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.: 113535 (Flu D-Pan-H1N1-017)

Title: Immunological equivalence between GSK2340272A and GSK2340274A influenza vaccines in adults aged 18 to 60 years.
GSK2340272A (Flu1): GlaxoSmithKline (GSK) Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain (manufactured in Dresden) with adjuvant.
GSK2340274A (Flu2): GSK Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain (manufactured in Quebec) with adjuvant.

Rationale: The present study was designed to assess equivalence of immunogenicity between Flu1 and Flu2 vaccines.

Phase: III

Study Period:
12 October 2009 to
- 09 November 2009 (Day 21)
- 04 December 2009 (Day 42)
- 04 November 2010 (Day 364)

Study Design: Observer-blind, randomised study with two parallel groups.

Centres: 7 centres (4 in France and 3 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
- Flu1 Group: Subjects received two doses of Flu1 vaccine at Day 0 and Day 21.
- Flu2 Group: Subjects received two doses of Flu2 vaccine at Day 0 and Day 21.

Vaccines were administered intramuscularly in the deltoid region of the non-dominant (Day 0) or dominant (Day 21) arm.

Objectives:
To assess the immunological equivalence (in terms of vaccine-homologous virus H1N1 HI antibody geometric mean titres [GMTs]) of Flu1 and Flu2 vaccines, 21 days after the first vaccination in healthy subjects aged 18 to 60 years.
Criterion for equivalence:
Immunological equivalence was demonstrated if the limits of two-sided 95% confidence interval (CI) for the GMT ratio (Flu1 vaccine over Flu2 vaccine) in terms of HI antibody titre against A/California/7/2009 (H1N1)v-like strain were within the 0.5 - 2.0 interval.

Primary Outcome/Efficacy Variable:
- Humoral immune response in terms of Haemagglutination Inhibition (HI) antibodies, in all subjects from both groups against A/California/7/2009 (H1N1)v-like antigen:
  - GMTs 21 days after the first dose of vaccine (Day 21).

Secondary Outcome/Efficacy Variable(s):
Immunogenicity
- Humoral immune response in terms of HI antibodies, in all subjects from both groups against A/California/7/2009 (H1N1)v-like antigen:
  - GMTs and seropositivity rates at Days 0, 21, 42, 182 and 364
  - Seroconversion rate (SCR)* at Days 21, 42, 182 and 364
  - Seroprotection rate (SPR)** at Days 0, 21, 42, 182 and 364
  - Geometric mean fold rise (GMFR)*** at Days 21, 42, 182 and 364

*SCR is defined as the percentage of vaccinees that have either a pre- vaccination titre < 1:10 and a post-vaccination titre ≥ 1:40 or a pre vaccination titre ≥ 1:10 and at least a four-fold increase in post-vaccination titre.
**SPR is defined as the percentage of vaccinees with a serum HI titre ≥ 1:40, that usually is accepted as indicating protection.
***GMFR (also called seroconversion factor [SCF]) is defined the fold increase in serum HI GMTs post-vaccination compared to pre-vaccination.

- Humoral immune response in terms of neutralizing antibodies, in all subjects from both groups against A/California/7/2009 (H1N1)v-like antigen: §
  - GMTs at Days 0 and 21
  - SCR* at Day 21

*SCR is defined as the percentage of vaccinees that have a four-fold increase between pre- and post-vaccination titres.

§Protocol Amendment 4 of 22 July 2010 cancelled testing of neutralizing antibodies.

Safety

- Occurrence, duration and intensity of each solicited local adverse event (AE) during the 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after each vaccination.
- Occurrence, duration, intensity and relation to vaccination of each solicited general AE during the 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after each vaccination.
- Occurrence, intensity and relationship to vaccination of unsolicited AEs within 21 days after the first vaccination and up to 63 days after the second vaccination (Day 0-Day 20 and Day 21-Day 84), according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence and relationship to vaccination of adverse events of specific interest (AESIs)/ potential immune-mediated diseases (pIMDs) and AEs of special interest* during the entire study period (up to Day 364).
- Occurrence and relationship to vaccination of serious adverse events (SAEs) during the entire study period (up to Day 364).

*AEs of special interest include convulsion and anaphylaxis.

Statistical Methods:

The analyses were performed on the Total Vaccinated cohort, the According-To-Protocol (ATP) cohort for immunogenicity at Day 21, the ATP cohort for immunogenicity at Day 42, the ATP cohort for persistence at Month 6 and the ATP cohort for persistence at Month 12.

- The Total Vaccinated cohort included all vaccinated subjects.
- The ATP cohort for immunogenicity at Day 21 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 1 dose was taken and assay results were available for antibodies against H1N1antigen for the blood sample taken 21 days after the first vaccine dose.
- The ATP cohort for immunogenicity at Day 42 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 2 doses were taken and assay results were available for antibodies against H1N1antigen for the blood sample taken 21 days after the second vaccine dose
- The ATP cohort for persistence at Month 6 included all evaluable subjects who met all eligibility criteria, who had received at least 1 dose of study/control vaccine according to their treatment assignment during the primary vaccination course, for whom the injection site of study/control vaccine was known, 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, who did not meet the elimination criteria during the entire study, for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against the study vaccine antigen component at Month 6.
- The ATP cohort for persistence at Month 12 included all evaluable subjects who met all eligibility criteria, who had received at least 1 dose of study/control vaccine according to their treatment assignment during the primary vaccination course, for whom the injection site of study/control vaccine was known, 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 12, who did not meet the elimination criteria during the entire study, for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against the study vaccine antigen component at Month 12.

Immunogenicity:

An unplanned analysis was initially performed on the Total Vaccinated cohort for Flu2 Group only in order to provide Public Health Authorities with the earliest possible data regarding the immunogenicity of Flu2 vaccine.

For the humoral response in terms of H1N1 HI antibodies in the Flu2 Group, the following parameters (with 95% confidence intervals [CI]) were calculated:

- GMTs of antibodies against vaccine homologous virus at Days 0 and 21.
- Seropositivity rates of antibodies against vaccine homologous virus at Days 0 and 21.
- SCR of antibodies against vaccine homologous virus at Day 21.
- SCF of H1N1 HI antibodies against vaccine homologous virus at Day 21.
- SPR of H1N1 HI antibodies against vaccine homologous virus at Days 0 and 21.

The next analysis was based on the ATP cohorts for immunogenicity at Day 21 and at Day 42 and the ATP cohorts for persistence at Month 6 and Month 12.

The 95% CIs of the GMT ratio (Flu1 vaccine over Flu2 vaccine) for HI antibodies against A/California/7/2009 (H1N1)v-like strain, 21 days after first vaccination were computed. The objective of immunological equivalence of Flu2 vaccine compared to Flu1 vaccine was reached if the two-sided 95% CIs for the GMT ratio (Flu1 vaccine over Flu2 vaccine) were within the 0.5 -

2 interval.
For the humoral response in terms of H1N1 HI antibodies, the following parameters (with 95% CIs) were calculated:

- GMTs of antibodies against vaccine homologous virus at Days 0, 21, 42, 182 and 364.
- Seropositivity rates of antibodies against vaccine homologous virus at Days 0, 21, 42, 182 and 364.
- SCR of antibodies against vaccine homologous virus at Days 21, 42, 182 and 364.
- SCF of H1N1 HI antibodies against vaccine homologous virus at Days 21, 42, 182 and 364.
- SPR of H1N1 HI antibodies against vaccine homologous virus at Days 0, 21, 42, 182 and 364.

Safety
The analysis was based on the Total Vaccinated cohort.
The percentage of subjects reporting each individual solicited local and general symptom during the solicited follow-up period following vaccination was tabulated with exact 95% CI for each treatment group and for all subjects aged 18 to 60 years.
The same tabulation was performed for grade 3 symptoms and for solicited general symptoms assessed by the investigators as related to vaccination. All solicited local symptoms were presumed to be causally related to vaccination.
The percentage of subjects with at least one report of an unsolicited AE classified by the Medical Dictionary for Regulatory Activities (MedDRA) and reported up to Day 84 after the first dose of vaccine was tabulated for each treatment group and for all subjects aged 18 to 60 years. The same tabulation was performed for grade 3 unsolicited AEs and for unsolicited AEs that were assessed by the investigators as possibly related to vaccination.
SAE(s), AESI(s) /pIMDs and AEs of special interest were collected and classified by MedDRA preferred terms up to Day 364.

Study Population: Healthy male or female adults 18 to 60 years of age at the time of first vaccination, inclusive. Written informed consent was obtained from the subjects prior to study entry.

Number of Subjects:	**Flu2 Group**	**Flu1 Group**
Planned, N	160	160
Randomised, N (Total Vaccinated cohort)	167	167
Completed to Day 42, n (%)	166 (99.4)	166 (99.4)
Completed to Day 364, n (%)	160 (95.8)	161 (96.4)
Total Number Subjects Withdrawn, n (%)	7 (4.2)	6 (3.6)
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 (%)	7 (4.2)	6 (3.6)
Demographics	**Flu2 Group**	**Flu1 Group**
N (Total Vaccinated cohort)	167	167
Females: Males	77: 90	87:80
Mean Age, years (SD)	39.7 (11.98)	40.1 (11.65)
White - Caucasian / European heritage, n (%)	161 (96.4)	165 (98.8)

Primary Efficacy Results: Adjusted GMT ratios for HI antibodies against Flu A/CAL/7/2009 strain, 21 days after the first vaccine dose, between Flu1 and Flu2 Groups (Flu1 / Flu 2) with their 95% CIs (ATP cohort for immunogenicity at Day 21)

						Adjusted GMT ratio			
								95% CI	
Group description	**N**	**Adjusted GMT**	**Group description**	**N**	**Adjusted GMT**	**Ratio order**	**Value**	**LL**	**UL**
Flu1	164	393.1	Flu2	164	328.0	Flu1 /Flu2	1.20	0.96	1.49

Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio; LL = lower limit, UL = upper limit
Immunological equivalence criterion: limits of two-sided 95% CI for the GMT ratio within the 0.5 - 2.0 interval.

Primary Efficacy Results: Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 by pre-vaccination status (Total Vaccinated cohort)

					≥ 1:10				**GMT**		
							95% CI			**95% CI**	
Antibodies against	**Group**	**Pre-vacc status**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	S-	PRE	95	0	0.0	0.0	3.8	5.00	5.00	5.00
			PI(D21)	95	95	100	96.2	100	251.50	203.12	311.39
		S+	PRE	72	72	100	95.0	100	27.41	22.27	33.75
			PI(D21)	71	71	100	94.9	100	484.49	380.45	616.97

		Total	PRE	167	72	43.1	35.5	51.0	10.41	8.90	12.18
			PI(D21)*	166	166	100	97.8	100	332.91	281.96	393.06

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination
S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Prevaccination (Day 0)
PI(D21) = Post dose 1 (Day 21)
*Primary outcome result

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

				≥ 1:10				GMT		
						95% CI			95% CI	
Antibodies against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	PRE	155	69	44.5	36.5	52.7	10.7	9.1	12.7
		PI(D21)*	155	155	100	97.6	100	339.1	285.4	403.0
		PII(D42)	155	155	100	97.6	100	678.3	599.3	767.6
	Flu1	PRE	155	60	38.7	31.0	46.9	9.5	8.1	11.2
		PI(D21)*	155	155	100	97.6	100	383.6	327.2	449.7
		PII(D42)	155	155	100	97.6	100	599.8	532.3	675.9

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
PRE= Pre-vaccination (Day 0)
PI(D21)= Post dose 1 (Day 21)
PII(D42)= Post dose 2 (Day 42)
* Primary outcome result

Secondary Outcome Variable(s): SCRs for HI antibodies against Flu A/CAL/7/09 at Day 21 (Total Vaccinated cohort)

					SCR			
							95% CI	
Antibodies against	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	S-	PI(D21)	95	92	96.8	91.0	99.3
		S+	PI(D21)	71	64	90.1	80.7	95.9
		Total	PI(D21)	166	156	94.0	89.2	97.1

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination
S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination
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(D21)= Post dose 1 (Day 21)

Secondary Outcome Variable(s): SPRs for HI antibodies against Flu A/CAL/7/09 at Day 0 and Day 21 (Total Vaccinated cohort)

					SPR			
							95% CI	
Antibodies against	**Group**	**Pre-vacc status**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	S-	PRE	95	0	0.0	0.0	3.8
			PI(D21)	95	92	96.8	91.0	99.3
		S+	PRE	72	22	30.6	20.2	42.5

			PI(D21)	71	70	98.6	92.4	100
		Total	PRE	167	22	13.2	8.4	19.3
			PI(D21)	166	162	97.6	93.9	99.3

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
PRE= Prevaccination (Day 0)
PI(D21)= Post dose 1 (Day 21)

Secondary Outcome Variable(s): SCFs for HI antibody titres at Day 21 (Total Vaccinated cohort)

					SCF		
						95% CI	
Antibodies against	**Group**	**Sub-group**	**Timing**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	S-	PI(D21)	95	50.3	40.6	62.3
		S+	PI(D21)	71	17.7	13.3	23.4
		Total	PI(D21)	166	32.2	26.7	38.8

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination
S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination
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 dose 1 (Day 21)

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/09 (ATP cohort for immunogenicity at Day 42)

				SCR			
						95% CI	
Antibodies against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	PI(D21)	155	145	93.5	88.5	96.9
		PII(D42)	155	153	98.7	95.4	99.8
	Flu1	PI(D21)	155	151	97.4	93.5	99.3
		PII(D42)	155	154	99.4	96.5	100

Seroconversion (SCR) 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(D21)= Post dose 1 (Day 21)
PII(D42)= Post dose 2 (Day 42)

Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/09 (ATP cohort for immunogenicity at Day 42)

				SPR			
						95% CI	
Antibodies against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	PRE	155	22	14.2	9.1	20.7
		PI(D21)	155	151	97.4	93.5	99.3
		PII(D42)	155	155	100	97.6	100
	Flu1	PRE	155	19	12.3	7.5	18.5
		PI(D21)	155	155	100	97.6	100
		PII(D42)	155	155	100	97.6	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
PRE= Pre-vaccination (Day 0)
PI(D21)= Post dose 1 (Day 21)
PII(D42)= Post dose 2 (Day 42)

Secondary Outcome Variable(s): SCF for HI antibodies against Flu A/CAL/7/09 (ATP cohort for immunogenicity at Day 42)

	SCF	
		95% CI

Antibodies against	Group	Timing	N	Value	LL	UL
Flu A/CAL/7/09	Flu2	PI(D21)	155	31.6	26.0	38.4
		PII(D42)	155	63.2	52.6	75.9
	Flu1	PI(D21)	155	40.3	33.2	49.0
		PII(D42)	155	63.0	52.2	76.1

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(D21)= Post dose 1 (Day 21)
PII(D42)= Post dose 2 (Day 42)

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 at Day 182 (ATP cohort for persistence at Month 6)

			≥ 1:10				GMT		
					95% CI			95% CI	
Antibodies against	**Group**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	154	154	100	97.6	100	233.0	196.0	276.9
	Flu1	156	155	99.4	96.5	100	202.5	173.1	236.9

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

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/09 at Day 182 (ATP cohort for persistence at Month 6)

			SCR			
					95% CI	
Antibodies against	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	154	141	91.6	86.0	95.4
	Flu1	156	144	92.3	86.9	96.0

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

Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/09 at Day 182 (ATP cohort for persistence at Month 6)

				SPR		
					95% CI	
Antibodies against	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	154	150	97.4	93.5	99.3
	Flu1	156	151	96.8	92.7	99.0

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

Secondary Outcome Variable(s): GMFR for HI antibodies against Flu A/CAL/7/09 at Day 182 (ATP cohort for persistence at Month 6)

			GMFR		
				95% CI	
Antibodies against	**Group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09.	Flu2	154	21.7	18.1	25.9
	Flu1	156	22.0	18.5	26.1

N = Number of subjects with pre- and post-vaccination results available
GMFR = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

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

				≥ 1:10				GMT		
						95% CI			95% CI	
Antibodies against	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	PII(D364)	146	145	99.3	96.2	100	107.6	89.2	129.7
	Flu1	PII(D364)	144	144	100	97.5	100	96.7	81.2	115.2

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
PII(D364) = Post dose 2 (Day 364)

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/09 at Day 364 (ATP cohort for persistence at Month 12)

			SCR			
					95% CI	
Antibodies against	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	146	106	72.6	64.6	79.7
	Flu1	144	109	75.7	67.9	82.4

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

Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/09 at Day 364 (ATP cohort for persistence at Month 12)

				SPR		
					95% CI	
Antibodies against	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	146	121	82.9	75.8	88.6
	Flu1	144	121	84.0	77.0	89.6

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

Secondary Outcome Variable(s): GMFR for HI antibodies against Flu A/CAL/7/09 at Day 364 (ATP cohort for persistence at Month 12)

			GMFR		
				95% CI	
Antibodies against	**Group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09	Flu2	146	11.0	9.1	13.3
	Flu1	144	11.0	9.2	13.2

N = Number of subjects with pre- and post-vaccination results available
GMFR = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
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)

		Flu2 Group					Flu1 Group				
					95 % CI					95 % CI	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Pain	Any	167	144	86.2	80.1	91.1	167	148	88.6	82.8	93.0
	Grade 3	167	4	2.4	0.7	6.0	167	6	3.6	1.3	7.7
Redness	Any	167	19	11.4	7.0	17.2	167	25	15.0	9.9	21.3
	>100 mm	167	0	0.0	0.0	2.2	167	0	0.0	0.0	2.2
Swelling	Any	167	29	17.4	11.9	24.0	167	32	19.2	13.5	26.0
	>100 mm	167	0	0.0	0.0	2.2	167	2	1.2	0.1	4.3
Dose 2											

Pain	Any	162	137	84.6	78.1	89.8	162	139	85.8	79.5	90.8
	Grade 3	162	4	2.5	0.7	6.2	162	5	3.1	1.0	7.1
Redness	Any	162	17	10.5	6.2	16.3	162	18	11.1	6.7	17.0
	>100 mm	162	0	0.0	0.0	2.3	162	0	0.0	0.0	2.3
Swelling	Any	162	21	13.0	8.2	19.1	162	17	10.5	6.2	16.3
	>100 mm	162	0	0.0	0.0	2.3	162	1	0.6	0.0	3.4
Across doses											
Pain	Any	167	151	90.4	84.9	94.4	167	153	91.6	86.3	95.3
	Grade 3	167	6	3.6	1.3	7.7	167	8	4.8	2.1	9.2
Redness	Any	167	28	16.8	11.4	23.3	167	35	21.0	15.1	27.9
	>100 mm	167	0	0.0	0.0	2.2	167	0	0.0	0.0	2.2
Swelling	Any	167	36	21.6	15.6	28.6	167	36	21.6	15.6	28.6
	>100 mm	167	0	0.0	0.0	2.2	167	2	1.2	0.1	4.3

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= 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 any local symptoms during the solicited post-vaccination period (Total Vaccinated cohort)

Solicited symptom	Dose	Group	N	Mean	Median
Pain	Dose 1	Flu2	144	3.5	3.0
		Flu1	148	3.4	3.0
	Dose 2	Flu2	137	3.2	3.0
		Flu1	139	3.0	3.0
	Overall/dose	Flu2	281	3.3	3.0
		Flu1	287	3.2	3.0
Redness	Dose 1	Flu2	19	2.9	3.0
		Flu1	25	3.6	3.0
	Dose 2	Flu2	17	2.6	2.0
		Flu1	18	3.2	3.0
	Overall/dose	Flu2	36	2.8	3.0
		Flu1	43	3.4	3.0
Swelling	Dose 1	Flu2	29	3.1	2.0
		Flu1	32	3.3	3.0
	Dose 2	Flu2	21	2.8	2.0
		Flu1	17	3.5	3.0
	Overall/dose	Flu2	50	3.0	2.0
		Flu1	49	3.4	3.0

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)

		Flu2 Group					Flu1 Group				
					95 % CI					95 % CI	
Symptom	**Intensity/ Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Fatigue	Any	167	55	32.9	25.9	40.6	167	60	35.9	28.7	43.7
	Grade 3	167	2	1.2	0.1	4.3	167	3	1.8	0.4	5.2
	Related	167	54	32.3	25.3	40.0	167	54	32.3	25.3	40.0
Headache	Any	167	48	28.7	22.0	36.2	167	55	32.9	25.9	40.6
	Grade 3	167	2	1.2	0.1	4.3	167	4	2.4	0.7	6.0
	Related	167	44	26.3	19.8	33.7	167	46	27.5	20.9	35.0
Joint pain at other location	Any	167	38	22.8	16.6	29.9	167	37	22.2	16.1	29.2
	Grade 3	167	2	1.2	0.1	4.3	167	1	0.6	0.0	3.3

	Related	167	37	22.2	16.1	29.2	167	33	19.8	14.0	26.6
Muscle aches	Any	167	81	48.5	40.7	56.3	167	57	34.1	27.0	41.9
	Grade 3	167	4	2.4	0.7	6.0	167	3	1.8	0.4	5.2
	Related	167	79	47.3	39.5	55.2	167	55	32.9	25.9	40.6
Shivering	Any	167	24	14.4	9.4	20.6	167	34	20.4	14.5	27.3
	Grade 3	167	2	1.2	0.1	4.3	167	0	0.0	0.0	2.2
	Related	167	24	14.4	9.4	20.6	167	32	19.2	13.5	26.0
Sweating	Any	167	14	8.4	4.7	13.7	167	13	7.8	4.2	12.9
	Grade 3	167	1	0.6	0.0	3.3	167	1	0.6	0.0	3.3
	Related	167	14	8.4	4.7	13.7	167	12	7.2	3.8	12.2
Temperature (Axillary)	≥ 37.5°C	167	5	3.0	1.0	6.8	167	2	1.2	0.1	4.3
	≥ 39.0- ≤40°C	167	2	1.2	0.1	4.3	167	1	0.6	0.0	3.3
	Related	167	5	3.0	1.0	6.8	167	2	1.2	0.1	4.3
Dose 2											
Fatigue	Any	162	60	37.0	29.6	45.0	162	61	37.7	30.2	45.6
	Grade 3	162	4	2.5	0.7	6.2	162	3	1.9	0.4	5.3
	Related	162	59	36.4	29.0	44.3	162	59	36.4	29.0	44.3
Headache	Any	162	51	31.5	24.4	39.2	162	57	35.2	27.9	43.1
	Grade 3	162	3	1.9	0.4	5.3	162	2	1.2	0.1	4.4
	Related	162	46	28.4	21.6	36.0	162	53	32.7	25.6	40.5
Joint pain at other location	Any	162	47	29.0	22.2	36.7	162	34	21.0	15.0	28.1
	Grade 3	162	4	2.5	0.7	6.2	162	5	3.1	1.0	7.1
	Related	162	45	27.8	21.0	35.3	162	33	20.4	14.5	27.4
Muscle aches	Any	162	71	43.8	36.1	51.8	162	64	39.5	31.9	47.5
	Grade 3	162	2	1.2	0.1	4.4	162	4	2.5	0.7	6.2
	Related	162	70	43.2	35.5	51.2	162	63	38.9	31.3	46.9
Shivering	Any	162	35	21.6	15.5	28.7	162	37	22.8	16.6	30.1
	Grade 3	162	4	2.5	0.7	6.2	162	5	3.1	1.0	7.1
	Related	162	32	19.8	13.9	26.7	162	37	22.8	16.6	30.1
Sweating	Any	162	16	9.9	5.8	15.5	162	24	14.8	9.7	21.2
	Grade 3	162	2	1.2	0.1	4.4	162	4	2.5	0.7	6.2
	Related	162	15	9.3	5.3	14.8	162	23	14.2	9.2	20.5
Temperature (Axillary)	≥ 37.5°C	162	8	4.9	2.2	9.5	162	11	6.8	3.4	11.8
	≥ 39.0- ≤40°C	162	3	1.9	0.4	5.3	162	2	1.2	0.1	4.4
	Related	162	8	4.9	2.2	9.5	162	11	6.8	3.4	11.8
Across doses											
Fatigue	Any	167	79	47.3	39.5	55.2	167	92	55.1	47.2	62.8
	Grade 3	167	5	3.0	1.0	6.8	167	6	3.6	1.3	7.7
	Related	167	78	46.7	39.0	54.6	167	87	52.1	44.2	59.9
Headache	Any	167	73	43.7	36.1	51.6	167	83	49.7	41.9	57.5
	Grade 3	167	5	3.0	1.0	6.8	167	6	3.6	1.3	7.7
	Related	167	69	41.3	33.8	49.2	167	74	44.3	36.6	52.2
Joint pain at other location	Any	167	66	39.5	32.1	47.4	167	53	31.7	24.8	39.4
	Grade 3	167	5	3.0	1.0	6.8	167	5	3.0	1.0	6.8
	Related	167	64	38.3	30.9	46.2	167	49	29.3	22.6	36.9
Muscle aches	Any	167	104	62.3	54.5	69.6	167	85	50.9	43.1	58.7
	Grade 3	167	5	3.0	1.0	6.8	167	6	3.6	1.3	7.7
	Related	167	102	61.1	53.2	68.5	167	83	49.7	41.9	57.5
Shivering	Any	167	47	28.1	21.5	35.6	167	57	34.1	27.0	41.9
	Grade 3	167	6	3.6	1.3	7.7	167	5	3.0	1.0	6.8
	Related	167	45	26.9	20.4	34.3	167	56	33.5	26.4	41.2
Sweating	Any	167	28	16.8	11.4	23.3	167	28	16.8	11.4	23.3
	Grade 3	167	3	1.8	0.4	5.2	167	5	3.0	1.0	6.8
	Related	167	27	16.2	10.9	22.6	167	27	16.2	10.9	22.6
Temperature	≥ 37.5°C	167	11	6.6	3.3	11.5	167	12	7.2	3.8	12.2

(Axillary)	≥ 39.0- ≤40°C	167	5	3.0	1.0	6.8	167	3	1.8	0.4	5.2
	Related	167	11	6.6	3.3	11.5	167	12	7.2	3.8	12.2

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= any general symptom, regardless of intensity grade or relationship 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 any general symptoms during the solicited post-vaccination period (Total Vaccinated cohort)

Solicited symptom	Dose	Group	N	Mean	Median
Fatigue	Dose 1	Flu2	55	2.5	2.0
		Flu1	60	2.1	2.0
	Dose 2	Flu2	60	2.1	2.0
		Flu1	61	2.0	1.0
	Overall/dose	Flu2	115	2.3	2.0
		Flu1	121	2.1	2.0
Headache	Dose 1	Flu2	48	1.9	2.0
		Flu1	55	2.0	1.0
	Dose 2	Flu2	51	2.0	2.0
		Flu1	57	2.0	1.0
	Overall/dose	Flu2	99	2.0	2.0
		Flu1	112	2.0	1.0
Joint pain at other location	Dose 1	Flu2	38	2.6	2.0
		Flu1	37	2.1	2.0
	Dose 2	Flu2	47	2.2	2.0
		Flu1	34	2.6	2.0
	Overall/dose	Flu2	85	2.4	2.0
		Flu1	71	2.3	2.0
Muscle aches	Dose 1	Flu2	81	2.5	2.0
		Flu1	57	2.5	2.0
	Dose 2	Flu2	71	2.4	2.0
		Flu1	64	2.3	2.0
	Overall/dose	Flu2	152	2.4	2.0
		Flu1	121	2.4	2.0
Sweating	Dose 1	Flu2	14	1.4	1.0
		Flu1	13	1.6	1.0
	Dose 2	Flu2	16	1.7	1.0
		Flu1	24	2.2	1.0
	Overall/dose	Flu2	30	1.5	1.0
		Flu1	37	2.0	1.0
Shivering	Dose 1	Flu2	24	1.5	1.0
		Flu1	34	1.4	1.0
	Dose 2	Flu2	35	1.6	1.0
		Flu1	37	1.4	1.0
	Overall/dose	Flu2	59	1.6	1.0
		Flu1	71	1.4	1.0
Temperature	Dose 1	Flu2	5	1.0	1.0
		Flu1	2	3.0	3.0
	Dose 2	Flu2	8	1.6	2.0
		Flu1	11	1.3	1.0
	Overall/dose	Flu2	13	1.4	1.0
		Flu1	13	1.5	1.0

N = number of doses with the symptom

Secondary Outcome Variable(s): Occurrence of AESIs/ pIMDs reported up to Day 42 (Total Vaccinated cohort)		
Most frequent AESIs/pIMDS- On-Therapy (occurring within Days 0-41 following vaccination)	**Flu2 Group N = 167**	**Flu1 Group N = 167**
Subjects with any AESI(s)/pIMD(s), n (%)	0 (0.0)	0 (0.0)
Secondary Outcome Variable(s): Occurrence of AESIs/ pIMDs reported up to Day 364 (Total Vaccinated cohort)		
Most frequent AESIs/pIMDS (occurring within Days 0-363 following vaccination)	**Flu2 Group N = 167**	**Flu1 Group N = 167**
Subjects with any AESI(s)/pIMD(s), n (%)	0 (0.0)	1 (0.6)
Subjects with related AESI(s)/pIMD(s), n (%)	0 (0.0)	0 (0.0)
VIIth nerve paralysis	-	1 (0.6)
Secondary Outcome Variable(s): Occurrence of AEs of special interest reported up to Day 364 (Total Vaccinated cohort)		
Most frequent adverse events of special interest (occurring within Days 0-363 following vaccination)	**Flu2 Group N = 167**	**Flu1 Group N = 167**
Subjects with any AE(s) of special interest, n (%)	0 (0.0)	0 (0.0)
Safety results: Number (%) of subjects with unsolicited adverse events reported up to Day 42 (Total Vaccinated cohort)		
Most frequent adverse events* - On-Therapy (occurring within Days 0-41 following vaccination)	**Flu2 Group N = 167**	**Flu1 Group N = 167**
Subjects with any AE(s), n (%)	52 (31.1)	52 (31.1)
Subjects with grade 3 AE(s), n (%)	5 (3.0)	9 (5.4)
Subjects with related AE(s), n (%)	19 (11.4)	19 (11.4)
Lymphadenopathy	-	2 (1.2)
Tachycardia	-	1 (0.6)
Vertigo	-	1 (0.6)
Vision blurred	-	1 (0.6)
Diarrhoea	2 (1.2)	1 (0.6)
Enteritis	-	1 (0.6)
Nausea	3 (1.8)	1 (0.6)
Asthenia	2 (1.2)	-
Axillary pain	-	1 (0.6)
Feeling hot	-	1 (0.6)
Influenza like illness	-	3 (1.8)
Injection site anaesthesia	-	1 (0.6)
Injection site exfoliation	-	1 (0.6)
Injection site haematoma	2 (1.2)	-
Injection site induration	-	1 (0.6)
Injection site lymphadenopathy	-	1 (0.6)
Injection site pain	2 (1.2)	-
Injection site paraesthesia	-	1 (0.6)
Injection site pruritus	-	5 (3.0)
Pyrexia	-	1 (0.6)
Bronchitis	2 (1.2)	-
Gastroenteritis	-	1 (0.6)
Influenza	-	2 (1.2)
Laryngitis	-	1 (0.6)
Nasopharyngitis	6 (3.6)	10 (6.0)
Oral herpes	-	1 (0.6)
Pharyngitis	-	1 (0.6)
Rhinitis	4 (2.4)	6 (3.6)
Sinusitis	-	1 (0.6)
Viral rhinitis	-	1 (0.6)
Vulvovaginal mycotic infection	2 (1.2)	1 (0.6)
Back pain	2 (1.2)	1 (0.6)
Musculoskeletal stiffness	-	1 (0.6)
Neck pain	-	1 (0.6)
Pain in extremity	-	1 (0.6)

Sacroiliitis	-	1 (0.6)
Tendonitis	2 (1.2)	1 (0.6)
Tenosynovitis	-	1 (0.6)
Dysgeusia	-	1 (0.6)
Headache	6 (3.6)	2 (1.2)
Migraine	2 (1.2)	-
Pseudoradicular syndrome	-	1 (0.6)
Sciatica	-	1 (0.6)
Sleep disorder	-	1 (0.6)
Cough	3 (1.8)	1 (0.6)
Dry throat	-	1 (0.6)
Epistaxis	-	1 (0.6)
Oropharyngeal pain	3 (1.8)	1 (0.6)
Dermatitis contact	-	1 (0.6)
Rash	-	1 (0.6)
Skin neoplasm excision	-	1 (0.6)
* Not all AEs were classified by MedDRA, however all subjects having AE are counted -: AE 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= AEs which prevented normal everyday activities Related= AEs assessed by the investigator as causally related to the study vaccination		
Safety results: Number (%) of subjects with unsolicited adverse events reported up to Day 84 (Total Vaccinated cohort)		
Most frequent adverse events - On-Therapy (occurring within Days 0-83 following vaccination)	**Flu2 Group N = 167**	**Flu1 Group N = 167**
Subjects with any AE(s), n (%)	71 (42.5)	68 (40.7)
Subjects with grade 3 AE(s), n (%)	8 (4.8)	16 (9.6)
Subjects with related AE(s), n (%)	20 (12.0)	20 (12.0)
Nasopharyngitis	9 (5.4)	13 (7.8)
Headache	12 (7.2)	6 (3.6)
Rhinitis	4 (2.4)	9 (5.4)
Back pain	7 (4.2)	2 (1.2)
Bronchitis	5 (3.0)	-
Injection site pruritus	-	5 (3.0)
Cough	4 (2.4)	-
Gastroenteritis	-	4 (2.4)
Influenza like illness	-	4 (2.4)
Diarrhoea	3 (1.8)	-
Influenza	-	3 (1.8)
Injection site pain	3 (1.8)	-
Nausea	3 (1.8)	-
Oropharyngeal pain	3 (1.8)	-
Sinusitis	-	3 (1.8)
Tonsillitis	3 (1.8)	-
Laryngitis	-	2 (1.2)
Lymphadenopathy	-	2 (1.2)
Neck pain	-	2 (1.2)
Pyrexia	-	2 (1.2)
Sciatica	-	2 (1.2)
-: AE 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= AEs which prevented normal everyday activities Related= AEs assessed by the investigator as causally related to the study vaccination		
Safety results: Number (%) of subjects with serious adverse events reported up to Day 42 (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	**Flu2 Group N = 167**	**Flu1 Group N = 167**

Subjects with any SAE(s), n (%) [n assessed by investigator as related]	1 (0.6) [0]	0 (0.0) [0]
Back pain	1 (0.6) [0]	0 (0.0) [0]
Fatal SAEs	**Flu2 Group N = 167**	**Flu1 Group N = 167**
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 serious adverse events reported up to Day 364 (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	**Flu2 Group N = 167**	**Flu1 Group N = 167**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	11 (6.6) [0]	9 (5.4) [0]
Nephrolithiasis	1 (0.6) [0]	1 (0.6) [0]
Abortion missed	1 (0.6) [0]	0 (0.0) [0]
Abortion spontaneous incomplete	0 (0.0) [0]	1 (0.6) [0]
Acute coronary syndrome	0 (0.0) [0]	1 (0.6) [0]
Adjustment disorder	0 (0.0) [0]	1 (0.6) [0]
Amnesia	1 (0.6) [0]	0 (0.0) [0]
Anal fissure	1 (0.6) [0]	0 (0.0) [0]
Appendicitis	1 (0.6) [0]	0 (0.0) [0]
Back pain	1 (0.6) [0]	0 (0.0) [0]
Foot fracture	1 (0.6) [0]	0 (0.0) [0]
Gastritis	1 (0.6) [0]	0 (0.0) [0]
Hypercholesterolaemia	0 (0.0) [0]	1 (0.6) [0]
Inguinal hernia	0 (0.0) [0]	1 (0.6) [0]
Intervertebral disc injury	0 (0.0) [0]	1 (0.6) [0]
Intervertebral disc protrusion	1 (0.6) [0]	0 (0.0) [0]
Ovarian cyst	0 (0.0) [0]	1 (0.6) [0]
Perirectal abscess	1 (0.6) [0]	0 (0.0) [0]
Pneumonia aspiration	0 (0.0) [0]	1 (0.6) [0]
Pulmonary embolism	1 (0.6) [0]	0 (0.0) [0]
Pyelonephritis	1 (0.6) [0]	0 (0.0) [0]
Sleep apnoea syndrome	0 (0.0) [0]	1 (0.6) [0]
Suicide attempt	0 (0.0) [0]	1 (0.6) [0]
Testicular injury	0 (0.0) [0]	1 (0.6) [0]
Thyroid neoplasm	0 (0.0) [0]	1 (0.6) [0]
Fatal SAEs	**Flu2 Group N = 167**	**Flu1 Group N = 167**
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:
21 days after the first dose vaccine (Day 21), GMT value for HI antibodies against Flu A/CAL/7/09 was 339.1 in Flu2 Group and 383.6 in Flu1 Group.
Up to Day 84, at least one unsolicited AE was reported by 71 (42.5%) subjects in Flu2 Group and 68 (40.7%) subjects in Flu1 Group. Over the course of the study, 11 (6.6%) subjects in the Flu2 Group and 9 (5.4%) subjects in the Flu1 Group reported at least one SAE. All the SAEs were assessed by the investigators as unrelated to the study vaccination. No fatal SAEs were reported.

Date updated: 17-September-2014