

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.: 113630 (FLU D-PAN H1N1-022)
Title: Safety and immunogenicity study of GSK Biologicals' influenza vaccine GSK2340272A in adults aged 18 years and above. GSK2340272 (Flu): GlaxoSmithKline (GSK) Biologicals' A/California/7/2009 (H1N1)v-like adjuvanted vaccine.
Rationale: The aim of this study was to assess the safety and immunogenicity of 2 different vaccination schedules of Flu vaccine in adults aged 18 years and above. This summary presents results up to Day 182/203 and will be updated when additional data become available.
Phase: III
Study Period: 14 September 2009 to 30 June 2010
Study Design: Open, randomised (1:1) study with 2 parallel groups. Subjects were stratified according to their age at study entry: 18-60 years and > 60 years of age.
Centres: 5 centres in France
Indication: Immunization against A/California/7/2009 (H1N1)v-like influenza.
Treatment: The study groups were as follows: <ul style="list-style-type: none"> • Flu D21 Group: subjects received 2 doses of Flu vaccine, at Day 0 and Day 21. • Flu M6 Group: subjects received 2 doses of Flu vaccine, at Day 0 and Month 6. Vaccines were administered intramuscularly in the deltoid region of the non-dominant arm (first dose) and of the dominant arm (second dose).
Objectives: To demonstrate that vaccination with one dose of Flu vaccine results in an Haemagglutination Inhibition (HI) immune response to the vaccine-homologous virus that meets or exceeds the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) guidance targets for pandemic vaccine seroconversion rate (SCR), seroprotection rate (SPR), and geometric mean fold rise (GMFR) at 21 days after the first dose of Flu vaccine in adults within the 18 to 60 years and above 60 years age strata.
Primary Outcome/Efficacy Variable: <i>Immunogenicity</i> <ul style="list-style-type: none"> • Humoral immune response in terms of HI antibodies in subjects receiving Flu vaccine: <ul style="list-style-type: none"> - SCR* at 21 days after first dose of Flu vaccine (Day 21) - SPR** at 21 days after first dose of Flu vaccine (Day 21) - GMFR*** at 21 days after first dose of Flu vaccine (Day 21) <p>*SCR: defined as the proportion of subjects who have either a pre-vaccination reciprocal HI titre < 10 and a post-vaccination reciprocal titre \geq 40, or a pre-vaccination reciprocal HI titre \geq 10 and at least a 4-fold increase in post-vaccination reciprocal titre against the vaccine virus. The CHMP criterion was fulfilled if the point estimate for SCR was > 40% in subjects 18 to 60 years of age or >30% for subjects above 60 years of age.</p> <p>**SPR: the proportion of subjects with H1N1 reciprocal HI titres \geq 40 against the vaccine-homologous virus. The CHMP criterion was fulfilled if the post-vaccination point estimate for SPR was > 70% in subjects 18 to 60 years of age or >60% for subjects above 60 years of age.</p> <p>***GMFR [also called seroconversion factor (SCF)]: the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination reciprocal HI titre for the vaccine virus. The criterion was fulfilled if the point estimate for GMFR was > 2.5 in subjects 18 to 60 years of age or >2 for subjects above 60 years of age.</p>
Secondary Outcome/Efficacy Variable(s): <i>Immunogenicity</i> <ul style="list-style-type: none"> • Humoral immune response in terms of HI antibodies in subjects receiving 2 doses of Flu vaccine: <ul style="list-style-type: none"> - Geometric Mean Titres (GMTs) and seropositivity rates at Day 0, 21, 42, 182, 203† and 364# - SCR* at Day 21, 42, 182, 203† and 364# - SPR* at Day 0, 21, 42, 182, 203† and 364# - GMFR* at Day 21, 42, 182, 203† and 364# <p>*See primary outcome variable section on criteria for evaluation for each age stratum.</p> <ul style="list-style-type: none"> • Humoral immune response in terms of neutralizing antibodies in a subset of subjects against A/California/7/2009 (H1N1) v-like antigen.§ <ul style="list-style-type: none"> - GMTs at Day 0, 21, 42, 182, 203† and 364

- SCR** at Day 21, 42, 182, 203† and 364

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

Safety

- Solicited local and general symptoms.
 - Occurrence, intensity and duration of each solicited local symptom during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after each vaccination.
 - Occurrence, intensity, duration and relationship to vaccination of each solicited general symptom during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after each vaccination.
- Unsolicited adverse events (AEs).
 - Occurrence, intensity and relationship to vaccination of unsolicited AEs within 21 days after the first vaccination (for all subjects) and 63 days after the second vaccination [Day 0 - Day 20 and either 63 days after the second vaccination (Day 21- Day 84, Flu D21 Group only) or 30 days after the second vaccination* (Day 182 - Day 212, Flu M6 Group only)], according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Adverse events of specific interest (AESIs) or potential Immune-Mediated Diseases (pIMDs) and AEs of special interest.
 - Occurrence and relationship to vaccination of AESIs/pIMDs and AEs of special interest during the entire study period (up to Day 364 for Flu D21 Group and up to Day 546 for Flu M6 Group). #
- Serious adverse events (SAEs).
 - Occurrence and relationship to vaccination of SAEs during the entire study (up to Day 364 for Flu D21 Group and up to Day 546 for Flu M6 Group). #
- Safety evaluation in terms of biochemical parameters.
 - The number and percentage of subjects with normal or abnormal values of biochemical parameters at Day 0, Day 21, Day 42, Day 182, Day 203† and Day 364#.

*Only 21 days follow-up post-vaccination 2 for Flu M6 Group at the time of writing this summary. The rest 9 days will be added when data are available.

†This only applies to subjects enrolled in the Flu M6 Group.

This CTRS presents the data up to Day 182/203. The study is ongoing and the CTRS will be updated for results from later time points with availability of the data.

§ Not available at the time of writing this summary.

Statistical Methods:

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 immunogenicity at Day 203 and the ATP cohort for antibody persistence at Day 182.

- The Total Vaccinated Cohort included all subjects with at least 1 vaccine administration documented.
- The ATP cohort for immunogenicity at Day 21 included all eligible subjects, who met all inclusion criteria and had no exclusion criteria, had not received a vaccine not specified or forbidden in the protocol and for whom 1 dose of study vaccine was taken and assay results were available for antibodies against H1N1 antigen for the blood sample taken 21 days after the first vaccine dose.
- The ATP cohort for immunogenicity at Day 42 included all eligible subjects, who had not received a vaccine not specified or forbidden in the protocol and for whom 2 (for Flu D21 Group)/1 (for Flu M6 Group) dose(s) of study vaccine were/was taken and assay results were available for antibodies against H1N1 antigen for the blood sample taken 21(for Flu D21 Group)/42 (for Flu M6 Group) days after the second/first vaccine dose (Flu D21 Group/Flu M6 Group accordingly).
- The ATP cohort for antibody persistence at Day 182 included all eligible subjects, who received at least 1 dose of study vaccine according to their treatment assignment, had not received a vaccine not specified or forbidden in the protocol and for whom assay results were available for the study vaccine antigen component at Month 6.
- The ATP cohort for immunogenicity at Day 203 included all eligible subjects from the Flu M6 Group, who had not received a vaccine not specified or forbidden in the protocol, for whom 2 doses were taken and for whom assay results were available for antibodies against H1N1 antigen for blood sample taken 21 days after the second dose at Day 182.

Analysis of immunogenicity

The analysis was based on the ATP cohort for immunogenicity at Day 21, the ATP cohort for immunogenicity at Day 42, the ATP cohort for immunogenicity at Day 203 and the ATP cohort for antibody persistence at Day 182.

The HI immune response to the vaccine homologous virus was described by estimating the following parameters (with 95%

confidence intervals [CIs]: GMT and SPR on Days 0, 21, 42, 182 and 203, SCR and SCF on Days 21, 42, 182 and 203. The HI immune response was described for pooled groups and per age stratum at Day 21, and per treatment group and per age stratum for each time point.

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 (Days 0-6) after each vaccine dose was tabulated with exact 95% CIs for both groups (Flu D21 and Flu M6 Groups) and per age stratum.

The same calculations were performed for symptoms of any intensity, those with Grade 3 intensity and for solicited general symptoms assessed by the investigator as related to vaccination. The duration of the symptoms was also computed.

The percentage of subjects with at least one report of an unsolicited adverse event classified by MedDRA and reported up to 21 days after the first dose for both groups and 63 days after the second dose (for Flu D21 Group) or 21 days after the second dose (for Flu M6 Group) was tabulated for each treatment group and per age stratum. The same tabulation was performed for Grade 3 unsolicited AEs and for unsolicited AEs that were assessed by the investigators to be possibly related to vaccination. SAEs, AESIs/pIMDs and AEs of special interest were summarized up to Day 203. The number and proportion of subjects with normal or abnormal values for each biochemistry parameter were tabulated for both groups at each scheduled time point, up to Day 182/203.

Study Population: Male or female subjects aged 18 years or above at the time of first vaccination were enrolled in the study if results from a baseline medical assessment by history and physical were satisfactory and that subject had a stable health status. If the subject was female and of childbearing potential, she had to be abstinent or to have used contraceptive precautions for 30 days prior to vaccination; she had to have a negative pregnancy test at study entry and had to agree to continue contraceptive precautions for 2 months after completion of the vaccination series. Written informed consent was obtained from the subject prior to study entry.

Number of Subjects:	Flu D21 Group		Flu M6 Group	
	18-60 years	>60 years	18-60 years	>60 years
Planned, N	150		150	
Randomized, N (Total Vaccinated Cohort)	93	91	70	52
Completed, n (%) (Day 21)	92 (98.9)	88 (96.7)	70 (100)	52 (100)
Completed, n (%) (Day 42)	92 (98.9)	88 (96.7)	68 (97.1)	52 (100)
Completed, n (%) (Day 182)	90 (96.8)	86 (94.5)	64 (91.4)	48 (92.3)
Completed, n (%) (Day 203)	-	-	63 (90.0)	47 (90.4)
Total Number Subjects Withdrawn, n (%)	3 (3.2)	5 (5.5)	7 (10.0)	5 (9.6)
Withdrawn due to Adverse Events n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0(0.0)
Withdrawn due to Lack of Efficacy n (%)	Not Applicable	Not applicable	Not Applicable	Not applicable
Withdrawn for other reasons n (%)	3 (3.2)	5 (5.5)	7 (10.0)	5 (9.6)
Demographics	Flu D21 Group		Flu M6 Group	
	18-60 years	>60 years	18-60 years	>60 years
N (Total Vaccinated Cohort)	93	91	70	52
Females: Males	50:43	42:49	37:33	26:26
Mean Age, years (SD)	39.0 (12.17)	66.8 (5.50)	40.8 (12.61)	66.1 (4.08)
White - Caucasian / European heritage, n (%)	86 (92.5)	88 (96.7)	64 (91.4)	50 (96.2)

Primary Efficacy Results: SCR for HI antibodies against Flu A/CAL/7/2009 at Day 21 (ATP cohort for immunogenicity at Day 21)

					SCR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/2009	Pooled groups	18-60	PI(D21)	160	154	96.3	92.0	98.6
		>60	PI(D21)	136	121	89.0	82.5	93.7

18-60 = Subjects aged between and including 18 years to 60 years

>60 = Subjects aged more than 60 years

Seroconversion defined as:

For initially seronegative subjects, antibody titre \geq 1:40 after vaccination

For initially seropositive subjects, antibody titre after vaccination \geq 4 fold the pre-vaccination antibody titre

N = Number of subjects with pre- and post-vaccination results available

n/% = Number/percentage of seroconverted subjects

95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

PI(D21)= Post-dose 1, Day 21

Primary Efficacy Results: SPR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 21)											
					SPR						
					95% CI						
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL			
Flu A/CAL/7/2009	Pooled groups	18-60	PRE	160	23	14.4	9.3	20.8			
			PI(D21)	160	156	97.5	93.7	99.3			
		>60	PRE	136	7	5.1	2.1	10.3			
			PI(D21)	136	125	91.9	86.0	95.9			
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years N = Number of subjects with available results n/% = Number/percentage of seroprotected subjects (HI titre \geq 1:40) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PRE= Pre-vaccination, Day 0 PI(D21)= Post-dose 1, Day 21											
Primary Efficacy Results: SCF for HI antibody titre (ATP cohort for immunogenicity at day 21)											
					SCF						
					95% CI						
Antibodies against	Group	Sub-group	Timing	N	Value	LL	UL				
Flu A/CAL/7/2009	Pooled groups	18-60	PI(D21)	160	45.0	37.2	54.5				
		>60	PI(D21)	136	23.4	19.1	28.7				
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years 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): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 42)											
					\geq 1:10				GMT		
					95% CI				95% CI		
Antibody against	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/CAL/7/2009	Flu D21	18-60	PRE	87	30	34.5	24.6	45.4	8.9	7.2	11.0
			PI(D21)	87	87	100	95.8	100	459.8	374.2	565.1
			PII(D42)	87	87	100	95.8	100	771.8	660.5	901.7
		>60	PRE	83	26	31.3	21.6	42.4	7.3	6.3	8.5
			PI(D21)	83	83	100	95.7	100	168.2	129.0	219.3
			PII(D42)	83	83	100	95.7	100	400.9	329.3	488.2
	Flu M6	18-60	PRE	67	25	37.3	25.8	50.0	9.3	7.4	11.8
			PI(D21)	67	65	97.0	89.6	99.6	366.1	266.7	502.7
			PI(D42)	67	65	97.0	89.6	99.6	297.6	218.6	405.2
		>60	PRE	48	20	41.7	27.6	56.8	8.0	6.6	9.8
			PI(D21)	48	48	100	92.6	100	187.5	136.6	257.4
			PI(D42)	48	48	100	92.6	100	132.6	94.3	186.6
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years 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 PI(D42)= Post-dose 1, Day 42 PII(D42)= Post-dose 2, Day 42											

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for antibody persistence at Day 182)											
							≥ 1:10		GMT		
							95% CI		95% CI		
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
FLU A/ CAL/7/2009	Flu D21	18-60	PII(D182)	85	85	100	95.8	100	240.5	193.6	298.8
		>60	PII(D182)	83	83	100	95.7	100	97.8	79.4	120.4
	Flu M6	18-60	PI(D182)	56	54	96.4	87.7	99.6	124.1	88.1	174.8
		>60	PI(D182)	30	28	93.3	77.9	99.2	48.6	30.0	78.9
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years 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 PII (D182) = Post-dose 2, Day 182 PI (D182) = Post-dose 1, Day 182											
Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 203)											
							≥ 1:10		GMT		
							95% CI		95% CI		
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/CAL/7/2009	Flu M6	18-60	PII(D203)	48	48	100	92.6	100	708.3	546.2	918.5
		>60	PII(D203)	28	28	100	87.7	100	512.1	354.5	740.0
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years 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 PII (D203) = Post-dose 2, Day 203											
Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 42)											
							SCR				
							n	%	95% CI		
Antibodies against	Group	Sub-group		Timing	N	n	%	LL	UL		
Flu A/CAL/7/2009	Flu D21	18-60		PI(D21)	87	87	100	95.8	100		
				PII(D42)	87	86	98.9	93.8	100		
		>60		PI(D21)	83	74	89.2	80.4	94.9		
				PII(D42)	83	82	98.8	93.5	100		
	Flu M6	18-60		PI(D21)	67	62	92.5	83.4	97.5		
				PI(D42)	67	61	91.0	81.5	96.6		
		>60		PI(D21)	48	43	89.6	77.3	96.5		
				PI(D42)	48	39	81.3	67.4	91.1		
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years 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 PI(D42)= Post-dose 1, Day 42											

PII(D42)= Post-dose 2, Day 42								
Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for antibody persistence at Day 182)								
					SCR			
					95% CI			
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL
FLU A/CAL/7/2009	Flu D21	18-60	PII(D182)	85	79	92.9	85.3	97.4
		>60	PII(D182)	83	72	86.7	77.5	93.2
	Flu M6	18-60	PI(D182)	56	47	83.9	71.7	92.4
		>60	PI(D182)	30	17	56.7	37.4	74.5
18-60 = Adults aged between and including 18 years to 60 years >60 = Adults aged more than 60 years Seroconversion defined as: For initially seronegative subjects, antibody titre \geq 1:40 after vaccination For initially seropositive subjects, antibody titre after vaccination \geq 4 fold the pre-vaccination antibody titre N = Number of subjects with pre- and post-vaccination results available n/% = Number/percentage of seroconverted subjects 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PII(D182) = Post-dose 2, Day 182 PI(D182) = Post-dose 1, Day 182								
Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 203)								
					SCR			
					95% CI			
Antibodies against	Group	Sub-Group	Timing	N	n	%	LL	UL
Flu A/CAL/7/2009	Flu M6	18-60	PII(D203)	48	48	100	92.6	100
		>60	PII(D203)	28	28	100	87.7	100
18-60 = Adults aged between and including 18 years to 60 years >60 = Adults aged more than 60 years Seroconversion defined as: For initially seronegative subjects, antibody titre \geq 1:40 after vaccination For initially seropositive subjects, antibody titre after vaccination \geq 4 fold the pre-vaccination antibody titre N = Number of subjects with pre- and post-vaccination results available n/% = Number/percentage of seroconverted subjects 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PII(D203) = Post-dose 2, Day 203								
Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 42)								
					SPR			
					95% CI			
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/2009	Flu D21	18-60	PRE	87	11	12.6	6.5	21.5
			PI(D21)	87	87	100	95.8	100
			PII(D42)	87	87	100	95.8	100
		>60	PRE	83	6	7.2	2.7	15.1
			PI(D21)	83	75	90.4	81.9	95.7
			PII(D42)	83	83	100	95.7	100
	Flu M6	18-60	PRE	67	10	14.9	7.4	25.7
			PI(D21)	67	63	94.0	85.4	98.3
			PI(D42)	67	64	95.5	87.5	99.1
		>60	PRE	48	1	2.1	0.1	11.1
			PI(D21)	48	46	95.8	85.7	99.5
			PI(D42)	48	43	89.6	77.3	96.5

18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years N = Number of subjects with available results n/% = Number/percentage of seroprotected subjects (HI titre \geq 1:40) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PRE= Pre-vaccination, Day 0 PI(D21)= Post-dose 1, Day 21 PI(D42)= Post-dose 1, Day 42 PII(D42)= Post-dose 2, Day 42								
Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for antibody persistence at Day 182)								
					SPR			
					95% CI			
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/ CAL/7/2009	Flu D21	18-60	PII(D182)	85	83	97.6	91.8	99.7
		>60	PII(D182)	83	75	90.4	81.9	95.7
	Flu M6	18-60	PI(D182)	56	48	85.7	73.8	93.6
		>60	PI(D182)	30	19	63.3	43.9	80.1
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years N = Number of subjects with available results n/% = Number/percentage of seroprotected subjects (HI titer \geq 1:40) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PII(D182) = Post-dose 2, Day 182 PI(D182) = Post-dose 1, Day 182								
Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 203)								
					SPR			
					95% CI			
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/2009	Flu M6	18-60	PII(D203)	48	48	100	92.6	100
		>60	PII(D203)	28	28	100	87.7	100
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years N = Number of subjects with available results n/% = Number/percentage of seroprotected subjects (HI titre \geq 1:40) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PII(D203) = Post-dose 2, Day 203								
Secondary Outcome Variable(s): SCF for HI antibody titre (ATP cohort for immunogenicity at Day 42)								
					SCF			
					95% CI			
Antibodies against	Group	Sub-group	Timing	N	Value	LL	UL	
Flu A/CAL/7/2009	Flu D21	18-60	PI(D21)	87	51.6	40.7	65.5	
			PII(D42)	87	86.7	68.6	109.5	
		>60	PI(D21)	83	23.0	17.7	29.9	
			PII(D42)	83	54.9	43.4	69.3	
	Flu M6	18-60	PI(D21)	67	39.2	28.3	54.2	
			PI(D42)	67	31.9	23.4	43.4	
		>60	PI(D21)	48	23.3	16.6	32.7	
			PI(D42)	48	16.5	11.8	23.0	
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years N = Number of subjects with pre- and post-vaccination results available SCF = Seroconversion Factor or geometric mean ratio (mean[log ₁₀ (POST/PRE)]) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI(D21)= Post-dose 1, Day 21								

PI(D42)= Post-dose 1, Day 42 PII(D42)= Post-dose 2, Day 42											
Secondary Outcome Variable(s): SCF for HI antibody titre (ATP cohort for antibody persistence at Day 182)											
						SCF					
						95% CI					
Antibodies against	Group	Sub-group	Timing	N	Value	LL	UL				
FLU A/ CAL/7/2009	Flu D21	18-60	PII(D182)	85	26.6	20.8	34.0				
		>60	PII(D182)	83	13.4	10.9	16.5				
	Flu M6	18-60	PI(D182)	56	14.6	10.8	19.7				
		>60	PI(D182)	30	6.1	3.9	9.4				
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years 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 PII (D182) = Post-dose 2, Day 182 PI (D182) = Post-dose 1, Day 182											
Secondary Outcome Variable(s): SCF for HI antibody titre (ATP cohort for immunogenicity at Day 203)											
						SCF					
						95% CI					
Antibodies against	Group	Sub-group	Timing	N	Value	LL	UL				
Flu A/CAL/7/2009	Flu M6	18-60	PII(D203)	48	79.0	58.0	107.7				
		>60	PII(D203)	28	65.7	41.4	104.1				
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years 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 PII (D203) = Post-dose 2, Day 203											
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 D21 Group											
18-60						> 60					
95% CI						95% CI					
Symptom	Intensity	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Pain	Any	92	87	94.6	87.8	98.2	90	71	78.9	69.0	86.8
	Grade 3	92	0	0.0	0.0	3.9	90	2	2.2	0.3	7.8
Redness (mm)	Any	92	10	10.9	5.3	19.1	90	8	8.9	3.9	16.8
	> 100	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Swelling (mm)	Any	92	11	12.0	6.1	20.4	90	6	6.7	2.5	13.9
	> 100	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Dose 2											
Pain	Any	91	80	87.9	79.4	93.8	85	62	72.9	62.2	82.0
	Grade 3	91	2	2.2	0.3	7.7	85	0	0.0	0.0	4.2
Redness (mm)	Any	91	6	6.6	2.5	13.8	85	11	12.9	6.6	22.0
	> 100	91	0	0.0	0.0	4.0	85	0	0.0	0.0	4.2
Swelling (mm)	Any	91	8	8.8	3.9	16.6	85	10	11.8	5.8	20.6
	> 100	91	0	0.0	0.0	4.0	85	0	0.0	0.0	4.2
Across doses											
Pain	Any	92	91	98.9	94.1	100	90	78	86.7	77.9	92.9
	Grade 3	92	2	2.2	0.3	7.6	90	2	2.2	0.3	7.8
Redness (mm)	Any	92	14	15.2	8.6	24.2	90	17	18.9	11.4	28.5
	> 100	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0

Swelling (mm)	Any	92	15	16.3	9.4	25.5	90	15	16.7	9.6	26.0
	> 100	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Flu M6 Group											
18-60						> 60					
95% CI						95% CI					
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Pain	Any	70	67	95.7	88.0	99.1	52	35	67.3	52.9	79.7
	Grade 3	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
Redness (mm)	Any	70	8	11.4	5.1	21.3	52	1	1.9	0.0	10.3
	> 100	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
Swelling (mm)	Any	70	6	8.6	3.2	17.7	52	1	1.9	0.0	10.3
	> 100	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
Dose 2											
Pain	Any	60	54	90.0	79.5	96.2	45	26	57.8	42.2	72.3
	Grade 3	60	3	5.0	1.0	13.9	45	0	0.0	0.0	7.9
Redness (mm)	Any	60	6	10.0	3.8	20.5	45	3	6.7	1.4	18.3
	> 100	60	2	3.3	0.4	11.5	45	1	2.2	0.1	11.8
Swelling (mm)	Any	60	10	16.7	8.3	28.5	45	4	8.9	2.5	21.2
	> 100	60	0	0.0	0.0	6.0	45	0	0.0	0.0	7.9
Across doses											
Pain	Any	70	68	97.1	90.1	99.7	52	40	76.9	63.2	87.5
	Grade 3	70	3	4.3	0.9	12.0	52	0	0.0	0.0	6.8
Redness (mm)	Any	70	13	18.6	10.3	29.7	52	4	7.7	2.1	18.5
	> 100	70	2	2.9	0.3	9.9	52	1	1.9	0.0	10.3
Swelling (mm)	Any	70	13	18.6	10.3	29.7	52	4	7.7	2.1	18.5
	> 100	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
<p>18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years 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 symptoms regardless of their intensity grade Grade 3 pain= significant pain at rest; prevented normal activities as assessed by inability to attend/do work or school</p>											
Secondary Outcome Variable(s): Number of days with local symptoms during the solicited post-vaccination period following each dose (Total Vaccinated Cohort)											
Solicited symptom	Dose	Group		Sub-group		N	Mean	Median			
Pain	Dose 1	Flu D21	18-60	18-60		87	3.3	3.0			
			>60	>60		71	3.0	3.0			
		Flu M6	18-60	18-60		67	3.3	3.0			
	Dose 2	Flu D21	18-60	18-60		80	3.0	3.0			
			>60	>60		62	3.3	3.0			
		Flu M6	18-60	18-60		54	3.3	3.0			
Redness	Dose 1	Flu D21	18-60	18-60		10	2.5	2.5			
			>60	>60		8	2.5	2.0			
		Flu M6	18-60	18-60		8	2.8	2.0			
	Dose 2	Flu D21	18-60	18-60		6	2.8	2.5			
			>60	>60		11	2.5	1.0			
		Flu M6	18-60	18-60		6	2.5	2.0			
Swelling	Dose 1	Flu D21	18-60	18-60		11	2.4	2.0			

			>60	6	2.2	2.0					
		Flu M6	18-60	6	3.5	3.0					
			>60	1	6.0	6.0					
	Dose 2	Flu D21	18-60	8	2.5	2.0					
			>60	10	3.2	3.0					
		Flu M6	18-60	10	2.5	2.0					
			>60	4	2.8	2.0					
18-60 = Subjects aged between and including 18 years to 60 years											
>60 = Subjects aged more than 60 years											
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 D21 Group											
18-60											
>60											
95% CI											
95% CI											
Symptom	Intensity/Relationship	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Fatigue	Any	92	40	43.5	33.2	54.2	90	26	28.9	19.8	39.4
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	35	38.0	28.1	48.8	90	22	24.4	16.0	34.6
Headache	Any	92	34	37.0	27.1	47.7	90	20	22.2	14.1	32.2
	Grade 3	92	0	0.0	0.0	3.9	90	1	1.1	0.0	6.0
	Related	92	29	31.5	22.2	42.0	90	17	18.9	11.4	28.5
Joint pain at other location	Any	92	21	22.8	14.7	32.8	90	19	21.1	13.2	31.0
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	17	18.5	11.1	27.9	90	15	16.7	9.6	26.0
Muscle aches	Any	92	43	46.7	36.3	57.4	90	26	28.9	19.8	39.4
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	36	39.1	29.1	49.9	90	23	25.6	16.9	35.8
Shivering	Any	92	17	18.5	11.1	27.9	90	12	13.3	7.1	22.1
	Grade 3	92	0	0.0	0.0	3.9	90	1	1.1	0.0	6.0
	Related	92	12	13.0	6.9	21.7	90	8	8.9	3.9	16.8
Sweating	Any	92	12	13.0	6.9	21.7	90	10	11.1	5.5	19.5
	Grade 3	92	1	1.1	0.0	5.9	90	0	0.0	0.0	4.0
	Related	92	8	8.7	3.8	16.4	90	6	6.7	2.5	13.9
Fever (Axillary) (°C)	≥ 37.5	92	1	1.1	0.0	5.9	90	1	1.1	0.0	6.0
	≥ 39.0	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Dose 2											
Fatigue	Any	91	49	53.8	43.1	64.4	85	27	31.8	22.1	42.8
	Grade 3	91	3	3.3	0.7	9.3	85	1	1.2	0.0	6.4
	Related	91	42	46.2	35.6	56.9	85	18	21.2	13.1	31.4
Headache	Any	91	41	45.1	34.6	55.8	85	19	22.4	14.0	32.7
	Grade 3	91	1	1.1	0.0	6.0	85	1	1.2	0.0	6.4
	Related	91	36	39.6	29.5	50.4	85	12	14.1	7.5	23.4
Joint pain at other location	Any	91	18	19.8	12.2	29.4	85	21	24.7	16.0	35.3
	Grade 3	91	0	0.0	0.0	4.0	85	0	0.0	0.0	4.2
	Related	91	14	15.4	8.7	24.5	85	17	20.0	12.1	30.1
Muscle aches	Any	91	39	42.9	32.5	53.7	85	25	29.4	20.0	40.3
	Grade 3	91	0	0.0	0.0	4.0	85	0	0.0	0.0	4.2
	Related	91	32	35.2	25.4	45.9	85	19	22.4	14.0	32.7
Shivering	Any	91	26	28.6	19.6	39.0	85	13	15.3	8.4	24.7
	Grade 3	91	1	1.1	0.0	6.0	85	1	1.2	0.0	6.4

	Related	91	24	26.4	17.7	36.7	85	9	10.6	5.0	19.2
Sweating	Any	91	19	20.9	13.1	30.7	85	14	16.5	9.3	26.1
	Grade 3	91	1	1.1	0.0	6.0	85	0	0.0	0.0	4.2
	Related	91	17	18.7	11.3	28.2	85	9	10.6	5.0	19.2
Fever (Axillary) (°C)	≥ 37.5	91	6	6.6	2.5	13.8	85	5	5.9	1.9	13.2
	≥ 39.0	91	0	0.0	0.0	4.0	85	2	2.4	0.3	8.2
	Related	91	5	5.5	1.8	12.4	85	4	4.7	1.3	11.6
Across doses											
Fatigue	Any	92	59	64.1	53.5	73.9	90	39	43.3	32.9	54.2
	Grade 3	92	3	3.3	0.7	9.2	90	1	1.1	0.0	6.0
	Related	92	52	56.5	45.8	66.8	90	29	32.2	22.8	42.9
Headache	Any	92	53	57.6	46.9	67.9	90	30	33.3	23.7	44.1
	Grade 3	92	1	1.1	0.0	5.9	90	2	2.2	0.3	7.8
	Related	92	45	48.9	38.3	59.6	90	22	24.4	16.0	34.6
Joint pain at other location	Any	92	27	29.3	20.3	39.8	90	27	30.0	20.8	40.6
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	22	23.9	15.6	33.9	90	21	23.3	15.1	33.4
Muscle aches	Any	92	53	57.6	46.9	67.9	90	34	37.8	27.8	48.6
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	46	50.0	39.4	60.6	90	28	31.1	21.8	41.7
Shivering	Any	92	34	37.0	27.1	47.7	90	22	24.4	16.0	34.6
	Grade 3	92	1	1.1	0.0	5.9	90	2	2.2	0.3	7.8
	Related	92	28	30.4	21.3	40.9	90	15	16.7	9.6	26.0
Sweating	Any	92	24	26.1	17.5	36.3	90	19	21.1	13.2	31.0
	Grade 3	92	2	2.2	0.3	7.6	90	0	0.0	0.0	4.0
	Related	92	18	19.6	12.0	29.1	90	13	14.4	7.9	23.4
Fever (Axillary) (°C)	≥ 37.5	92	7	7.6	3.1	15.1	90	5	5.6	1.8	12.5
	≥ 39.0	92	0	0.0	0.0	3.9	90	2	2.2	0.3	7.8
	Related	92	5	5.4	1.8	12.2	90	4	4.4	1.2	11.0
Flu M6 Group											
18-60											
>60											
95% CI											
Symptom	Intensity/Relationship	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Fatigue	Any	70	27	38.6	27.2	51.0	52	18	34.6	22.0	49.1
	Grade 3	70	1	1.4	0.0	7.7	52	0	0.0	0.0	6.8
	Related	70	21	30.0	19.6	42.1	52	11	21.2	11.1	34.7
Headache	Any	70	22	31.4	20.9	43.6	52	9	17.3	8.2	30.3
	Grade 3	70	1	1.4	0.0	7.7	52	0	0.0	0.0	6.8
	Related	70	13	18.6	10.3	29.7	52	6	11.5	4.4	23.4
Joint pain at other location	Any	70	10	14.3	7.1	24.7	52	8	15.4	6.9	28.1
	Grade 3	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
	Related	70	9	12.9	6.1	23.0	52	5	9.6	3.2	21.0
Muscle aches	Any	70	23	32.9	22.1	45.1	52	15	28.8	17.1	43.1
	Grade 3	70	0	0.0	0.0	5.1	52	1	1.9	0.0	10.3
	Related	70	20	28.6	18.4	40.6	52	12	23.1	12.5	36.8
Shivering	Any	70	14	20.0	11.4	31.3	52	6	11.5	4.4	23.4
	Grade 3	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
	Related	70	9	12.9	6.1	23.0	52	2	3.8	0.5	13.2
Sweating	Any	70	7	10.0	4.1	19.5	52	7	13.5	5.6	25.8
	Grade 3	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
	Related	70	4	5.7	1.6	14.0	52	3	5.8	1.2	15.9
Fever (Axillary) (°C)	≥ 37.5	70	2	2.9	0.3	9.9	52	1	1.9	0.0	10.3

	≥ 39.0	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
	Related	70	1	1.4	0.0	7.7	52	0	0.0	0.0	6.8
Dose 2											
Fatigue	Any	60	31	51.7	38.4	64.8	44	13	29.5	16.8	45.2
	Grade 3	60	2	3.3	0.4	11.5	44	0	0.0	0.0	8.0
	Related	60	31	51.7	38.4	64.8	44	11	25.0	13.2	40.3
Headache	Any	60	21	35.0	23.1	48.4	44	11	25.0	13.2	40.3
	Grade 3	60	3	5.0	1.0	13.9	44	0	0.0	0.0	8.0
	Related	60	19	31.7	20.3	45.0	44	9	20.5	9.8	35.3
Joint pain at other location	Any	60	16	26.7	16.1	39.7	44	12	27.3	15.0	42.8
	Grade 3	60	0	0.0	0.0	6.0	44	0	0.0	0.0	8.0
	Related	60	16	26.7	16.1	39.7	44	7	15.9	6.6	30.1
Muscle aches	Any	60	31	51.7	38.4	64.8	44	15	34.1	20.5	49.9
	Grade 3	60	1	1.7	0.0	8.9	44	0	0.0	0.0	8.0
	Related	60	28	46.7	33.7	60.0	44	10	22.7	11.5	37.8
Shivering	Any	60	11	18.3	9.5	30.4	44	7	15.9	6.6	30.1
	Grade 3	60	0	0.0	0.0	6.0	44	0	0.0	0.0	8.0
	Related	60	11	18.3	9.5	30.4	44	4	9.1	2.5	21.7
Sweating	Any	60	8	13.3	5.9	24.6	44	4	9.1	2.5	21.7
	Grade 3	60	0	0.0	0.0	6.0	44	0	0.0	0.0	8.0
	Related	60	8	13.3	5.9	24.6	44	2	4.5	0.6	15.5
Fever (Axillary) (°C)	≥ 37.5	60	1	1.7	0.0	8.9	44	0	0.0	0.0	8.0
	≥ 39.0	60	0	0.0	0.0	6.0	44	0	0.0	0.0	8.0
	Related	60	1	1.7	0.0	8.9	44	0	0.0	0.0	8.0
Across doses											
Fatigue	Any	70	41	58.6	46.2	70.2	52	25	48.1	34.0	62.4
	Grade 3	70	3	4.3	0.9	12.0	52	0	0.0	0.0	6.8
	Related	70	38	54.3	41.9	66.3	52	18	34.6	22.0	49.1
Headache	Any	70	31	44.3	32.4	56.7	52	15	28.8	17.1	43.1
	Grade 3	70	3	4.3	0.9	12.0	52	0	0.0	0.0	6.8
	Related	70	24	34.3	23.3	46.6	52	12	23.1	12.5	36.8
Joint pain at other location	Any	70	20	28.6	18.4	40.6	52	17	32.7	20.3	47.1
	Grade 3	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
	Related	70	20	28.6	18.4	40.6	52	11	21.2	11.1	34.7
Muscle aches	Any	70	40	57.1	44.7	68.9	52	25	48.1	34.0	62.4
	Grade 3	70	1	1.4	0.0	7.7	52	1	1.9	0.0	10.3
	Related	70	37	52.9	40.6	64.9	52	20	38.5	25.3	53.0
Shivering	Any	70	20	28.6	18.4	40.6	52	10	19.2	9.6	32.5
	Grade 3	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
	Related	70	18	25.7	16.0	37.6	52	6	11.5	4.4	23.4
Sweating	Any	70	13	18.6	10.3	29.7	52	11	21.2	11.1	34.7
	Grade 3	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
	Related	70	10	14.3	7.1	24.7	52	5	9.6	3.2	21.0
Fever (Axillary) (°C)	≥ 37.5	70	3	4.3	0.9	12.0	52	1	1.9	0.0	10.3
	≥ 39.0	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
	Related	70	2	2.9	0.3	9.9	52	0	0.0	0.0	6.8
<p>18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years 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 symptoms, regardless of their intensity grade or their relationship to vaccination Grade 3 symptoms= 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</p>											

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 following each dose (Total Vaccinated Cohort)						
Solicited symptom	Dose	Group	Sub-group	N	Mean	Median
Fatigue	Dose 1	Flu D21	18-60	40	2.2	2.0
			>60	26	2.5	2.0
		Flu M6	18-60	27	2.8	2.0
			>60	18	2.0	1.5
	Dose 2	Flu D21	18-60	49	2.1	2.0
			>60	27	2.8	2.0
		Flu M6	18-60	31	2.5	2.0
			>60	13	2.7	2.0
Headache	Dose 1	Flu D21	18-60	34	1.5	1.0
			>60	20	2.0	1.0
		Flu M6	18-60	22	1.7	1.0
			>60	9	2.0	1.0
	Dose 2	Flu D21	18-60	41	2.2	2.0
			>60	19	2.2	2.0
		Flu M6	18-60	21	2.2	2.0
			>60	11	2.8	3.0
Joint pain at other location	Dose 1	Flu D21	18-60	21	2.0	2.0
			>60	19	2.9	2.0
		Flu M6	18-60	10	2.2	2.0
			>60	8	3.3	3.0
	Dose 2	Flu D21	18-60	18	2.2	2.0
			>60	21	2.6	2.0
		Flu M6	18-60	16	2.6	2.0
			>60	12	2.5	2.0
Muscle aches	Dose 1	Flu D21	18-60	43	2.1	2.0
			>60	26	2.4	2.0
		Flu M6	18-60	23	2.6	2.0
			>60	15	2.5	2.0
	Dose 2	Flu D21	18-60	39	2.2	2.0
			>60	25	2.6	2.0
		Flu M6	18-60	31	3.1	3.0
			>60	15	3.1	3.0
Sweating	Dose 1	Flu D21	18-60	12	1.8	1.5
			>60	10	2.4	2.0
		Flu M6	18-60	7	1.4	1.0
			>60	7	1.6	1.0
	Dose 2	Flu D21	18-60	19	2.1	2.0
			>60	14	1.9	1.5
		Flu M6	18-60	8	1.3	1.0
			>60	4	1.0	1.0
Shivering	Dose 1	Flu D21	18-60	17	1.3	1.0
			>60	12	2.1	1.0
		Flu M6	18-60	14	1.5	1.0
			>60	6	1.7	1.5
	Dose 2	Flu D21	18-60	26	1.5	1.0
			>60	13	1.6	2.0
		Flu M6	18-60	11	1.7	1.0
			>60	7	1.1	1.0
Temperature	Dose 1	Flu D21 Group	18-60	1	1.0	1.0
			>60	1	1.0	1.0

		Flu M6	18-60	2	1.5	1.5													
			>60	1	1.0	1.0													
	Dose 2	Flu D21	18-60	6	1.5	1.0													
			>60	5	1.0	1.0													
		Flu M6	18-60	1	2.0	2.0													
			Total	1	2.0	2.0													
18-60 = Subjects aged between and including 18 years to 60 years																			
>60 = Subjects aged more than 60 years																			
N = number of doses with the symptom																			
Secondary Outcome Variable(s): Number (%) of subjects with adverse events of specific interest or potential immune-mediated diseases and adverse events of special interest reporting up to Day 203 (Total Vaccinated Cohort)																			
Most frequent adverse events - On-Therapy [occurring up to Day 203 following vaccination]		Flu D21 Group								Flu M6 Group									
		18-60 years N = 93				>60 years N = 91				18-60 years N = 70				>60 years N = 52					
Subjects with any AESI(s)/pIMDs or AEs of special interest, n (%)		0 (0.0)				0 (0.0)				0 (0.0)				0 (0.0)					
Secondary Outcome Variable(s): Distribution of haematology and biochemistry with respect to normal laboratory ranges (Total Vaccinated Cohort)																			
Flu D21 Group																			
		18-60 N = 93								> 60 N = 91									
		Unknown		Below		Within		Above		Unknown		Below		Within		Above			
Laboratory parameter	Timing	N	n	%	n	%	n	%	n	%	N	n	%	n	%	n	%	n	%
ALAT	PRE	93	0	0.0	4	4.3	83	89.2	4	4.3	91	2	2.2	0	0.0	83	91.2	5	5.5
	PI(D21)	91	1	1.1	3	3.3	83	91.2	3	3.3	88	0	0.0	0	0.0	74	84.1	10	11.4
	PII(D42)	92	0	0.0	3	3.3	84	91.3	5	5.4	86	0	0.0	0	0.0	79	91.9	6	7.0
	PII(D182)	88	0	0.0	2	2.3	84	95.5	2	2.3	85	0	0.0	0	0.0	76	89.4	9	10.6
AP	PRE	93	1	1.1	3	3.2	85	91.4	2	2.2	91	0	0.0	2	2.2	86	94.5	2	2.2
	PI(D21)	91	0	0.0	3	3.3	86	94.5	1	1.1	88	0	0.0	2	2.3	79	89.8	3	3.4
	PII(D42)	92	0	0.0	2	2.2	88	95.7	2	2.2	86	0	0.0	2	2.3	82	95.3	1	1.2
	PII(D182)	88	1	1.1	4	4.5	81	92.0	2	2.3	85	1	1.2	2	2.4	81	95.3	1	1.2
ASAT	PRE	93	0	0.0	1	1.1	87	93.5	3	3.2	91	2	2.2	0	0.0	81	89.0	7	7.7
	PI(D21)	91	1	1.1	0	0.0	85	93.4	4	4.4	88	1	1.1	0	0.0	75	85.2	8	9.1
	PII(D42)	92	0	0.0	0	0.0	88	95.7	4	4.3	86	0	0.0	0	0.0	79	91.9	6	7.0
	PII(D182)	88	0	0.0	0	0.0	86	97.7	2	2.3	85	0	0.0	0	0.0	79	92.9	6	7.1
Bilirubin	PRE	93	0	0.0	0	0.0	86	92.5	5	5.4	91	2	2.2	0	0.0	87	95.6	1	1.1
	PI(D21)	91	1	1.1	0	0.0	86	94.5	3	3.3	88	0	0.0	0	0.0	82	93.2	2	2.3
	PII(D42)	92	0	0.0	0	0.0	89	96.7	3	3.3	86	0	0.0	0	0.0	84	97.7	1	1.2
	PII(D182)	88	1	1.1	0	0.0	84	95.5	3	3.4	85	4	4.7	0	0.0	80	94.1	1	1.2
Creatinine	PRE	93	0	0.0	1	1.1	86	92.5	4	4.3	91	0	0.0	1	1.1	75	82.4	14	15.4
	PI(D21)	91	0	0.0	2	2.2	83	91.2	5	5.5	88	0	0.0	0	0.0	73	83.0	11	12.5
	PII(D42)	92	0	0.0	5	5.4	84	91.3	3	3.3	86	0	0.0	2	2.3	75	87.2	8	9.3
	PII(D182)	88	0	0.0	4	4.5	81	92.0	3	3.4	85	0	0.0	0	0.0	76	89.4	9	10.6
BUN	PRE	93	2	2.2	1	1.1	87	93.5	1	1.1	91	1	1.1	0	0.0	67	73.6	22	24.2
	PI(D21)	91	0	0.0	0	0.0	87	95.6	3	3.3	88	0	0.0	0	0.0	60	68.2	24	27.3
	PII(D42)	92	3	3.3	0	0.0	84	91.3	5	5.4	86	2	2.3	0	0.0	66	76.7	17	19.8
	PII(D182)	88	1	1.1	1	1.1	81	92.0	5	5.7	85	2	2.4	0	0.0	59	69.4	24	28.2
Flu M6 Group																			
		18-60 N = 70								> 60 N = 52									
		Unknown		Below		Within		Above		Unknown		Below		Within		Above			
Laboratory parameter	Timing	N	n	%	n	%	n	%	n	%	N	n	%	n	%	n	%	n	%
ALAT	PRE	70	0	0.0	0	0.0	60	85.7	9	12.9	52	0	0.0	0	0.0	46	88.5	6	11.5

	PI(D21)	70	0	0.0	0	0.0	59	84.3	9	12.9	52	0	0.0	0	0.0	49	94.2	3	5.8
	PI(D42)	68	0	0.0	0	0.0	61	89.7	7	10.3	52	0	0.0	0	0.0	47	90.4	4	7.7
	PI(D182)	63	0	0.0	0	0.0	53	84.1	10	15.9	47	0	0.0	0	0.0	42	89.4	4	8.5
	PII(D203)	62	0	0.0	1	1.6	50	80.6	10	16.1	46	3	6.5	0	0.0	41	89.1	2	4.3
AP	PRE	70	0	0.0	4	5.7	64	91.4	1	1.4	52	0	0.0	3	5.8	49	94.2	0	0.0
	PI(D21)	70	0	0.0	5	7.1	62	88.6	1	1.4	52	0	0.0	3	5.8	49	94.2	0	0.0
	PI(D42)	68	1	1.5	3	4.4	63	92.6	1	1.5	52	0	0.0	4	7.7	47	90.4	0	0.0
	PI(D182)	63	0	0.0	1	1.6	62	98.4	0	0.0	47	1	2.1	2	4.3	43	91.5	0	0.0
ASAT	PII(D203)	62	0	0.0	3	4.8	57	91.9	1	1.6	46	0	0.0	3	6.5	43	93.5	0	0.0
	PRE	70	0	0.0	1	1.4	61	87.1	7	10.0	52	0	0.0	0	0.0	49	94.2	3	5.8
	PI(D21)	70	0	0.0	0	0.0	61	87.1	7	10.0	52	0	0.0	0	0.0	50	96.2	2	3.8
	PI(D42)	68	0	0.0	1	1.5	58	85.3	9	13.2	52	0	0.0	0	0.0	49	94.2	2	3.8
Bilirubin	PI(D182)	63	0	0.0	0	0.0	59	93.7	4	6.3	47	0	0.0	0	0.0	44	93.6	2	4.3
	PII(D203)	62	0	0.0	0	0.0	55	88.7	6	9.7	46	1	2.2	0	0.0	44	95.7	1	2.2
	PRE	70	1	1.4	0	0.0	66	94.3	2	2.9	52	0	0.0	0	0.0	49	94.2	3	5.8
	PI(D21)	70	0	0.0	0	0.0	64	91.4	4	5.7	52	0	0.0	0	0.0	49	94.2	3	5.8
Creatinine	PI(D42)	68	1	1.5	0	0.0	63	92.6	4	5.9	52	0	0.0	0	0.0	49	94.2	2	3.8
	PI(D182)	63	1	1.6	0	0.0	59	93.7	3	4.8	47	1	2.1	0	0.0	41	87.2	4	8.5
	PII(D203)	62	0	0.0	0	0.0	58	93.5	3	4.8	46	1	2.2	0	0.0	44	95.7	1	2.2
	PRE	70	0	0.0	4	5.7	63	90.0	2	2.9	52	0	0.0	1	1.9	45	86.5	6	11.5
BUN	PI(D21)	70	0	0.0	3	4.3	62	88.6	3	4.3	52	0	0.0	3	5.8	46	88.5	3	5.8
	PI(D42)	68	0	0.0	4	5.9	62	91.2	2	2.9	52	0	0.0	1	1.9	47	90.4	3	5.8
	PI(D182)	63	0	0.0	2	3.2	57	90.5	4	6.3	47	0	0.0	1	2.1	42	89.4	3	6.4
	PII(D203)	62	0	0.0	4	6.5	53	85.5	4	6.5	46	0	0.0	1	2.2	41	89.1	4	8.7
BUN	PRE	70	0	0.0	0	0.0	65	92.9	4	5.7	52	0	0.0	2	3.8	43	82.7	7	13.5
	PI(D21)	70	0	0.0	0	0.0	64	91.4	4	5.7	52	0	0.0	1	1.9	42	80.8	9	17.3
	PI(D42)	68	2	2.9	1	1.5	60	88.2	5	7.4	52	1	1.9	1	1.9	43	82.7	6	11.5
	PI(D182)	63	1	1.6	2	3.2	54	85.7	6	9.5	47	1	2.1	1	2.1	36	76.6	8	17.0
PII(D203)	62	0	0.0	2	3.2	48	77.4	11	17.7	46	0	0.0	0	0.0	33	71.7	13	28.3	

18-60 = Subjects aged between and including 18 years to 60 years

>60 = Subjects aged more than 60 years

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

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

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

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

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

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

ALAT= Alanine aminotransferase

AP= Alkaline phosphatase

ASAT=Aspartate aminotransferase

BUN= Blood urea nitrogen

Safety results: Number (%) of subjects with unsolicited adverse events within the 21-days post-vaccination 1 (Days 0-20; both groups) and either 63 days post-vaccination 2 (Days 21-84; Flu D21 Group) or 21 days post-vaccination 2* (Days 182-203; Flu M6 Group) (Total Vaccinated Cohort)

Most frequent adverse events - On-Therapy (occurring within 21 days post-vaccination 1 and either 63 days post-dose 2 (for Flu D21 Group only) or 21 days post-dose 2* (for Flu M6 Group only))	Flu D21 Group		Flu M6 Group	
	18-60 N = 93	> 60 N = 91	18-60 N = 70	> 60 N = 52
Subjects with any AE(s), n (%)	52 (55.9)	53 (58.2)	30 (42.9)	15 (28.8)
Nasopharyngitis	12 (12.9)	7 (7.7)	5 (7.1)	2 (3.8)
Rhinitis	10 (10.8)	10 (11.0)	5 (7.1)	1 (1.9)
Headache	8 (8.6)	6 (6.6)	3 (4.3)	1 (1.9)
Back pain	-	4 (4.4)	-	1 (1.9)
Diarrhoea	5 (5.4)	-	-	1 (1.9)

Bronchitis	-	-	2 (2.9)	3 (5.8)
Arthralgia	-	-	2 (2.9)	1 (1.9)
Oropharyngeal pain	-	-	2 (2.9)	1 (1.9)
Rhinotracheitis	-	-	-	2 (3.8)
Vertigo	5 (5.4)	-	-	-
Migraine	-	3 (3.3)	-	-
Gastroenteritis	-	-	2 (2.9)	-
Abdominal pain	-	-	-	1 (1.9)
Azotaemia	-	-	-	1 (1.9)
Conjunctivitis	-	-	-	1 (1.9)
Dermatitis contact	-	-	-	1 (1.9)
Epicondylitis	-	-	-	1 (1.9)
Eye irritation	-	-	-	1 (1.9)
Gastritis	-	-	-	1 (1.9)
Haematoma	-	-	-	1 (1.9)
Injection site joint pain	-	-	-	1 (1.9)
Joint injury	-	-	-	1 (1.9)
Lymphadenopathy	-	-	-	1 (1.9)
Post procedural infection	-	-	-	1 (1.9)
Presyncope	-	-	-	1 (1.9)

18-60 = Adults aged between and including 18 years to 60 years

>60 = Adults aged more than 60 years

-: Adverse event absent or not meeting the selected rule: If more than 30 subjects per group and > 3 groups, then only the 5 most frequent adverse events in each group are to be listed.

Grade 3= event that prevented normal activity

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

*only 21 days follow-up post-vaccination 2 for Flu M6 Group at the time of writing this summary, the rest 9 days will be added when data are available

Safety results: Number (%) of subjects with SAEs up to Day 203 (Total Vaccinated Cohort)

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

All SAEs	Flu D21 Group		Flu M6 Group	
	18-60 years N = 93	>60 years N = 91	18-60 years N = 70	>60 years N = 52
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	2 (2.2) [0]	4 (4.4) [1]	4 (5.7) [1]	2 (3.8) [0]
Vertigo	1 (1.1) [0]	1 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]
Chest pain	0 (0.0) [0]	1 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]
Coronary artery disease	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.9) [0]
Hepatic enzyme increased	0 (0.0) [0]	1 (1.1) [1]	0 (0.0) [0]	0 (0.0) [0]
Herpes zoster	0 (0.0) [0]	0 (0.0) [0]	1 (1.4) [1]	0 (0.0) [0]
Intervertebral disc disorder	0 (0.0) [0]	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Lentigo maligna stage unspecified	0 (0.0) [0]	1 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]
Nephrolithiasis	0 (0.0) [0]	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Post procedural infection	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.9) [0]
Prostatic adenoma	1 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Pyelonephritis	0 (0.0) [0]	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Spinal fracture	0 (0.0) [0]	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Fatal SAEs	Flu D21 Group		Flu M6 Group	
	18-60 years N = 93	>60 years N = 91	18-60 years N = 70	>60 years N = 52
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:

21 days after Flu vaccine administration, SCR for HI antibodies against vaccine-homologous virus was of 96.3% in subjects aged 18-60 years and 89.0% in subjects above 60 years. At the same time point, SPR was of 97.5% for subjects aged 18-

60 years and 91.9% in subjects above 60 years, and SCF was 45.0 in subjects aged 18-60 years and 23.4 in subjects above 60 years.

Within the 21-days post-vaccination 1 (Days 0-20; for both groups) and either 63 days post-vaccination 2 (Days 21-84; for Flu D21 Group) or 21 days post-vaccination 2 (Days 182-203; for Flu M6 Group), 52 (55.9%) subjects of Flu D21 (18-60 years) Group, 53 (58.2%) subjects of Flu D21 (>60 years) Group, 30 (42.9%) subjects of Flu M6 (18-60 years) Group and 15 (28.8%) subjects of Flu M6 (>60 years) Group reported at least one unsolicited adverse event.

Up to Day 203, SAEs were reported for 2 subjects from the Flu D21 (18-60 years) Group, 4 subjects from the Flu D21 (>60 years) Group, 4 subjects from the Flu M6 (18-60 years) Group and 2 subjects from the Flu M6 (> 60 years) Group. In both the Flu D21 (> 60 years) Group and the Flu M6 (18-60 years) Group one of the SAEs was assessed by the investigator as related to the study vaccination. No fatal SAE have been reported up to Day 203.

Publications: None

Date updated: 08 September 2010