pIMD(s), n (%)	0 (0.0)	0 (0.0)

**Secondary Outcome Variable(s):** Distribution of haematology and biochemistry with respect to normal laboratory ranges (Total Vaccinated cohort)

		Flu 2 Group N= 53									Flu 1 Group N = 104								
		Unkno wn			Below		Within		Above		Unkno wn			Below		Within		Above	
Laboratory parameter	Timing	N	n	%	n	%	n	%	n	%	N	n	%	n	%	n	%	n	%
ALAT	PRE	53	4	7.5	0	0.0	49	92.5	0	0.0	104	3	2.9	0	0.0	101	97.1	0	0.0
	PI(D21)	52	1	1.9	0	0.0	50	96.2	1	1.9	104	1	1.0	0	0.0	100	96.2	3	2.9
	PII(D42)	53	0	0.0	0	0.0	53	100	0	0.0	103	1	1.0	0	0.0	98	95.1	4	3.9
ASAT	PRE	53	3	5.7	0	0.0	49	92.5	1	1.9	104	3	2.9	0	0.0	100	96.2	1	1.0
	PI(D21)	52	3	5.8	0	0.0	48	92.3	1	1.9	104	4	3.8	0	0.0	94	90.4	6	5.8
	PII(D42)	53	0	0.0	0	0.0	53	100	0	0.0	103	1	1.0	0	0.0	96	93.2	6	5.8
Bilirubin*	PRE	53	4	7.5	0	0.0	49	92.5	0	0.0	104	3	2.9	0	0.0	101	97.1	0	0.0
		53	4	7.5	0	0.0	49	92.5	0	0.0	104	3	2.9	0	0.0	101	97.1	0	0.0
	PI(D21)	52	1	1.9	0	0.0	51	98.1	0	0.0	104	2	1.9	0	0.0	102	98.1	0	0.0
		52	1	1.9	0	0.0	51	98.1	0	0.0	104	1	1.0	0	0.0	103	99.0	0	0.0
	PII(D42)	53	0	0.0	0	0.0	53	100	0	0.0	103	1	1.0	0	0.0	102	99.0	0	0.0
		53	0	0.0	0	0.0	53	100	0	0.0	103	1	1.0	0	0.0	102	99.0	0	0.0
Creatinine	PRE	53	3	5.7	16	30.2	34	64.2	0	0.0	104	3	2.9	32	30.8	67	64.4	2	1.9
	PI(D21)	52	2	3.8	19	36.5	30	57.7	1	1.9	104	1	1.0	34	32.7	69	66.3	0	0.0
	PII(D42)	53	0	0.0	16	30.2	37	69.8	0	0.0	103	1	1.0	37	35.9	65	63.1	0	0.0
BUN	PRE	53	4	7.5	0	0.0	36	67.9	13	24.5	104	3	2.9	1	1.0	77	74.0	23	22.1
	PI(D21)	52	1	1.9	0	0.0	37	71.2	14	26.9	104	1	1.0	0	0.0	79	76.0	24	23.1
	PII(D42)	53	0	0.0	0	0.0	41	77.4	12	22.6	103	1	1.0	1	1.0	76	73.8	25	24.3

N = number of subjects with laboratory results for the specified time point and laboratory parameter

n/% = number/percentage of subjects in a given category

Unknown = value unknown for the specified time point and laboratory parameter

Below = value below the laboratory reference range defined for the specified time point and laboratory parameter

Within = value within the laboratory reference range defined for the specified time point and laboratory parameter

Above = value above the laboratory reference range defined for the specified time point and laboratory parameter

ALAT = Alanine Amino Transferase

ASAT = Aspartate Amino Transferase

BUN = Blood Urea Nitrogen  
 PRE = Pre-vaccination (Day 0)  
 PI (D21) = Post-dose 1 (Day 21)  
 PII (D42) = Post-dose 2 (Day 42)  
 \*Bilirubin: at each time point, the first row is "Bilirubin Total" measurement and the second is "Bilirubin Direct" measurement.

**Safety results:** Number (%) of subjects with unsolicited adverse events up to Day 42 (Total Vaccinated cohort)

<b>Most frequent adverse events - On-Therapy (occurring within day 0-41 following vaccination)</b>	<b>Flu 2 Group N = 53</b>	<b>Flu 1 Group N = 104</b>
Subjects with any AE(s), n (%)	43 (81.1)	91 (87.5)
Subjects with grade 3 AE(s), n (%)	2 (3.8)	13 (12.5)
Subjects with related AE(s), n (%)	8 (15.1)	12 (11.5)
Upper respiratory tract infection	17 (32.1)	44 (42.3)
Diarrhoea	3 (5.7)	12 (11.5)
Vomiting	9 (17.0)	5 (4.8)
Gastroenteritis	4 (7.5)	9 (8.7)
Pyrexia	3 (5.7)	7 (6.7)
Cough	2 (3.8)	7 (6.7)
Laryngitis	2 (3.8)	6 (5.8)
Otitis media acute	-	7 (6.7)
Pharyngitis	2 (3.8)	5 (4.8)
Respiratory tract infection	2 (3.8)	5 (4.8)
Asthma	5 (9.4)	-
Otitis media	-	5 (4.8)
Rash	-	5 (4.8)
Toothache	-	5 (4.8)
Herpangina	2 (3.8)	-
Nasal congestion	2 (3.8)	-
Prurigo	2 (3.8)	-
Urticaria	2 (3.8)	-

-: adverse event absent or not meeting the selected rule: If more than 30 subjects per group and ≤ 3 groups, then only the 10 most frequent adverse events in each group are to be listed.

Grade 3= event that prevented normal activities

Related= event assessed by the investigator as causally related to the study vaccination

**Safety results:** Number (%) of subjects with serious adverse events up to Day 42 (Total Vaccinated cohort)

**Serious adverse event, n (%) [n considered by the investigator to be related to study medication]**

<b>All SAEs</b>	<b>Flu 2 Group N = 53</b>	<b>Flu 1 Group N = 104</b>
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	1 (1.9) [0]	0 (0.0) [0]
Traumatic brain injury	1 (1.9) [0]	0 (0.0) [0]
<b>Fatal SAE(s)</b>	<b>Flu 2 Group N = 53</b>	<b>Flu 1 Group N = 104</b>
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]

**Conclusion:** At Day 42, the GMT value was 2007.70 in Flu 1 Group. At Day 42, all subjects of Flu 1 Group have shown seroconversion and reached HI antibody titres usually accepted as indicating seroprotection. The SCF at Day 42 was of 346.86 in Flu 1 Group.

Up to Day 42, at least one unsolicited AE was reported for 43 (81.1%) subjects in Flu 2 Group and 91 (87.5%) subjects in Flu 1 Group. One SAE (in Flu 2 Group) was reported during this period of the study and assessed by the investigator as unrelated to the study vaccination.

**Publications:** None

Date updated: 06 April 2010