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.

Study No.: 113574 (FLU D-PAN H1N1-021)

Title: Safety and immunogenicity study of GSK Biologicals' influenza vaccine GSK2340272A in adults aged 18 to 60 years.
GSK2340272A (Flu 1): GlaxoSmithKline (GSK) Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain.

Rationale: The aim of the study was to assess the immunogenicity and safety of Flu 1 vaccine compared to GSK Biologicals' Pandemic influenza vaccine GSK2340269A.
GSK2340269A (Flu 2): Alternative formulation of GSK Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain.

Phase: II

Study Period: 11 August 2009 to 30 August 2010

Study Design: Randomized (1:1), observer-blind study with 2 parallel groups.

Centers: 3 centers in Germany.

Indication: Immunization against A/California/7/2009 (H1N1)v-like influenza in male and female subjects aged 18 to 60 years.

Treatment: Study groups were as follows:

- Flu 1 Group: subjects received two doses of Flu 1 vaccine (one at Day 0 and one at Day 21).
- Flu 2 Group: subjects received two doses of Flu 2 vaccine (one at Day 0 and one at Day 21).

Vaccines were administered intramuscularly in the deltoid region of the non-dominant arm at Day 0 and of the dominant arm at Day 21.

Objectives:
To evaluate the humoral response of two doses of Flu 1 vaccine in terms of hemagglutination inhibition (HI) against the vaccine-homologous virus at 14 days after the second dose in adults 18 to 60 years of age.

Primary Outcome/Efficacy Variable:
Humoral immune response in terms of HI antibodies:
In subjects vaccinated with the Flu 1 vaccine, 14 days after the second dose (Day 35):

- Geometric mean titers (GMTs) with 95% confidence intervals (CIs).
- Seroconversion rates (SCR, defined as the percentage of vaccinees with either a pre-vaccination titer < 1:10 and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least 4-fold increase in post-vaccination titer) with 95% CI.
- Seroprotection rates (SPR, defined as the percentage of vaccinees with a serum HI titer ≥ 1:40, that is usually accepted as indicating protection) with 95% CI.
- Geometric mean fold rise (GMFR, also called seroconversion factor [SCF]) defined as the fold increase in serum HI GMTs post-vaccination compared to pre-vaccination) with 95% CI.

Secondary Outcome/Efficacy Variable(s):
Humoral immune response in terms of HI antibodies:
In subjects of both groups, at Days 0, 21, 35 (for subjects vaccinated with Flu 2 vaccine), 182 and 364:

- GMTs with 95% CI.
- SCR with 95% CI.
- SPR with 95% CI.
- SCF with 95% CI.

Safety:

- Occurrence, duration and intensity of each solicited local symptom within 7 days (Day 0 – Day 6) after each vaccination.
- Occurrence, duration, intensity and relation to vaccination of each solicited general symptom within 7 days (Day 0 – Day 6) after each vaccination.
- Occurrence, intensity and relationship to vaccination of unsolicited adverse events (AEs) within 21 days after the first vaccination and 63 days after the second vaccination (Day 0 – Day 20 and Day 21 – Day 83), according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence and relationship to vaccination of AEs of specific interest (AESIs) and serious adverse events (SAEs) during the entire study period (up to Day 364).

Statistical Methods:

Analyses were performed on the Total Vaccinated cohort, the According-To-Protocol (ATP) cohort for immunogenicity and the ATP cohort for persistence (Month 6).

- 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) who received two doses of vaccine and for whom assay results were available for antibodies against H1N1 antigen for blood sample taken 14 days after the second vaccine dose.
- The ATP cohort for persistence (Month 6) 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) who received at least one dose of the vaccine and for whom assay results were available for antibodies against H1N1 antigen for blood sample taken at Month 6.
- The ATP cohort for persistence (Month 12) 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) who received at least one dose of the vaccine and for whom assay results were available for antibodies against H1N1 antigen for blood sample taken at Month 12.

Analysis of immunogenicity:

The analysis was based on the ATP cohort for immunogenicity and on the ATP cohort for persistence. The analysis of immunogenicity was done as a descriptive analysis of the humoral immune response in adults 18 to 60 years of age.

For each treatment group, the following parameters (with 95% confidence intervals) were calculated:

- GMTs of H1N1 antibody titers at Day 0, 21, 35, 182, and 364.
- SCRs at Day 21, 35, 182, and 364.
- SCFs at Day 21, 35, 182, and 364.
- SPRs at Day 0, 21, 35, 182, and 364.

Analysis of safety:

The analysis was based on the Total Vaccinated cohort.

The incidence of solicited local and general symptoms occurring during 7 days after each vaccination was tabulated with exact 95% CI for each treatment group. The same calculations were performed for symptoms of any intensity, those with intensity grade of grade 3, as well as for solicited general events with relationship to vaccination. All solicited local AEs were considered to be causally related. Duration of local and general symptoms was also calculated.

The percentage of subjects with at least one report of an unsolicited adverse event classified by MedDRA up to 21 days after first dose and 63 days after second dose of vaccine was tabulated for each treatment group. The same tabulation was performed for grade 3 unsolicited adverse events and for unsolicited adverse events that were assessed by the investigator as possibly related to vaccination. SAEs and AESIs were collected and summarized through the entire follow-up period up to Day 364.

Study Population: Healthy male or female adults 18 to 60 years of age at the time of first vaccination. Women were to be of non-childbearing potential or if of childbearing potential, had to practice adequate contraception for 30 days prior to vaccination, to have a negative pregnancy test, and to continue such precautions during the entire treatment period and for 2 months after completion of the vaccination series. A written informed consent was obtained from the subjects prior to study entry.

Number of subjects	**Flu 1 Group**	**Flu 2 Group**
Planned, N	64	64
Randomized, N (Total Vaccinated cohort)	64	66
Completed (Day 364), n (%)	59 (92.2)	65 (98.5)
Total Number Subjects Withdrawn, n (%)	5 (7.8)	1 (1.5)
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 (%)	5 (7.8)	1 (1.5)
Demographics	**Flu 1 Group**	**Flu 2 Group**
N (Total Vaccinated cohort)	64	66
Females:Males	27:37	31:35
Mean Age, years (SD)	39.9 (11.72)	39.3 (13.16)
White - Caucasian / European heritage, n (%)	64 (100)	66 (100)

Primary Efficacy Results: Seropositivity rates and GMTs for HI antibodies against A/California/7/2009 antibodies, (ATP cohort for immunogenicity)

	≥1:10		**GMT***	
		95% CI		**95% CI**

Antibody against	Group	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/California/7/2009	Flu 1	PRE	56	28	50.0	36.3	63.7	10.6	8.2	13.6
		PI(D21)	56	56	100	93.6	100	541.7	415.7	706.0
		PII(D35)*	56	56	100	93.6	100	780.2	650.3	936.0
	Flu 2	PRE	61	30	49.2	36.1	62.3	11.7	8.7	15.8
		PI(D21)	61	61	100	94.1	100	530.5	391.6	718.6
		PII(D35)	61	61	100	94.1	100	533.6	412.2	690.7

GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
PI (D21) = Post-vaccination at Day 21
PII (D35) = Post-vaccination at Day 35
* Primary outcome variable

Primary Efficacy Results: SCR for HI antibody titer, (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/California/7/2009	Flu 1	PI(D21)	56	55	98.2	90.4	100
		PII(D35)*	56	56	100	93.6	100
	Flu 2	PI(D21)	61	58	95.1	86.3	99.0
		PII(D35)	61	60	98.4	91.2	100

Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥1:40 after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
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-vaccination at Day 21
PII (D35) = Post-vaccination at Day 35
* Primary outcome variable

Primary Efficacy Results: SPR for HI antibodies against Flu A/California/7/2009 antibodies at each time point, (ATP cohort for immunogenicity)

				SPR			
						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/California/7/2009	Flu 1	PRE	56	7	12.5	5.2	24.1
		PI(D21)	56	55	98.2	90.4	100
		PII(D35)*	56	56	100	93.6	100
	Flu 2	PRE	61	8	13.1	5.8	24.2
		PI(D21)	61	60	98.4	91.2	100
		PII(D35)	61	61	100	94.1	100

N = Number of subjects with available results
n (%) = Number (percentage) of seroprotected subjects (HI titer ≥1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
PI (D21) = Post-vaccination at Day 21
PII (D35) = Post-vaccination at Day 35
* Primary outcome variable

Primary Efficacy Results: SCF for HI antibody titer at each post-vaccination time point, (ATP cohort for immunogenicity)

				SCF		
					95% CI	
Antibody against	**Group**	**Timing**	**N**	**Value**	**LL**	**UL**
Flu A/California/7/2009	Flu 1	PI(D21)	56	51.3	36.2	72.9

		PII(D35)*	56	73.9	55.1	99.2
	Flu 2	PI(D21)	61	45.3	32.6	63.0
		PII(D35)	61	45.6	33.3	62.2

N = Number of subjects with pre- and post-vaccination results available
SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI (D21) = Post-vaccination at Day 21
PII (D35) = Post-vaccination at Day 35
* Primary outcome variable

Secondary Outcome variable(s): Seropositivity rates and GMTs for HI antibodies against A/California/7/2009 antibodies (ATP cohort for persistence at Month 6)

				≥1:10				GMT		
						95% CI			95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/California/7/2009	Flu1	PII(D182)	59	59	100	93.9	100	161.9	125.8	208.4
	Flu 2	PII(D182)	62	61	98.4	91.3	100	149.7	109.9	203.8

GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PII(D182) = Post-vaccination at Day 182

Secondary Outcome variable(s): Seropositivity rates and GMTs for HI antibodies against A/California/7/2009 antibodies (ATP cohort for persistence at Month 12)

				≥1:10				GMT		
						95% CI			95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/09 H1N1	Flu 1	PII(D364)	58	58	100	93.8	100	90.1	68.9	117.8
	Flu 2	PII(D364)	63	62	98.4	91.5	100	96.0	68.7	134.2

GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PII(D364) = Post-vaccination at Day 364

Secondary Outcome variable(s): SCR for HI antibodies against A/California/7/2009 antibodies at Day 182 (ATP cohort for persistence at Month 6)

			SCR			
					95% CI	
Antibody	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/California/7/2009	Flu1	59	53	89.8	79.2	96.2
	Flu 2	62	49	79.0	66.8	88.3

Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 1:40 after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
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

Secondary Outcome variable(s): SCR for HI antibodies against A/California/7/2009 antibodies at Day 364 (ATP cohort for persistence at Month 12)

			SCR			
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09 H1N1	Flu 1	58	38	65.5	51.9	77.5
	Flu 2	63	41	65.1	52.0	76.7

Seroconversion defined as:

For initially seronegative subjects, antibody titer ≥ 1:40 after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
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

Secondary Outcome variable(s): SPR for HI antibodies against A/California/7/2009 antibodies at Day 182 (ATP cohort for persistence at Month 6)

				SPR			
						95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/California/7/2009	Flu 1	PII(D182)	59	56	94.9	85.9	98.9
	Flu 2	PII(D182)	62	56	90.3	80.1	96.4

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PII(D182) = Post-vaccination at Day 182

Secondary Outcome variable(s): SPR for HI antibodies against A/California/7/2009 antibodies at Day 0 and Day 364 (ATP cohort for persistence at Month 12)

				SPR			
						95% CI	
Strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09 H1N1	Flu 1	PII(D364)	58	48	82.8	70.6	91.4
	Flu 2	PII(D364)	63	51	81.0	69.1	89.8

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PII(D364) = Post-vaccination at Day 364

Secondary Outcome variable(s): SCF for HI antibodies against A/California/7/2009 antibodies at Day 182 (ATP cohort for persistence at Month 6)

		SCF			
				95% CI	
Antibody	**Group**	**N**	**Value**	**LL**	**UL**
Flu A/California/7/2009	Flu 1	59	15.3	11.5	20.3
	Flu 2	62	11.7	8.7	15.9

N = Number of subjects with pre- and post-vaccination results available
SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome variable(s): SCF for HI antibodies against A/California/7/2009 antibodies at Day 364 (ATP cohort for persistence at Month 12)

			SCF		
				95% CI	
Strain	**Group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09 H1N1	Flu 1	58	8.4	6.2	11.3
	Flu 2	63	7.6	5.6	10.4

N = Number of subjects with pre- and post-vaccination results available
SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome variable(s): Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and across doses (Total Vaccinated cohort)

		Flu 1 Group					Flu 2 Group				
					95 % CI					95 % CI	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Pain	Any	63	56	88.9	78.4	95.4	66	39	59.1	46.3	71.0
	Grade 3	63	1	1.6	0.0	8.5	66	0	0.0	0.0	5.4

Redness	Any	63	20	31.7	20.6	44.7	66	3	4.5	0.9	12.7
	> 100 mm	63	0	0.0	0.0	5.7	66	0	0.0	0.0	5.4
Swelling	Any	63	20	31.7	20.6	44.7	66	1	1.5	0.0	8.2
	> 100 mm	63	0	0.0	0.0	5.7	66	0	0.0	0.0	5.4
Dose 2											
Pain	Any	62	53	85.5	74.2	93.1	65	33	50.8	38.1	63.4
	Grade 3	62	0	0.0	0.0	5.8	65	1	1.5	0.0	8.3
Redness	Any	62	16	25.8	15.5	38.5	65	2	3.1	0.4	10.7
	> 100 mm	62	0	0.0	0.0	5.8	65	0	0.0	0.0	5.5
Swelling	Any	62	12	19.4	10.4	31.4	65	1	1.5	0.0	8.3
	> 100 mm	62	0	0.0	0.0	5.8	65	0	0.0	0.0	5.5
Across Doses											
Pain	Any	63	57	90.5	80.4	96.4	66	41	62.1	49.3	73.8
	Grade 3	63	1	1.6	0.0	8.5	66	1	1.5	0.0	8.2
Redness	Any	63	24	38.1	26.1	51.2	66	3	4.5	0.9	12.7
	> 100 mm	63	0	0.0	0.0	5.7	66	0	0.0	0.0	5.4
Swelling	Any	63	21	33.3	22.0	46.3	66	2	3.0	0.4	10.5
	> 100 mm	63	0	0.0	0.0	5.7	66	0	0.0	0.0	5.4

N= number of subjects with at least one documented 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= pain that prevented normal activity

Secondary Outcome variable(s): Number of days with any local symptom during the solicited post-vaccination period (Total Vaccinated cohort)

Solicited symptom	Dose	Group	N	Mean	Median
Pain	Dose 1	Flu 1	56	3.8	3.0
		Flu 2	39	2.1	2.0
	Dose 2	Flu 1	53	3.2	3.0
		Flu 2	33	2.0	2.0
	Overall/dose	Flu 1	109	3.5	3.0
		Flu 2	72	2.1	2.0
Redness	Dose 1	Flu 1	20	2.8	2.0
		Flu 2	3	3.0	4.0
	Dose 2	Flu 1	16	2.8	2.0
		Flu 2	2	1.5	1.5
	Overall/dose	Flu 1	36	2.8	2.0
		Flu 2	5	2.4	2.0
Swelling	Dose 1	Flu 1	20	3.4	3.0
		Flu 2	1	4.0	4.0
	Dose 2	Flu 1	12	2.8	3.0
		Flu 2	1	1.0	1.0
	Overall/dose	Flu 1	32	3.2	3.0
		Flu 2	2	2.5	2.5

N = number of doses with the symptom

Secondary Outcome variable(s): Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and across doses (Total Vaccinated cohort)

		Flu 1 Group					Flu 2 Group				
					95 % CI					95 % CI	
Symptom	**Intensity/ Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Fatigue	Any	63	26	41.3	29.0	54.4	66	18	27.3	17.0	39.6
	Grade 3	63	2	3.2	0.4	11.0	66	1	1.5	0.0	8.2

	Related	63	10	15.9	7.9	27.3	66	7	10.6	4.4	20.6
Headache	Any	63	19	30.2	19.2	43.0	66	10	15.2	7.5	26.1
	Grade 3	63	1	1.6	0.0	8.5	66	1	1.5	0.0	8.2
	Related	63	9	14.3	6.7	25.4	66	5	7.6	2.5	16.8
Joint pain at other location	Any	63	15	23.8	14.0	36.2	66	5	7.6	2.5	16.8
	Grade 3	63	1	1.6	0.0	8.5	66	0	0.0	0.0	5.4
	Related	63	9	14.3	6.7	25.4	66	2	3.0	0.4	10.5
Muscle aches	Any	63	22	34.9	23.3	48.0	66	12	18.2	9.8	29.6
	Grade 3	63	1	1.6	0.0	8.5	66	0	0.0	0.0	5.4
	Related	63	10	15.9	7.9	27.3	66	3	4.5	0.9	12.7
Shivering	Any	63	7	11.1	4.6	21.6	66	7	10.6	4.4	20.6
	Grade 3	63	0	0.0	0.0	5.7	66	0	0.0	0.0	5.4
	Related	63	2	3.2	0.4	11.0	66	3	4.5	0.9	12.7
Sweating	Any	63	9	14.3	6.7	25.4	66	11	16.7	8.6	27.9
	Grade 3	63	0	0.0	0.0	5.7	66	1	1.5	0.0	8.2
	Related	63	4	6.3	1.8	15.5	66	3	4.5	0.9	12.7
Temperature/ (Axillary)	≥ 37.5°C	63	1	1.6	0.0	8.5	66	0	0.0	0.0	5.4
	> 40 °C	63	0	0.0	0.0	5.7	66	0	0.0	0.0	5.4
	Related	63	1	1.6	0.0	8.5	66	0	0.0	0.0	5.4
Dose 2											
Fatigue	Any	62	29	46.8	34.0	59.9	65	13	20.0	11.1	31.8
	Grade 3	62	3	4.8	1.0	13.5	65	0	0.0	0.0	5.5
	Related	62	16	25.8	15.5	38.5	65	7	10.8	4.4	20.9
Headache	Any	62	19	30.6	19.6	43.7	65	12	18.5	9.9	30.0
	Grade 3	62	3	4.8	1.0	13.5	65	0	0.0	0.0	5.5
	Related	62	11	17.7	9.2	29.5	65	5	7.7	2.5	17.0
Joint pain at other location	Any	62	23	37.1	25.2	50.3	65	7	10.8	4.4	20.9
	Grade 3	62	2	3.2	0.4	11.2	65	1	1.5	0.0	8.3
	Related	62	15	24.2	14.2	36.7	65	3	4.6	1.0	12.9
Muscle aches	Any	62	30	48.4	35.5	61.4	65	7	10.8	4.4	20.9
	Grade 3	62	2	3.2	0.4	11.2	65	0	0.0	0.0	5.5
	Related	62	17	27.4	16.9	40.2	65	2	3.1	0.4	10.7
Shivering	Any	62	12	19.4	10.4	31.4	65	4	6.2	1.7	15.0
	Grade 3	62	1	1.6	0.0	8.7	65	0	0.0	0.0	5.5
	Related	62	10	16.1	8.0	27.7	65	2	3.1	0.4	10.7
Sweating	Any	62	12	19.4	10.4	31.4	65	7	10.8	4.4	20.9
	Grade 3	62	1	1.6	0.0	8.7	65	0	0.0	0.0	5.5
	Related	62	8	12.9	5.7	23.9	65	1	1.5	0.0	8.3
Temperature/ (Axillary)	≥ 37.5°C	62	2	3.2	0.4	11.2	65	0	0.0	0.0	5.5
	> 40 °C	62	0	0.0	0.0	5.8	65	0	0.0	0.0	5.5
	Related	62	1	1.6	0.0	8.7	65	0	0.0	0.0	5.5
Across Doses											
Fatigue	Any	63	35	55.6	42.5	68.1	66	23	34.8	23.5	47.6
	Grade 3	63	5	7.9	2.6	17.6	66	1	1.5	0.0	8.2
	Related	63	20	31.7	20.6	44.7	66	11	16.7	8.6	27.9
Headache	Any	63	30	47.6	34.9	60.6	66	18	27.3	17.0	39.6
	Grade 3	63	4	6.3	1.8	15.5	66	1	1.5	0.0	8.2
	Related	63	17	27.0	16.6	39.7	66	8	12.1	5.4	22.5
Joint pain at other location	Any	63	27	42.9	30.5	56.0	66	10	15.2	7.5	26.1
	Grade 3	63	2	3.2	0.4	11.0	66	1	1.5	0.0	8.2
	Related	63	18	28.6	17.9	41.3	66	5	7.6	2.5	16.8
Muscle aches	Any	63	35	55.6	42.5	68.1	66	14	21.2	12.1	33.0
	Grade 3	63	2	3.2	0.4	11.0	66	0	0.0	0.0	5.4
	Related	63	18	28.6	17.9	41.3	66	5	7.6	2.5	16.8

Shivering	Any	63	16	25.4	15.3	37.9	66	10	15.2	7.5	26.1
	Grade 3	63	1	1.6	0.0	8.5	66	0	0.0	0.0	5.4
	Related	63	10	15.9	7.9	27.3	66	4	6.1	1.7	14.8
Sweating	Any	63	17	27.0	16.6	39.7	66	14	21.2	12.1	33.0
	Grade 3	63	1	1.6	0.0	8.5	66	1	1.5	0.0	8.2
	Related	63	11	17.5	9.1	29.1	66	4	6.1	1.7	14.8
Temperature/ (Axillary)	≥ 37.5°C	63	3	4.8	1.0	13.3	66	0	0.0	0.0	5.4
	> 40 °C	63	0	0.0	0.0	5.7	66	0	0.0	0.0	5.4
	Related	63	2	3.2	0.4	11.0	66	0	0.0	0.0	5.4

N= number of subjects with at least one documented 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 and relationship to vaccination
Grade 3 = symptom that prevented normal everyday activities
Related = general symptom assessed by the investigator as causally related to the study vaccination

Secondary Outcome variable(s): Number of days with any general symptoms during the solicited post-vaccination period (Total Vaccinated cohort)

Solicited symptom	Dose	Group	N	Mean	Median
Fatigue	Dose 1	Flu 1	26	1.8	1.0
		Flu 2	18	1.9	2.0
	Dose 2	Flu 1	29	2.1	2.0
		Flu 2	13	2.2	2.0
	Overall/dose	Flu 1	55	1.9	1.0
		Flu 2	31	2.0	2.0
Headache	Dose 1	Flu 1	19	2.1	2.0
		Flu 2	10	1.7	1.5
	Dose 2	Flu 1	19	2.1	2.0
		Flu 2	12	2.6	2.0
	Overall/dose	Flu 1	38	2.1	2.0
		Flu 2	22	2.2	2.0
Joint pain at other location	Dose 1	Flu 1	15	2.3	2.0
		Flu 2	5	3.0	2.0
	Dose 2	Flu 1	23	2.6	2.0
		Flu 2	7	2.4	2.0
	Overall/dose	Flu 1	38	2.5	2.0
		Flu 2	12	2.7	2.0
Muscle aches	Dose 1	Flu 1	22	2.4	2.0
		Flu 2	12	1.9	1.5
	Dose 2	Flu 1	30	2.6	2.0
		Flu 2	7	2.1	3.0
	Overall/dose	Flu 1	52	2.5	2.0
		Flu 2	19	2.0	2.0
Sweating	Dose 1	Flu 1	9	1.8	1.0
		Flu 2	11	1.8	2.0
	Dose 2	Flu 1	12	1.5	1.0
		Flu 2	7	1.7	2.0
	Overall/dose	Flu 1	21	1.6	1.0
		Flu 2	18	1.8	2.0
Shivering	Dose 1	Flu 1	7	1.1	1.0
		Flu 2	7	1.3	1.0
	Dose 2	Flu 1	12	1.3	1.0
		Flu 2	4	1.8	2.0
	Overall/dose	Flu 1	19	1.3	1.0
		Flu 2	11	1.5	1.0

Temperature	Dose 2	Flu 1	2	1.0	1.0
	Overall/Dose	Flu 1	2	1.0	1.0
N = number of doses with the symptom					
Secondary Outcome variable(s): Number (%) of subjects with adverse events of specific interest within the 364-day (Days 0-363) post-vaccination period (Total Vaccinated cohort)					

Most frequent AESIs - On-Therapy (occurring within Day 0-363 following vaccination)	**Flu 1 Group N = 64**	**Flu 2 Group N = 66**
Subjects with any AESI(s), n (%)	0 (0.0)	0 (0.0)

Safety results: Number (%) of subjects with unsolicited adverse events within 84 days follow-up after the first vaccination and 63 days follow-up after the second vaccination (Total Vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-83 following vaccination)	**Flu 1 Group N = 64**	**Flu 2 Group N = 66**
Subjects with any AE(s), n (%)	22 (34.4)	27 (40.9)
Subjects with grade 3 AE(s), n (%)	1 (1.6)	4 (6.1)
Subjects with related AE(s), n (%)	5 (7.8)	6 (9.1)
Nasopharyngitis	5 (7.8)	4 (6.1)
Influenza like illness	1 (1.6)	6 (9.1)
Diarrhoea	2 (3.1)	2 (3.0)
Arthralgia	1 (1.6)	2 (3.0)
Gastritis	1 (1.6)	2 (3.0)
Gastroenteritis	2 (3.1)	1 (1.5)
Nausea	1 (1.6)	2 (3.0)
Oropharyngeal pain	-	3 (4.5)
Rhinitis	1 (1.6)	2 (3.0)
Abdominal pain upper	1 (1.6)	1 (1.5)
Acute tonsillitis	1 (1.6)	1 (1.5)
Dizziness	2 (3.1)	-
Lymphadenopathy	1 (1.6)	1 (1.5)
Migraine	-	2 (3.0)
Oral herpes	1 (1.6)	1 (1.5)
Borrelia infection	-	1 (1.5)
Bronchitis	1 (1.6)	-
Cervicobrachial syndrome	-	1 (1.5)
Cough	1 (1.6)	-
Cystitis	-	1 (1.5)
Dry mouth	1 (1.6)	-
Dysphagia	1 (1.6)	-
Ear infection	-	1 (1.5)
Ear pain	-	1 (1.5)
Folliculitis	1 (1.6)	-
Groin abscess	1 (1.6)	-
Haemorrhoids	-	1 (1.5)
Headache	1 (1.6)	-
Hypersensitivity	-	1 (1.5)
Hypoaesthesia	-	1 (1.5)
Injection site haematoma	-	1 (1.5)
Injection site lymphadenopathy	1 (1.6)	-
Intertrigo	1 (1.6)	-
Intervertebral disc disorder	1 (1.6)	-
Laryngitis	1 (1.6)	-
Muscle contractions involuntary	1 (1.6)	-
Musculoskeletal pain	-	1 (1.5)
Myalgia	1 (1.6)	-
Neck pain	-	1 (1.5)

Ovarian cyst ruptured	-	1 (1.5)
Pruritus	1 (1.6)	-
Restless legs syndrome	1 (1.6)	-
Salpingo-oophoritis	-	1 (1.5)
Sinusitis	1 (1.6)	-
Tonsillitis	-	1 (1.5)
Wound	-	1 (1.5)
- : Adverse event absent Grade 3 = event that prevented normal everyday 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 364 (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	**Flu 1 Group N = 64**	**Flu 2 Group N = 66**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	3 (4.5) [1]
Hypersensitivity	0 (0.0) [0]	1 (1.5) [1]
Ovarian cyst ruptured	0 (0.0) [0]	1 (1.5) [0]
Wound	0 (0.0) [0]	1 (1.5) [0]
Fatal SAEs	**Flu 1 Group N = 64**	**Flu 2 Group N = 66**
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion: At Day 35, all subjects in Flu 1 Group, presented hemagglutination-inhibition titers that exceeded the regulatory threshold, with a 1:40 seroconversion in 100% of subjects. In the Flu 2 group, 98.4% of the subjects reached the same threshold.
Up to Day 83, 22 (34.4%) and 27 (40.9%) subjects in the Flu 1 and Flu 2 Groups, respectively, reported at least one unsolicited AE. Up to Day 364, 3 SAEs were reported in Flu 2 group, one of which was assessed by the investigator as related to study vaccination. No fatal SAE was reported up to Day 364.
Please also refer to the publication.

Date updated: 05-September-2014