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.: 113572 (FLU D-PAN H1N1-020)

Title: Immunogenicity and safety of GSK Biologicals' pandemic influenza candidate vaccine GSK2340272A GSK234072A (H1N1): 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 a two-dose schedule with H1N1 vaccine with or without previous administration of *Fluarix*™ in subjects aged 61 years and older.
Fluarix™ (Flu S): GSK Biologicals' licensed seasonal Trivalent Influenza Vaccine (TIV)

Phase: III

Study Period: From 08 September 2009 to 08 October 2010

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

Centres: 6 centres in Germany.

Indication: Immunisation against A/California/7/2009 (H1N1)v-like influenza in male and female subjects aged 61 years or above.

Treatment: Study groups were as follows:

- Group A: Subjects received 1 placebo dose at Day -21 (Visit 1), 2 doses of H1N1 vaccine, 1 at Day 0 & 1 at Day 21 (Visits 2 and 3) and 1 dose of Flu S vaccine at Day 42 (Visit 4).
- Group B: Subjects received 1 dose of Flu S vaccine at Day -21 (Visit 1), 2 doses of H1N1 vaccine 1 at Day 0 & 1 at Day 21 (Visits 2 and 3) and 1 dose of placebo at Day 42, after the second H1N1 vaccine dose (Visit 4).

Vaccines were administered intramuscularly in the deltoid region of the dominant (Flu and Placebo) or non-dominant (H1N1) arm.

Objectives: To assess whether vaccination with 2 doses of the H1N1 vaccine results in an HI immune response that meets or exceeds the European Medicines Agency (EMEA) Committee for Medicinal Products for Human Use (CHMP) guidance targets for pandemic influenza vaccines (seroconversion rate (SCR), seroprotection rate (SPR), and seroconversion factor (SCF)) at 21 days after the second dose of H1N1 vaccine when Flu has been administered or not at least 21 days before in subjects aged 61 years and older.

Primary Outcome/Efficacy Variable:
Humoral immune response in terms of Haemagglutination Inhibition (HI) antibodies
• HI antibodies against the vaccine-strain at Day 42.
Derived variables [with 95% Confidence Intervals (CI) for each study group]:
• Geometric mean titres (GMTs) and seropositivity rates of HI antibody titres at Day 42.
• Seroconversion rate (SCR*) at Day 42.
• Seroconversion factor (SCF**) at Day 42.
• Seroprotection rate (SPR***) at Day 42.
*SCR for HI antibody response is defined as the percentage of subjects who have either a prevaccination (Day -21) titre < 1:10 and a post-vaccination titre ≥ 1:40 or a prevaccination titre ≥ 1:10 and at least a 4-fold increase in post-vaccination titre.
**SCF is defined as the fold increase in serum HI antibody GMTs post-vaccination compared to prevaccination (Day -21).
***SPR is defined as the percentage of subjects with a serum HI antibody titre ≥1:40 that usually is accepted as indicating protection.
The CHMP criteria in subjects > 60 years of age are fulfilled if the point estimate for SCR ≥ 30%, the point estimate for SPR is ≥ 60% and the point estimate for SCF is ≥ 2.0.

Secondary Outcome/Efficacy Variable(s):
Humoral immune response in terms of HI antibodies
• HI antibodies against vaccine strain at Day -21, Day 0, Day 21, Day 42, Day 63, Month 6 and Month 12.
Derived variables (with 95% CI for each study group):
• GMTs and seropositivity rates of HI antibodies at Day -21, Day 0, Day 21, Day 42, Day 63, Month 6 and Month 12.
• SCR* at Day 0, Day 21, Day 42, Day 63, Month 6 and Month 12.
• SCF* at Day 0, Day 21, Day 42, Day 63, Month 6 and Month 12.
• SPR* at Day -21, Day 0, Day 21, Day 42, Day 63, Month 6 and Month 12.
*Criteria for evaluation were the same as that for the primary outcome variables.
Safety
• Occurrence of solicited local signs and symptoms, intensity and duration during a 7-Day follow-up period (i.e. Day of

vaccination and 6 subsequent days) after each vaccination.
• Occurrence of solicited general signs and symptoms, intensity, duration and relationship to vaccination during a 7-Day follow-up period (i.e. Day of vaccination and 6 subsequent days) after each vaccination.
• Occurrence of unsolicited adverse events, intensity and relationship to vaccination during the 21 days after each vaccination.
• Occurrence of SAEs, relationship to vaccination during the entire study period.
• Occurrence of AEs of specific interest (AESIs), during the entire study period.

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

- The Total Vaccinated cohort included all subjects with at least 1 vaccine administration documented.
- 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 blood samples were taken and assay results were available for antibodies against at least one study vaccine antigen component after vaccination.
- The ATP cohort for persistence included all evaluable subjects, who met all eligibility criteria, who complied with the procedures defined in the protocol during the entire study period and with the intervals defined in the protocol for visit at Month 6 and Month 12, who did not meet the elimination criteria during the entire study and for whom data concerning immunogenicity outcome measures were available. This cohort included subjects for whom assay results were available for antibodies against the study vaccine antigen component at Month 6 and Month 12.

Analysis of immunogenicity:
The analysis was based on the ATP cohort for immunogenicity and the ATP cohort for persistence.
Point estimate for SCR, SPR, SCF and the associated 95% CI was computed at Day 21 after the second dose of the H1N1 vaccine.
For the humoral immune response in terms of HI antibodies against the different vaccines strains (with 95% confidence intervals [CIs]), for each treatment group, the following parameters were calculated based on different pre-vaccination time points for each strain and group (Pre-vaccination for H1N1 is at Day 0 for both groups; for Flu S, it is at Day 42 for Group A and Day -21 for Group B):

- GMTs of H1N1 HI antibody titres at Day -21, Day 0, Day 21, Day 42 and Day 63.
- SCR at Day 0, Day 21, Day 42 and Day 63.
- SCF at Day 0, Day 21, Day 42 and Day 63.
- SPR at Day -21, Day 0, Day 21, Day 42 and Day 63.

The same parameters were calculated at Month 6 and Month 12 for H1N1 vaccine strain.

Analysis of safety:
The analysis was based on the Total Vaccinated cohort.
The incidence of solicited local and general symptoms occurring during the 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 of grade 3, as well as for solicited general symptoms assessed by the investigator as related to vaccination. All solicited local AEs were assessed as causally related to the vaccination. Duration of local and general symptoms was also calculated within the solicited period after each vaccination.
The percentages of subjects with at least one report of an unsolicited AE classified by Medical Dictionary for Regulatory Activities (MedDRA) preferred term up to 21 days after each vaccination were tabulated for each treatment group. The same tabulation was performed for grade 3 unsolicited adverse events and for unsolicited adverse events that are considered by the investigator to be possibly related to vaccination.
SAEs and AESIs were collected and summarized by MedDRA preferred terms.

Study Population: Male or female adults aged 61 years and above at the time of first vaccination with satisfactory baseline medical assessment by history and physical examination. A written informed consent was obtained from the subjects prior to study entry.

Number of subjects	**Group A**	**Group B**
Planned, N	72	72
Randomised, N (Total Vaccinated cohort)	72	73
Completed, n (%) (Day 21)	72 (100)	72 (98.6)
Completed to Day 63, n(%)	71 (98.6)	72 (98.6)

Completed to Day 364, n (%)	71 (98.6)	71 (97.3)
Total Number Subjects Withdrawn, n (%)	1 (1.4)	2 (2.7)
Withdrawn due to Adverse Events n (%)	1 (1.4)	1 (1.4)
Withdrawn due to Lack of Efficacy n (%)	Not applicable	Not applicable
Withdrawn for other reasons n (%)	0 (0.0)	1 (1.4)
Demographics	**Group A**	**Group B**
N (Total Vaccinated Cohort)	72	73
Females:Males	39:33	34:39
Mean Age, years (SD)	69.1 (5.16)	69.7 (5.59)
White - Caucasian / European heritage, n (%)	71 (98.6)	73 (100)

Primary Efficacy Results: Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 (ATP cohort for immunogenicity)

				≥ 1:10				GMT		
						95% CI			95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/09	Group A	PRE	64	22	34.4	22.9	47.3	8.7	6.9	11.1
		PI(D0)	64	26	40.6	28.5	53.6	9.2	7.3	11.7
		PII(D21)	64	64	100	94.4	100	147.5	111.9	194.4
		PIII(D42)*	64	64	100	94.4	100	309.8	246.4	389.6
		PIII(D63)	63	63	100	94.3	100	223.8	181.2	276.5
	Group B	PRE	67	21	31.3	20.6	43.8	7.4	6.3	8.7
		PI(D0)	67	50	74.6	62.5	84.5	13.8	11.3	16.9
		PII(D21)	67	67	100	94.6	100	109.6	82.4	145.8
		PIII(D42)*	67	67	100	94.6	100	227.5	181.5	285.3
		PIII(D63)	66	66	100	94.6	100	174.0	138.7	218.4

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
PI(D0) = Post-dose 1 Day 0
PII(D21) = Post-dose 2 Day 21
PIII(D42) = Post-dose 3 Day 42
PIII(D63) = Post-dose 3 Day 63
PRE = Pre-vaccination Day -21
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.
* Primary outcome variable

Primary Efficacy Results: SCR for HI antibodies against Flu A/CAL/7/09 at Day 21 and Day 42 (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Group A	PII(D21)	64	57	89.1	78.8	95.5
		PIII(D42)*	64	61	95.3	86.9	99.0
	Group B	PII(D21)	67	43	64.2	51.5	75.5
		PIII(D42)*	67	59	88.1	77.8	94.7

Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 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
PII(D21) = Post-dose 2 Day 21
PIII(D42) = Post-dose 3 Day 42
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-

vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.
* Primary outcome variable

Primary Efficacy Results: SCF for HI antibodies against Flu A/CAL/7/09 at Day 21 and Day 42 (ATP cohort for immunogenicity)

				SCF		
					95% CI	
Antibody against	**Group**	**Timing**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09	Group A	PII(D21)	64	16.0	12.2	21.0
		PIII(D42)*	64	33.6	25.5	44.3
	Group B	PII(D21)	67	7.9	5.8	10.8
		PIII(D42)*	67	16.5	12.4	21.9

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
PII(D21) = Post-dose 2 Day 21
PIII(D42) = Post-dose 3 Day 42
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.
* Primary outcome variable

Primary Efficacy Results: SPR for HI antibodies against Flu A/CAL/7/09 at Day -21, Day 0, Day 21, Day 42 and Day 63 (ATP cohort for immunogenicity)

				SPR			
						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Group A	PRE	64	9	14.1	6.6	25.0
		PI(D0)	64	9	14.1	6.6	25.0
		PII(D21)	64	60	93.8	84.8	98.3
		PIII(D42)*	64	64	100	94.4	100
		PIII(D63)	63	63	100	94.3	100
	Group B	PRE	67	4	6.0	1.7	14.6
		PI(D0)	67	12	17.9	9.6	29.2
		PII(D21)	67	58	86.6	76.0	93.7
		PIII(D42)*	67	67	100	94.6	100
		PIII(D63)	66	65	98.5	91.8	100

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D0) = Post-dose 1 Day 0
PII(D21) = Post-dose 2 Day 21
PIII(D42) = Post-dose 3 Day 42
PIII(D63) = Post-dose 3 Day 63
PRE = Pre-vaccination Day -21
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.
* Primary outcome variable

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/Bri/59/07 (ATP cohort for immunogenicity)

				≥ 1:10				**GMT**		
						95% CI			**95% CI**	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/Bri/59/07	Group A	PRE	64	57	89.1	78.8	95.5	23.1	18.9	28.4
		PI(D0)	64	56	87.5	76.8	94.4	22.4	18.2	27.5
		PIII(D42)	64	62	96.9	89.2	99.6	32.3	26.4	39.7
		PIII(D63)	63	62	98.4	91.5	100	55.7	45.1	68.7
	Group	PRE	67	58	86.6	76.0	93.7	20.8	16.7	25.9

	B	PI(D0)	67	67	100	94.6	100	64.0	50.8	80.5
		PIII(D42)	67	67	100	94.6	100	56.5	45.3	70.5
		PIII(D63)	66	66	100	94.6	100	49.8	40.1	61.9

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
PI(D0) = Post-dose 1 Day 0
PIII(D42) = Post-dose 3 Day 42
PIII(D63) = Post-dose 3 Day 63
PRE = Pre-vaccination Day -21
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against FluB/Bri/60/08 (ATP cohort for immunogenicity)

					≥ 1:10			**GMT**		
						95% CI			**95% CI**	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
FluB/Bri/60/08	Group A	PRE	64	64	100	94.4	100	120.7	98.7	147.7
		PI(D0)	64	64	100	94.4	100	118.8	97.7	144.5
		PIII(D42)	64	64	100	94.4	100	182.2	154.7	214.6
		PIII(D63)	63	63	100	94.3	100	291.3	246.2	344.7
	Group B	PRE	67	67	100	94.6	100	135.6	107.2	171.6
		PI(D0)	67	67	100	94.6	100	351.2	285.6	431.9
		PIII(D42)	67	67	100	94.6	100	291.5	238.8	355.8
		PIII(D63)	66	66	100	94.6	100	273.3	225.3	331.6

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
PI(D0) = Post-dose 1 Day 0
PIII(D42) = Post-dose 3 Day 42
PIII(D63) = Post-dose 3 Day 63
PRE = Pre-vaccination Day -21
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/Uru/716/07.(ATP cohort for immunogenicity)

					≥ 1:10			**GMT**		
						95% CI			**95% CI**	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/Uru/716/07	Group A	PRE	64	51	79.7	67.8	88.7	26.2	19.2	35.7
		PI(D0)	64	51	79.7	67.8	88.7	25.5	18.8	34.6
		PIII(D42)	64	57	89.1	78.8	95.5	27.1	20.7	35.4
		PIII(D63)	63	63	100	94.3	100	85.9	65.2	113.2
	Group B	PRE	67	52	77.6	65.8	86.9	22.5	16.2	31.2
		PI(D0)	67	66	98.5	92.0	100	100.9	75.9	134.1
		PIII(D42)	67	66	98.5	92.0	100	69.2	51.0	93.7
		PIII(D63)	66	65	98.5	91.8	100	62.4	46.9	83.2

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
PI(D0) = Post-dose 1 Day 0
PIII(D42) = Post-dose 3 Day 42

PIII(D63) = Post-dose 3 Day 63
PRE = Pre-vaccination Day -21
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 (ATP cohort for persistence)

				≥ 1:10				GMT		
						95% CI			95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/09	Group A	PIII(M6)	60	60	100	94.0	100	102.0	78.6	132.3
		PIII(M12)	60	57	95.0	86.1	99.0	35.6	27.0	47.0
	Group B	PIII(M6)	63	63	100	94.3	100	74.1	59.0	92.9
		PIII(M12)	64	60	93.8	84.8	98.3	25.7	20.8	31.9

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
PIII(M6) = Post-vaccination at Month 6
PIII(M12) = Post-vaccination at Month 12

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/Bri/59/07 at Day 0 and Day 63 (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Bri/59/07	Group A	PIII(D63)	63	9	14.3	6.7	25.4
	Group B	PI(D0)	67	21	31.3	20.6	43.8

Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 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(D0) = Post-dose 1 Day 0
PIII(D63) = Post-dose 3 Day 63
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): SCR for HI antibodies against FluB/Bri/60/08 at Day 0 and Day 63 (ATP cohort for immunogenicity)

					SCR		
						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
FluB/Bri/60/08	Group A	PIII(D63)	63	4	6.3	1.8	15.5
	Group B	PI(D0)	67	18	26.9	16.8	39.1

Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 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(D0) = Post-dose 1 Day 0
PIII(D63) = Post-dose 3 Day 63
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/Uru/716/07 at Day 0 and Day 63 (ATP cohort for immunogenicity)

	SCR

						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Uru/716/07	Group A	PIII(D63)	63	25	39.7	27.6	52.8
	Group B	PI(D0)	67	34	50.7	38.2	63.2

Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 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(D0) = Post-dose 1 Day 0
PIII(D63) = Post-dose 3 Day 63
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/09 at Month 6 and Month 12 (ATP cohort for persistence)

				SCR			
						95% CI	
Strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Group A	PIII(M6)	60	48	80.0	67.7	89.2
		PIII(M12)	60	19	31.7	20.3	45.0
	Group B	PIII(M6)	63	39	61.9	48.8	73.9
		PIII(M12)	64	11	17.2	8.9	28.7

Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 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
PIII(M6) = Post-vaccination at Month 6
PIII(M12) = Post-vaccination at Month 12

Secondary Outcome Variable(s): SCF for HI antibodies against Flu A/Bri/59/07 at Day 0 and Day 63 (ATP cohort for immunogenicity)

				SCF		
					95% CI	
Antibody against	**Group**	**Timing**	**N**	**Value**	**LL**	**UL**
Flu A/Bri/59/07	Group A	PIII(D63)	63	1.7	1.4	2.1
	Group B	PI(D0)	67	3.1	2.3	4.1

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(D0) = Post-dose 1 Day 0
PIII(D63) = Post-dose 3 Day 63
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): SCF for HI antibodies against FluB/Bri/60/08 at Day 0 and Day 63 (ATP cohort for immunogenicity)

				SCF		
					95% CI	
Antibody against	**Group**	**Timing**	**N**	**Value**	**LL**	**UL**
FluB/Bri/60/08	Group A	PIII(D63)	63	1.6	1.4	1.8
	Group B	PI(D0)	67	2.6	2.1	3.2

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(D0) = Post-dose 1 Day 0

PIII(D63) = Post-dose 3 Day 63
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): SCF for HI antibodies against Flu A/Uru/716/07 at Day 0 and Day 63 (ATP cohort for immunogenicity)

				SCF		
					95% CI	
Antibody against	**Group**	**Timing**	**N**	**Value**	**LL**	**UL**
Flu A/Uru/716/07	Group A	PIII(D63)	63	3.1	2.5	4.0
	Group B	PI(D0)	67	4.5	3.3	6.0

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(D0) = Post-dose 1 Day 0
PIII(D63) = Post-dose 3 Day 63
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): SCF for HI antibodies against Flu A/CAL/7/09 at Month 6 and Month 12 (ATP cohort for persistence)

				SCF		
					95% CI	
Strain	**Group**	**Timing**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09	Group A	PIII(M6)	60	10.9	8.5	14.1
		PIII(M12)	60	3.8	2.9	5.0
	Group B	PIII(M6)	63	5.2	3.8	6.9
		PIII(M12)	64	1.8	1.4	2.4

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
PIII(M6) = Post-vaccination at Month 6
PIII(M12) = Post-vaccination at Month 12

Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/Bri/59/07 at Day -21, Day 0, Day 42 and Day 63 (ATP cohort for immunogenicity)

				SPR			
						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Bri/59/07	Group A	PRE	64	25	39.1	27.1	52.1
		PI(D0)	64	26	40.6	28.5	53.6
		PIII(D42)	64	30	46.9	34.3	59.8
		PIII(D63)	63	50	79.4	67.3	88.5
	Group B	PRE	67	21	31.3	20.6	43.8
		PI(D0)	67	50	74.6	62.5	84.5
		PIII(D42)	67	47	70.1	57.7	80.7
		PIII(D63)	66	42	63.6	50.9	75.1

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D0) = Post-dose 1 Day 0
PIII(D42) = Post-dose 3 Day 42
PIII(D63) = Post-dose 3 Day 63
PRE = Pre-vaccination Day -21
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): SPR for HI antibodies against FluB/Bri/60/08 at Day -21, Day 0, Day 42 and Day 63 (ATP cohort for immunogenicity)

	SPR

						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
FluB/Bri/60/08	Group A	PRE	64	61	95.3	86.9	99.0
		PI(D0)	64	61	95.3	86.9	99.0
		PIII(D42)	64	64	100	94.4	100
		PIII(D63)	63	63	100	94.3	100
	Group B	PRE	67	63	94.0	85.4	98.3
		PI(D0)	67	67	100	94.6	100
		PIII(D42)	67	67	100	94.6	100
		PIII(D63)	66	66	100	94.6	100

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D0) = Post-dose 1 Day 0
PIII(D42) = Post-dose 3 Day 42
PIII(D63) = Post-dose 3 Day 63
PRE = Pre-vaccination Day -21
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/Uru/716/07 at Day -21, Day 0, Day 42 and Day 63 (ATP cohort for immunogenicity)

				SPR			
						95% CI	
Antibody against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Uru/716/07	Group A	PRE	64	30	46.9	34.3	59.8
		PI(D0)	64	29	45.3	32.8	58.3
		PIII(D42)	64	30	46.9	34.3	59.8
		PIII(D63)	63	54	85.7	74.6	93.3
	Group B	PRE	67	22	32.8	21.8	45.4
		PI(D0)	67	57	85.1	74.3	92.6
		PIII(D42)	67	47	70.1	57.7	80.7
		PIII(D63)	66	46	69.7	57.1	80.4

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D0) = Post-dose 1 Day 0
PIII(D42) = Post-dose 3 Day 42
PIII(D63) = Post-dose 3 Day 63
PRE = Pre-vaccination Day -21
Note: Seropositivity rates are computed based on different pre-vaccination time points for each strain and group. Pre-vaccination for H1N1 is at Day 0 for both groups. For Flu S vaccine, it is at Day 42 for Group A and Day -21 for Group B.

Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/09 at Month 6 and Month 12 (ATP cohort for persistence)

				SPR			
						95% CI	
Strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09 H1N1.HA Ab	Group A	PIII(M6)	60	52	86.7	75.4	94.1
		PIII(M12)	60	28	46.7	33.7	60.0
	Group B	PIII(M6)	63	53	84.1	72.7	92.1
		PIII(M12)	64	19	29.7	18.9	42.4

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PIII(M6) = Post-vaccination at Month 6
PIII(M12) = Post-vaccination at Month 12

Secondary Outcome Variable(s): Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-

vaccination period following each dose of H1N1 candidate vaccine and across doses (Total Vaccinated cohort)

		Group A					Group B				
					95 % CI					95 % CI	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 2											
Pain	Any	71	44	62.0	49.7	73.2	71	40	56.3	44.0	68.1
	Grade 3	71	1	1.4	0.0	7.6	71	1	1.4	0.0	7.6
Redness	Any	71	7	9.9	4.1	19.3	71	8	11.3	5.0	21.0
	> 100 mm	71	0	0.0	0.0	5.1	71	0	0.0	0.0	5.1
Swelling	Any	71	4	5.6	1.6	13.8	71	10	14.1	7.0	24.4
	> 100 mm	71	0	0.0	0.0	5.1	71	0	0.0	0.0	5.1
Dose 3											
Pain	Any	70	42	60.0	47.6	71.5	70	33	47.1	35.1	59.4
	Grade 3	70	0	0.0	0.0	5.1	70	1	1.4	0.0	7.7
Redness	Any	70	6	8.6	3.2	17.7	70	5	7.1	2.4	15.9
	> 100 mm	70	0	0.0	0.0	5.1	70	1	1.4	0.0	7.7
Swelling	Any	70	5	7.1	2.4	15.9	70	5	7.1	2.4	15.9
	> 100 mm	70	0	0.0	0.0	5.1	70	1	1.4	0.0	7.7
Across doses											
Pain	Any	72	49	68.1	56.0	78.6	71	43	60.6	48.3	72.0
	Grade 3	72	1	1.4	0.0	7.5	71	2	2.8	0.3	9.8
Redness	Any	72	11	15.3	7.9	25.7	71	10	14.1	7.0	24.4
	> 100 mm	72	0	0.0	0.0	5.0	71	1	1.4	0.0	7.6
Swelling	Any	72	8	11.1	4.9	20.7	71	11	15.5	8.0	26.0
	> 100 mm	72	0	0.0	0.0	5.0	71	1	1.4	0.0	7.6

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= Significant pain at rest; prevented normal activities as assessed by inability to attend/do work or school

Secondary Outcome Variable(s): Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose of Placebo or Flu S vaccine at Day -21 (Total Vaccinated cohort)

		Group A					Group B				
					95 % CI					95 % CI	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Pain	Any	72	5	6.9	2.3	15.5	72	12	16.7	8.9	27.3
	Grade 3	72	0	0.0	0.0	5.0	72	0	0.0	0.0	5.0
Redness	Any	72	2	2.8	0.3	9.7	72	1	1.4	0.0	7.5
	> 100 mm	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
Swelling	Any	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
	> 100 mm	72	0	0.0	0.0	5.0	72	0	0.0	0.0	5.0

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= Significant pain at rest; prevented normal activities as assessed by inability to attend/do work or school

Secondary Outcome Variable(s): Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose of Flu S vaccine or Placebo at Day 42 (Total Vaccinated cohort)

		Group A					Group B				
					95 % CI					95 % CI	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Pain	Any	69	17	24.6	15.1	36.5	71	4	5.6	1.6	13.8
	Grade 3	69	0	0.0	0.0	5.2	71	0	0.0	0.0	5.1
Redness	Any	69	1	1.4	0.0	7.8	71	0	0.0	0.0	5.1
	> 100 mm	69	0	0.0	0.0	5.2	71	0	0.0	0.0	5.1

Swelling	Any	69	2	2.9	0.4	10.1	71	0	0.0	0.0	5.1
	> 100 mm	69	0	0.0	0.0	5.2	71	0	0.0	0.0	5.1

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= Significant pain at rest; prevented normal activities as assessed by inability to attend/do work or school

Secondary Outcome Variable(s): Number of days with local symptoms during the solicited post-vaccination period of H1N1 candidate vaccine (Total Vaccinated cohort)

Solicited symptom	Dose	Group	N	Mean	Median
Pain	Dose 2	Group A	44	2.9	3.0
		Group B	40	3.2	3.0
	Dose 3	Group A	42	2.8	2.0
		Group B	33	3.1	3.0
Redness	Dose 2	Group A	7	2.7	3.0
		Group B	8	3.9	3.5
	Dose 3	Group A	6	2.8	2.5
		Group B	5	3.2	3.0
Swelling	Dose 2	Group A	4	3.0	3.0
		Group B	10	3.0	3.0
	Dose 3	Group A	5	2.6	3.0
		Group B	5	2.8	3.0

N = number of doses with the symptom

Secondary Outcome Variable(s): Number of days with local symptoms during the solicited post-vaccination period of Placebo or Flu S vaccine at Day -21 (Total Vaccinated cohort)

Solicited symptom	Group	N	Mean	Median
Pain	Group A	5	1.8	1.0
	Group B	12	2.2	2.0
Redness	Group A	2	4.0	4.0
	Group B	1	2.0	2.0
Swelling	Group B	1	2.0	2.0

N = number of doses with the symptom

Secondary Outcome Variable(s): Number of days with local symptoms during the solicited post-vaccination period of Flu S vaccine or Placebo at Day 42 (Total Vaccinated cohort)

Solicited symptom	Group	N	Mean	Median
Pain	Group A	17	1.8	2.0
	Group B	4	3.0	3.0
Redness	Group A	1	1.0	1.0
Swelling	Group A	2	1.5	1.5

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 of H1N1 candidate vaccine and across doses (Total Vaccinated cohort)

		Group A					Group B				
					95 % CI					95 % CI	
Symptom	**Intensity/ Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 2											
Fatigue	Any	71	13	18.3	10.1	29.3	71	10	14.1	7.0	24.4
	Grade 3	71	2	2.8	0.3	9.8	71	0	0.0	0.0	5.1
	Related	71	12	16.9	9.0	27.7	71	8	11.3	5.0	21.0
Headache	Any	71	14	19.7	11.2	30.9	71	9	12.7	6.0	22.7
	Grade 3	71	2	2.8	0.3	9.8	71	0	0.0	0.0	5.1
	Related	71	14	19.7	11.2	30.9	71	8	11.3	5.0	21.0
Joint pain at other location	Any	71	11	15.5	8.0	26.0	71	4	5.6	1.6	13.8
	Grade 3	71	2	2.8	0.3	9.8	71	0	0.0	0.0	5.1

	Related	71	9	12.7	6.0	22.7	71	4	5.6	1.6	13.8
Muscle aches	Any	71	15	21.1	12.3	32.4	71	15	21.1	12.3	32.4
	Grade 3	71	2	2.8	0.3	9.8	71	1	1.4	0.0	7.6
	Related	71	13	18.3	10.1	29.3	71	14	19.7	11.2	30.9
Shivering	Any	71	4	5.6	1.6	13.8	71	8	11.3	5.0	21.0
	Grade 3	71	1	1.4	0.0	7.6	71	0	0.0	0.0	5.1
	Related	71	4	5.6	1.6	13.8	71	4	5.6	1.6	13.8
Sweating	Any	71	4	5.6	1.6	13.8	71	7	9.9	4.1	19.3
	Grade 3	71	1	1.4	0.0	7.6	71	0	0.0	0.0	5.1
	Related	71	3	4.2	0.9	11.9	71	3	4.2	0.9	11.9
Temperature/ (Axillary)	≥ 37.5°C	71	0	0.0	0.0	5.1	71	1	1.4	0.0	7.6
	≥ 39.0°C	71	0	0.0	0.0	5.1	71	0	0.0	0.0	5.1
	Related	71	0	0.0	0.0	5.1	71	0	0.0	0.0	5.1
Dose 3											
Fatigue	Any	70	13	18.6	10.3	29.7	70	12	17.1	9.2	28.0
	Grade 3	70	2	2.9	0.3	9.9	70	0	0.0	0.0	5.1
	Related	70	13	18.6	10.3	29.7	70	11	15.7	8.1	26.4
Headache	Any	70	16	22.9	13.7	34.4	70	14	20.0	11.4	31.3
	Grade 3	70	2	2.9	0.3	9.9	70	0	0.0	0.0	5.1
	Related	70	16	22.9	13.7	34.4	70	13	18.6	10.3	29.7
Joint pain at other location	Any	70	15	21.4	12.5	32.9	70	13	18.6	10.3	29.7
	Grade 3	70	0	0.0	0.0	5.1	70	0	0.0	0.0	5.1
	Related	70	15	21.4	12.5	32.9	70	10	14.3	7.1	24.7
Muscle aches	Any	70	17	24.3	14.8	36.0	70	17	24.3	14.8	36.0
	Grade 3	70	0	0.0	0.0	5.1	70	0	0.0	0.0	5.1
	Related	70	17	24.3	14.8	36.0	70	16	22.9	13.7	34.4
Shivering	Any	70	11	15.7	8.1	26.4	70	11	15.7	8.1	26.4
	Grade 3	70	0	0.0	0.0	5.1	70	0	0.0	0.0	5.1
	Related	70	11	15.7	8.1	26.4	70	10	14.3	7.1	24.7
Sweating	Any	70	9	12.9	6.1	23.0	70	6	8.6	3.2	17.7
	Grade 3	70	2	2.9	0.3	9.9	70	1	1.4	0.0	7.7
	Related	70	9	12.9	6.1	23.0	70	6	8.6	3.2	17.7
Temperature/ (Axillary)	≥ 37.5°C	70	2	2.9	0.3	9.9	70	2	2.9	0.3	9.9
	≥ 39.0°C	70	0	0.0	0.0	5.1	70	0	0.0	0.0	5.1
	Related	70	2	2.9	0.3	9.9	70	2	2.9	0.3	9.9
Across doses											
Fatigue	Any	72	22	30.6	20.2	42.5	71	18	25.4	15.8	37.1
	Grade 3	72	3	4.2	0.9	11.7	71	0	0.0	0.0	5.1
	Related	72	22	30.6	20.2	42.5	71	15	21.1	12.3	32.4
Headache	Any	72	23	31.9	21.4	44.0	71	19	26.8	16.9	38.6
	Grade 3	72	3	4.2	0.9	11.7	71	0	0.0	0.0	5.1
	Related	72	23	31.9	21.4	44.0	71	17	23.9	14.6	35.5
Joint pain at other location	Any	72	20	27.8	17.9	39.6	71	13	18.3	10.1	29.3
	Grade 3	72	2	2.8	0.3	9.7	71	0	0.0	0.0	5.1
	Related	72	19	26.4	16.7	38.1	71	10	14.1	7.0	24.4
Muscle aches	Any	72	23	31.9	21.4	44.0	71	22	31.0	20.5	43.1
	Grade 3	72	2	2.8	0.3	9.7	71	1	1.4	0.0	7.6
	Related	72	21	29.2	19.0	41.1	71	20	28.2	18.1	40.1
Shivering	Any	72	14	19.4	11.1	30.5	71	15	21.1	12.3	32.4
	Grade 3	72	1	1.4	0.0	7.5	71	0	0.0	0.0	5.1
	Related	72	14	19.4	11.1	30.5	71	10	14.1	7.0	24.4
Sweating	Any	72	12	16.7	8.9	27.3	71	13	18.3	10.1	29.3
	Grade 3	72	3	4.2	0.9	11.7	71	1	1.4	0.0	7.6
	Related	72	11	15.3	7.9	25.7	71	9	12.7	6.0	22.7
Temperature/	≥ 37.5°C	72	2	2.8	0.3	9.7	71	3	4.2	0.9	11.9

(Axillary)	≥ 39.0°C	72	0	0.0	0.0	5.0	71	0	0.0	0.0	5.1
	Related	72	2	2.8	0.3	9.7	71	2	2.8	0.3	9.8

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 or relation to vaccination
Grade 3= general symptom that prevented normal everyday activities as assessed by inability to attend/do work or school, or required intervention of a physician/healthcare provider
Related= general symptom assessed by the investigator as causally related to the study vaccination

Secondary Outcome Variable(s): Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose of Placebo or Flu S vaccine at Day -21 (Total Vaccinated cohort)

		Group A					**Group B**				
					95 % CI					**95 % CI**	
Symptom	**Intensity/ Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Fatigue	Any	72	9	12.5	5.9	22.4	72	7	9.7	4.0	19.0
	Grade 3	72	1	1.4	0.0	7.5	72	0	0.0	0.0	5.0
	Related	72	6	8.3	3.1	17.3	72	6	8.3	3.1	17.3
Headache	Any	72	5	6.9	2.3	15.5	72	10	13.9	6.9	24.1
	Grade 3	72	0	0.0	0.0	5.0	72	0	0.0	0.0	5.0
	Related	72	3	4.2	0.9	11.7	72	8	11.1	4.9	20.7
Joint pain at other location	Any	72	7	9.7	4.0	19.0	72	2	2.8	0.3	9.7
	Grade 3	72	1	1.4	0.0	7.5	72	1	1.4	0.0	7.5
	Related	72	4	5.6	1.5	13.6	72	2	2.8	0.3	9.7
Muscle aches	Any	72	4	5.6	1.5	13.6	72	6	8.3	3.1	17.3
	Grade 3	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
	Related	72	3	4.2	0.9	11.7	72	5	6.9	2.3	15.5
Shivering	Any	72	2	2.8	0.3	9.7	72	4	5.6	1.5	13.6
	Grade 3	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
	Related	72	2	2.8	0.3	9.7	72	3	4.2	0.9	11.7
Sweating	Any	72	5	6.9	2.3	15.5	72	6	8.3	3.1	17.3
	Grade 3	72	0	0.0	0.0	5.0	72	2	2.8	0.3	9.7
	Related	72	3	4.2	0.9	11.7	72	4	5.6	1.5	13.6
Temperature/ (Axillary)	≥ 37.5°C	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
	≥ 39.0°C	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
	Related	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5

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 or relation to vaccination
Grade 3= general symptom that prevented normal everyday activities as assessed by inability to attend/do work or school, or required intervention of a physician/healthcare provider
Related= general symptom assessed by the investigator as causally related to the study vaccination

Secondary Outcome Variable(s): Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose of Flu S vaccine or Placebo at Day 42 (Total Vaccinated cohort)

		Group A					**Group B**				
					95 % CI					**95 % CI**	
Symptom	**Intensity/ Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Fatigue	Any	69	10	14.5	7.2	25.0	71	4	5.6	1.6	13.8
	Grade 3	69	1	1.4	0.0	7.8	71	0	0.0	0.0	5.1
	Related	69	10	14.5	7.2	25.0	71	3	4.2	0.9	11.9
Headache	Any	69	10	14.5	7.2	25.0	71	8	11.3	5.0	21.0
	Grade 3	69	0	0.0	0.0	5.2	71	0	0.0	0.0	5.1
	Related	69	10	14.5	7.2	25.0	71	5	7.0	2.3	15.7
Joint pain at	Any	69	8	11.6	5.1	21.6	71	6	8.5	3.2	17.5

other location	Grade 3	69	0	0.0	0.0	5.2	71	1	1.4	0.0	7.6
	Related	69	8	11.6	5.1	21.6	71	4	5.6	1.6	13.8
Muscle aches	Any	69	7	10.1	4.2	19.8	71	5	7.0	2.3	15.7
	Grade 3	69	0	0.0	0.0	5.2	71	1	1.4	0.0	7.6
	Related	69	7	10.1	4.2	19.8	71	3	4.2	0.9	11.9
Shivering	Any	69	3	4.3	0.9	12.2	71	3	4.2	0.9	11.9
	Grade 3	69	0	0.0	0.0	5.2	71	0	0.0	0.0	5.1
	Related	69	3	4.3	0.9	12.2	71	3	4.2	0.9	11.9
Sweating	Any	69	3	4.3	0.9	12.2	71	4	5.6	1.6	13.8
	Grade 3	69	0	0.0	0.0	5.2	71	0	0.0	0.0	5.1
	Related	69	3	4.3	0.9	12.2	71	4	5.6	1.6	13.8
Temperature/ (Axillary)	≥ 37.5°C	69	0	0.0	0.0	5.2	71	0	0.0	0.0	5.1
	≥ 39.0°C	69	0	0.0	0.0	5.2	71	0	0.0	0.0	5.1
	Related	69	0	0.0	0.0	5.2	71	0	0.0	0.0	5.1

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 or relation to vaccination
Grade 3= general symptom that prevented normal everyday activities as assessed by inability to attend/do work or school, or required intervention of a physician/healthcare provider
Related= general symptom assessed by the investigator as causally related to the study vaccination

Secondary Outcome Variable(s): Number of days with general symptoms during the solicited post-vaccination period of H1N1 candidate vaccine (Total Vaccinated cohort)

Solicited symptom	**Dose**	**Group**	**N**	**Mean**	**Median**
Fatigue	Dose 2	Group A	13	2.4	2.0
		Group B	10	2.6	2.0
	Dose 3	Group A	13	2.4	2.0
		Group B	12	2.2	2.0
Headache	Dose 2	Group A	14	2.4	2.0
		Group B	9	2.6	2.0
	Dose 3	Group A	16	2.9	2.0
		Group B	14	2.1	2.0
Joint pain at other location	Dose 2	Group A	11	3.5	3.0
		Group B	4	2.5	2.5
	Dose 3	Group A	15	3.5	3.0
		Group B	13	3.0	2.0
Muscle aches	Dose 2	Group A	15	2.9	3.0
		Group B	15	2.5	2.0
	Dose 3	Group A	17	3.4	3.0
		Group B	17	2.6	2.0
Sweating	Dose 2	Group A	4	1.3	1.0
		Group B	7	1.7	2.0
	Dose 3	Group A	9	1.8	2.0
		Group B	6	2.7	2.0
Shivering	Dose 2	Group A	4	2.0	1.5
		Group B	8	1.6	1.5
	Dose 3	Group A	11	1.5	1.0
		Group B	11	1.6	1.0
Temperature	Dose 2	Group B	1	2.0	2.0
	Dose 3	Group A	2	1.0	1.0
		Group B	2	1.0	1.0

N = number of doses with the symptom

Secondary Outcome Variable(s): Number of days with general symptoms during the solicited post-vaccination period of Placebo or Flu S vaccine at Day -21 (Total Vaccinated cohort)

Solicited symptom	**Group**	**N**	**Mean**	**Median**

Fatigue	Group A	9	2.0	1.0
	Group B	7	2.1	1.0
Headache	Group A	5	2.6	2.0
	Group B	10	1.7	1.0
Joint pain at other location	Group A	7	3.6	3.0
	Group B	2	4.5	4.5
Muscle aches	Group A	4	1.8	1.5
	Group B	6	2.3	1.5
Sweating	Group A	5	2.4	1.0
	Group B	6	3.5	3.5
Shivering	Group A	2	4.5	4.5
	Group B	4	2.3	2.5
Temperature	Group B	1	3.0	3.0
N = number of doses with the symptom				
Secondary Outcome Variable(s): Number of days with general symptoms during the solicited post-vaccination period of Flu S vaccine or Placebo at Day 42 (Total Vaccinated cohort)				
Solicited symptom	**Group**	**N**	**Mean**	**Median**
Fatigue	Group A	10	2.6	1.5
	Group B	4	2.0	1.0
Headache	Group A	10	2.9	2.5
	Group B	8	2.3	1.5
Joint pain at other location	Group A	8	3.3	3.0
	Group B	6	2.8	1.5
Muscle aches	Group A	7	3.0	3.0
	Group B	5	4.2	4.0
Sweating	Group A	3	1.7	2.0
	Group B	4	1.5	1.5
Shivering	Group A	3	1.3	1.0
	Group B	3	1.7	1.0
N = number of doses with the symptom				
Secondary Outcome Variable(s): Percentage of subjects reporting the occurrence of AEs of specific interest up to Day 63 (Total Vaccinated cohort)				
Most frequent AEs of specific interest		**Group A N = 72**	**Group B N = 73**	
Subjects with any AE(s) of specific interest, n (%)		0 (0.0)	0 (0.0)	
Secondary Outcome Variable(s): Percentage of subjects reporting the occurrence of AEs of specific interest during the entire study period (Total Vaccinated cohort)				
Most frequent AEs of specific interest		**Group A N = 72**	**Group B N = 73**	
Subjects with any AE(s) of specific interest, n (%)		0 (0.0)	1 (1.4)	
VIth nerve paralysis		0 (0.0)	1 (1.4)	
Safety results: Number (%) of subjects with adverse events occurring within Day 0-20 following each vaccination (Total Vaccinated cohort)				
Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)		**Group A N = 72**	**Group B N = 73**	
Subjects with any AE(s), n (%)		33 (45.8)	37 (50.7)	
Subjects with grade 3 AE(s), n (%)		4 (5.6)	10 (13.7)	
Subjects with related AE(s), n (%)		14 (19.4)	9 (12.3)	
Nasopharyngitis		11 (15.3)	8 (11.0)	
Cough		3 (4.2)	2 (2.7)	
Cystitis		1 (1.4)	3 (4.1)	
Abdominal pain upper		1 (1.4)	2 (2.7)	
Back pain		-	3 (4.1)	
Bronchitis		3 (4.2)	-	
Contusion		1 (1.4)	2 (2.7)	

Diarrhoea	1 (1.4)	2 (2.7)
Eczema	1 (1.4)	2 (2.7)
Gastroenteritis	-	3 (4.1)
Headache	3 (4.2)	-
Gingivitis	-	2 (2.7)
Injection site pruritus	2 (2.8)	-
Migraine	2 (2.8)	-
Osteoarthritis	2 (2.8)	-
Rhinorrhoea	-	2 (2.7)
Sleep disorder	2 (2.8)	-
Arthralgia	1 (1.4)	-
Arthropod bite	1 (1.4)	-
Basal cell carcinoma	1 (1.4)	-
Blood glucose decreased	1 (1.4)	-
Cataract operation	1 (1.4)	-
Dental prosthesis user	1 (1.4)	-
Dizziness	1 (1.4)	-
Dysgeusia	1 (1.4)	-
Dyspepsia	1 (1.4)	-
Dysphonia	1 (1.4)	-
Ear pain	1 (1.4)	-
Fatigue	1 (1.4)	-
Feeling cold	1 (1.4)	-
Hyperhidrosis	1 (1.4)	-
Hypertension	1 (1.4)	-
Insomnia	1 (1.4)	-
Intercostal neuralgia	1 (1.4)	-
Joint sprain	1 (1.4)	-
Lumbar vertebral fracture	1 (1.4)	-
Myalgia	1 (1.4)	-
Oropharyngeal pain	1 (1.4)	-
Palpitations	1 (1.4)	-
Peripheral coldness	1 (1.4)	-
Radius fracture	1 (1.4)	-
Rash macular	1 (1.4)	-
Respiratory disorder	1 (1.4)	-
Skeletal injury	1 (1.4)	-
Skin laceration	1 (1.4)	-
Thrombophlebitis	1 (1.4)	-
Tinea pedis	1 (1.4)	-
Tooth disorder	1 (1.4)	-
Toothache	1 (1.4)	-
Wound	1 (1.4)	-
- : Adverse event absent or not meeting the selected rule: more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed. 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 SAEs up to Day 63 (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	**Group A N = 72**	**Group B N = 73**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	2 (2.8) [0]	4 (5.5) [1]
Cardiac failure	0 (0.0) [0]	1 (1.4) [0]
Femoral arterial stenosis	0 (0.0) [0]	1 (1.4) [0]
Gastroenteritis	0 (0.0) [0]	1 (1.4) [0]

Lumbar vertebral fracture	1 (1.4) [0]	0 (0.0) [0]
Myalgia	0 (0.0) [0]	1 (1.4) [1]
Radius fracture	1 (1.4) [0]	0 (0.0) [0]
Spinal compression fracture	0 (0.0) [0]	1 (1.4) [0]
Fatal SAEs	**Group A N = 72**	**Group B N = 73**
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]
Safety results: Number (%) of subjects with SAEs during the entire study period (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		

All SAEs	**Group A N = 72**	**Group B N = 73**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	11 (15.3) [0]	14 (19.2) [1]
Osteoarthritis	0 (0.0) [0]	2 (2.7) [0]
Sciatica	0 (0.0) [0]	2 (2.7) [0]
Atrial fibrillation	1 (1.4) [0]	0 (0.0) [0]
Breast mass	1 (1.4) [0]	0 (0.0) [0]
Cardiac failure	0 (0.0) [0]	1 (1.4) [0]
Cerebrovascular accident	1 (1.4) [0]	0 (0.0) [0]
Chronic obstructive pulmonary disease	0 (0.0) [0]	1 (1.4) [0]
Colon cancer	0 (0.0) [0]	1 (1.4) [0]
Death	0 (0.0) [0]	1 (1.4) [0]
Enterocolitis	0 (0.0) [0]	1 (1.4) [0]
Eyelid ptosis	1 (1.4) [0]	0 (0.0) [0]
Faecaloma	0 (0.0) [0]	1 (1.4) [0]
Femoral arterial stenosis	0 (0.0) [0]	1 (1.4) [0]
Gastroenteritis	0 (0.0) [0]	1 (1.4) [0]
Gastroenteritis norovirus	1 (1.4) [0]	0 (0.0) [0]
Hypertensive crisis	1 (1.4) [0]	0 (0.0) [0]
Inguinal hernia	0 (0.0) [0]	1 (1.4) [0]
Intervertebral disc protrusion	1 (1.4) [0]	0 (0.0) [0]
Ligament rupture	0 (0.0) [0]	1 (1.4) [0]
Lumbar spinal stenosis	0 (0.0) [0]	1 (1.4) [0]
Lumbar vertebral fracture	1 (1.4) [0]	0 (0.0) [0]
Meniscus lesion	0 (0.0) [0]	1 (1.4) [0]
Myalgia	0 (0.0) [0]	1 (1.4) [1]
Myocardial infarction	1 (1.4) [0]	0 (0.0) [0]
Radius fracture	1 (1.4) [0]	0 (0.0) [0]
Spinal compression fracture	0 (0.0) [0]	1 (1.4) [0]
Syncope	1 (1.4) [0]	0 (0.0) [0]
Tachycardia paroxysmal	1 (1.4) [0]	0 (0.0) [0]
Urinary tract infection	0 (0.0) [0]	1 (1.4) [0]
VIth nerve paralysis	0 (0.0) [0]	1 (1.4) [0]
Vertigo	1 (1.4) [0]	0 (0.0) [0]
Fatal SAEs	**Group A N = 72**	**Group B N = 73**
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	1 (1.4) [0]
Death	0 (0.0) [0]	1 (1.4) [0]

Conclusion:
At 21 days after the second dose of H1N1 vaccine (Day 42), the GMT value for HI antibodies against Flu A/CAL/7/09 strain was 309.8 in Group A and 227.5 in Group B and the SCF value was 33.6 in Group A and 16.5 in Group B. At the same time point, all subjects had HI titres ≥ 1:40 and 95.3% of the subjects in Group A and 88.1% of the subjects in Group B seroconverted.

During the 21-day follow-up period after each vaccination, 33 (45.8%) subjects in Group A and 37 (50.7%) subjects in Group B reported at least one unsolicited AE. SAEs were reported for 11 (15.3%) subjects in Group A and 14 (19.2%) subjects in Group B. One of the SAEs reported in Group B, myalgia was assessed by investigator as related to study vaccination. 1 fatal SAE was reported in Group B; the fatal SAE was not assessed by the investigator as related to study vaccination.

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