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**.**
Pandemrix™ - 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.

Phase: III

Study Period: 14 September 2009 to:

- 03 November 2009 (Day 42)
- 30 April 2010 (Day 203)
- 08 October 2010 (Day 364)
- 25 March 2011 (Day 546)

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: Immunisation against A/California/7/2009 (H1N1)v-like influenza.

Treatment: The study groups were as follows:

- 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 1 dose of Flu vaccine results in an Haemagglutination Inhibition (HI) immune response to the vaccine-homologous virus that would meet or exceed the European Medicines Agency (EMEA) 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:
Immunogenicity

- Humoral immune response in terms of HI antibodies in subjects receiving Flu vaccine:
  - 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)

*SCR: defined as the proportion of subjects who have either a pre-vaccination reciprocal HI titre < 10 and a post-vaccination reciprocal titre ≥ 40, or a pre-vaccination reciprocal HI titre ≥ 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.
**SPR: the proportion of subjects with H1N1 reciprocal HI titres ≥ 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.
***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.

Secondary Outcome/Efficacy Variable(s):
Immunogenicity

- Humoral immune response in terms of HI antibodies in subjects receiving 2 doses of Flu vaccine:
  - 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

*See primary outcome variable section on criteria for evaluation for each age stratum.

- Humoral immune response in terms of neutralizing antibodies in a subset of subjects against A/California/7/2009 (H1N1) v-like antigen.§
    - 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.
  Adverse events of specific interest for safety monitoring also called potential Immune-Mediated Diseases (pIMDs), are a subset of AEs that include both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which may or may not have an autoimmune aetiology.
    - 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.

† This only applies to subjects enrolled in the Flu M6 Group.
§ Results of neutralizing antibody testing at Days 182, 203 and 364 were cancelled.

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, the ATP cohort for antibody persistence at Day 182 and the ATP cohort for persistence at Day 364.

- 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 administered 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 administered 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, respectively).
- 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 administered 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.
- The ATP cohort for persistence at Day 364 included all evaluable subjects, who met all eligibility criteria, complied with the procedures defined in the protocol during the entire study period and with the intervals defined in the protocol for visit

at Day 364, 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 Day 364.

At Day 21, no distinction was made in terms of study groups as all subjects had received 1 dose of Flu vaccine. Results were therefore presented for the pooled groups.

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, the ATP cohort for antibody persistence at Day 182 and the ATP cohort for persistence at Day 364.

Point estimates for SCR, SPR and GMFR and the associated 95% confidence interval (CI) were computed at Day 21 after the first dose.

The HI immune response to the vaccine homologous virus was described by estimating the following parameters per age stratum (with 95% CIs):

- GMT, Seropositivity rate and SPR on Days 0, 21, 42, 182, 203 and 364,
- SCR and GMFR (SCF) on Days 21, 42, 182, 203 and 364.

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.

GMT on Days 0, 21 and 42 and vaccine response rate on Days 21 and 42 for neutralising antibodies were also tabulated with 95 % CI.

Analysis of safety

The analysis was based on the Total Vaccinated Cohort.

The percentages of subjects reporting solicited local and general symptoms occurring during the 7 days (Days 0-6) after each vaccine dose were tabulated with exact 95% CIs for the pooled groups (after first vaccination) and 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 investigators as related to vaccination. The duration of the symptoms was also computed within the solicited period.

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 30 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 related to vaccination.

SAEs, AESIs/pIMDs and AEs of special interest were summarized per age stratum, up to Day 364 for the Flu D21 Group and up to Day 546 for the Flu M6 Group. The number and proportion of subjects with normal or abnormal values for each biochemistry parameter were tabulated for each group and per age stratum at each scheduled time point, up to Day 364.

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	75	75	75	75
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)	86 (94.5)	68 (97.1)	52 (100)
Completed, n (%) (Day 182)	90 (96.8)	85 (93.4)	63 (90.0)	48 (92.3)
Completed, n (%) (Day 203)	Not Applicable	Not Applicable	62 (88.6)	46 (88.5)
Completed, n (%) (Day 364)	85 (91.4)	83 (91.2)	62 (88.6)	47 (90.4)
Completed, n (%) (Day 546)	Not Applicable	Not Applicable	60 (85.7)	47 (90.4)*
Total Number Subjects Withdrawn, n (%)	8 (8.6)	8 (8.8)	10 (14.3)	5 (9.6)*
Withdrawn due to Adverse Events n (%)	0 (0.0)	1 (1.1)	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 (%)	8 (8.6)	7 (7.7)	10 (14.3)	5 (9.6)

* 1 fatal SAE was reported at the time of the Day 546 phone contact but the subject was not recorded as withdrawn in the database; hence this SAE was not considered in the statistical analysis of the demography at Day 546.

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 ≥ 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

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 ≥ 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)

	≥ 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): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 (ATP cohort for persistence at Day 364)

					≥ 1:10				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/ CAL/7/2009	Flu D21	18-60	PII(D364)	79	79	100	95.4	100	107.8	82.9	140.1
		>60	PII(D364)	76	73	96.1	88.9	99.2	35.8	28.0	45.7
	Flu M6	18-6	PII(D364)	60	60	100	94.0	100	155.5	116.8	207.0
		>60	PII(D364)	46	46	100	92.3	100	68.8	51.2	92.5

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
PII(D364) = Post-Dose 2, Day 364

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 42)

					SCR			
							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 ≥ 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(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 ≥ 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(D203) = Post-Dose 2, Day 203

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

				SCR			
						95% CI	
Strain	**Group**	**Sub-group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu D21	18-60	79	60	75.9	65.0	84.9
		>60	76	31	40.8	29.6	52.7
	Flu M6	18-60	60	54	90.0	79.5	96.2
		>60	46	34	73.9	58.9	85.7

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 ≥ 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/7/2009 (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 ≥ 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 titre ≥ 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 ≥ 1:40)
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/7/09 at Day 364 (ATP cohort for persistence at Day 364)

				SPR			
						95% CI	
Strain	**Group**	**Sub-group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09	Flu D21	18-60	79	65	82.3	72.1	90.0
		>60	76	38	50.0	38.3	61.7
	Flu M6	18-60	60	56	93.3	83.8	98.2
		>60	46	37	80.4	66.1	90.6

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 ≥ 1:40)

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

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[log10(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): SCF for HI antibodies against Flu A/CAL/7/09 at Day 364 (ATP cohort for persistence at Day 364)

				SCF		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09	Flu D21	18-60	79	11.9	9.2	15.5
		>60	76	4.8	3.8	6.1

	Flu M6	18-60	60	17.3	13.0	23.0
		>60	46	8.3	6.0	11.3

18-60 = Subjects aged between and including 18 years to 60 years
>60 = Subjects aged more than 60 years
N = Number of subjects with pre- and post-vaccination results available
SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): GMTs of neutralizing antibody titres against Flu A/Netherlands/602/09 (H1N1) strain for the two groups by each age category 18-60Y and >60Y (ATP cohort for immunogenicity at Day 42)

					≥ 1:8				GMT		
							95% CI			95% CI	
Antibodies against	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/Netherlands/602/09 (H1N1)	Flu D21	18-60Y	PRE	24	6	25.0	9.8	46.7	6.0	4.2	8.6
			PI(D21)	24	24	100	85.8	100	163.0	84.3	315.2
			PII(D42)	24	24	100	85.8	100	408.2	257.0	648.4
		>60Y	PRE	24	15	62.5	40.6	81.2	10.2	7.0	14.8
			PI(D21)	24	24	100	85.8	100	96.4	56.0	166.1
			PII(D42)	24	24	100	85.8	100	207.8	136.0	317.4
	Flu M6	18-60Y	PRE	19	5	26.3	9.1	51.2	5.5	4.1	7.4
			PI(D21)	19	18	94.7	74.0	99.9	164.2	64.0	420.7
			PI(D42)	19	18	94.7	74.0	99.9	165.3	70.7	386.1
		>60Y	PRE	18	15	83.3	58.6	96.4	17.9	11.3	28.5
			PI(D21)	18	18	100	81.5	100	168.3	86.3	328.3
			PI(D42)	18	18	100	81.5	100	105.0	58.3	189.3

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): Vaccine response rate for neutralising antibodies against Flu A/Netherlands/602/09 (H1N1) strain at Day 21 and Day 42 by each age category 18-60Y, >60Y (ATP cohort for immunogenicity at Day 42)

					Vaccine response			
							95% CI	
Antibodies against	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Netherlands/602/09 (H1N1)	Flu D21	18-60Y	PI(D21)	24	18	75.0	53.3	90.2
			PII(D42)	24	24	100	85.8	100
		>60Y	PI(D21)	24	15	62.5	40.6	81.2
			PII(D42)	24	21	87.5	67.6	97.3
	Flu M6	18-60Y	PI(D21)	19	16	84.2	60.4	96.6
			PI(D42)	19	16	84.2	60.4	96.6
		>60Y	PI(D21)	18	11	61.1	35.7	82.7
			PI(D42)	18	11	61.1	35.7	82.7

18-60 = Subjects aged between and including 18 years to 60 years
>60 = Subjects aged more than 60 years
Vaccine response rate defined as the percentage of vaccines with a minimum 4-fold increase in titre at post-vaccination for neutralising antibody response
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of responders
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): Percentage of subjects with solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following first dose (Total Vaccinated cohort – Pooled Groups) - *Interim Analysis posted at Day 42*

		Pooled Groups									
		18-60 years					>60 years				
					95 % CI					95 % CI	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Pain	Any	162	154	95.1	90.5	97.8	142	106	74.6	66.7	81.6
	Grade 3	162	0	0.0	0.0	2.3	142	2	1.4	0.2	5.0
Redness	Any	162	18	11.1	6.7	17.0	142	9	6.3	2.9	11.7
	> 100 mm	162	0	0.0	0.0	2.3	142	0	0.0	0.0	2.6
Swelling	Any	162	17	10.5	6.2	16.3	142	7	4.9	2.0	9.9
	> 100 mm	162	0	0.0	0.0	2.3	142	0	0.0	0.0	2.6

N= number of subjects with the 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
Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Number of days with local symptoms during the solicited post-vaccination period following first dose (Total Vaccinated cohort – Pooled Groups) - *Interim Analysis posted at Day 42*

Solicited symptom	**Group**	**Sub-group**	**N**	**Mean**	**Median**
Pain	Pooled Groups	18-60	154	3.3	3.0
		>60	106	2.9	3.0
Redness	Pooled Groups	18-6	18	2.6	2.0
		>60	9	2.6	2.0
Swelling	Pooled Groups	18-60	17	2.8	3.0
		>60	7	2.7	2.0

N = number of doses with the symptom
Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Percentage of subjects with 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) - *Interim analysis posted at Day 42*

		Flu D21 Group									
		18-60 years					>60 years				
					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	Any	92	10	10.9	5.3	19.1	90	8	8.9	3.9	16.8
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Swelling	Any	92	11	12.0	6.1	20.4	90	6	6.7	2.5	13.9

	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Dose 2											
Pain	Any	90	80	88.9	80.5	94.5	84	62	73.8	63.1	82.8
	Grade 3	90	2	2.2	0.3	7.8	84	0	0.0	0.0	4.3
Redness	Any	90	6	6.7	2.5	13.9	84	11	13.1	6.7	22.2
	> 100 mm	90	0	0.0	0.0	4.0	84	0	0.0	0.0	4.3
Swelling	Any	90	8	8.9	3.9	16.8	84	10	11.9	5.9	20.8
	> 100 mm	90	0	0.0	0.0	4.0	84	0	0.0	0.0	4.3
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	Any	92	14	15.2	8.6	24.2	90	17	18.9	11.4	28.5
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Swelling	Any	92	15	16.3	9.4	25.5	90	15	16.7	9.6	26.0
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0

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 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
Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Percentage of subjects with 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 years					**>60 years**				
					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	Any	92	10	10.9	5.3	19.1	90	8	8.9	3.9	16.8
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Swelling	Any	92	11	12.0	6.1	20.4	90	6	6.7	2.5	13.9
	> 100 mm	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	Any	91	6	6.6	2.5	13.8	85	11	12.9	6.6	22.0
	> 100 mm	91	0	0.0	0.0	4.0	85	0	0.0	0.0	4.2
Swelling	Any	91	8	8.8	3.9	16.6	85	10	11.8	5.8	20.6
	> 100 mm	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	Any	92	14	15.2	8.6	24.2	90	17	18.9	11.4	28.5
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Swelling	Any	92	15	16.3	9.4	25.5	90	15	16.7	9.6	26.0
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
		Flu M6 Group									
		18-60 years					**>60 years**				
					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	Any	70	8	11.4	5.1	21.3	52	1	1.9	0.0	10.3
	> 100 mm	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8
Swelling	Any	70	6	8.6	3.2	17.7	52	1	1.9	0.0	10.3
	> 100 mm	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	Any	60	6	10.0	3.8	20.5	45	3	6.7	1.4	18.3
	> 100 mm	60	2	3.3	0.4	11.5	45	1	2.2	0.1	11.8
Swelling	Any	60	10	16.7	8.3	28.5	45	4	8.9	2.5	21.2
	> 100 mm	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	Any	70	13	18.6	10.3	29.7	52	4	7.7	2.1	18.5
	> 100 mm	70	2	2.9	0.3	9.9	52	1	1.9	0.0	10.3
Swelling	Any	70	13	18.6	10.3	29.7	52	4	7.7	2.1	18.5
	> 100 mm	70	0	0.0	0.0	5.1	52	0	0.0	0.0	6.8

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 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

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	87	3.3	3.0
			>60	71	3.0	3.0
		Flu M6	18-60	67	3.3	3.0
			>60	35	2.7	3.0
	Dose 2	Flu D21	18-60	80	3.0	3.0
			>60	62	3.3	3.0
		Flu M6	18-60	54	3.3	3.0
			>60	26	2.7	3.0
Redness	Dose 1	Flu D21	18-60	10	2.5	2.5
			>60	8	2.5	2.0
		Flu M6	18-60	8	2.8	2.0
			>60	1	3.0	3.0
	Dose 2	Flu D21	18-60	6	2.8	2.5
			>60	11	2.5	1.0
		Flu M6	18-60	6	2.5	2.0
			>60	3	4.3	4.0
Swelling	Dose 1	Flu D21	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): Percentage of subjects with solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following first dose (Total Vaccinated cohort – Pooled Groups) - *Interim analysis posted at Day 42*

		Pooled Groups									
		18-60 years					>60 years				
					95 % CI					95 % CI	
Symptom	**Intensity/ Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Fatigue	Any	162	67	41.4	33.7	49.4	142	44	31.0	23.5	39.3
	Grade 3	162	1	0.6	0.0	3.4	142	0	0.0	0.0	2.6
	Related	162	56	34.6	27.3	42.4	142	34	23.9	17.2	31.8
Headache	Any	162	56	34.6	27.3	42.4	142	29	20.4	14.1	28.0
	Grade 3	162	1	0.6	0.0	3.4	142	1	0.7	0.0	3.9
	Related	162	43	26.5	19.9	34.0	142	23	16.2	10.6	23.3
Joint pain at other location	Any	162	31	19.1	13.4	26.0	142	27	19.0	12.9	26.4
	Grade 3	162	0	0.0	0.0	2.3	142	0	0.0	0.0	2.6
	Related	162	26	16.0	10.8	22.6	142	20	14.1	8.8	20.9
Muscle aches	Any	162	66	40.7	33.1	48.7	142	41	28.9	21.6	37.1
	Grade 3	162	0	0.0	0.0	2.3	142	1	0.7	0.0	3.9
	Related	162	56	34.6	27.3	42.4	142	35	24.6	17.8	32.6
Shivering	Any	162	31	19.1	13.4	26.0	142	18	12.7	7.7	19.3
	Grade 3	162	0	0.0	0.0	2.3	142	1	0.7	0.0	3.9
	Related	162	22	13.6	8.7	19.8	142	11	7.7	3.9	13.4
Sweating	Any	162	19	11.7	7.2	17.7	142	17	12.0	7.1	18.5
	Grade 3	162	1	0.6	0.0	3.4	142	0	0.0	0.0	2.6
	Related	162	13	8.0	4.3	13.3	142	9	6.3	2.9	11.7
Temperature/ (Axillary)	≥37.5°C	162	3	1.9	0.4	5.3	142	2	1.4	0.2	5.0
	≥ 39.0°C	162	0	0.0	0.0	2.3	142	0	0.0	0.0	2.6
	Related	162	1	0.6	0.0	3.4	142	0	0.0	0.0	2.6

N= number of subjects with the 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= 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
Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Number of days with general symptoms during the solicited post-vaccination period following first dose (Total Vaccinated cohort – Pooled Groups) - *Interim analysis posted at Day 42*

Solicited symptom	**Group**	**Sub-group**	**N**	**Mean**	**Median**
Fatigue	Pooled Groups	18-60	67	2.4	2.0
		>60	44	2.3	2.0
Headache	Pooled Groups	18-60	56	1.6	1.0
		>60	29	2.0	1.0
Joint pain at other location	Pooled Groups	18-60	31	2.1	2.0
		>60	27	3.0	2.0
Muscle aches	Pooled Groups	18-60	66	2.3	2.0
		>60	41	2.4	2.0
Sweating	Pooled Groups	18-60	19	1.7	1.0
		>60	17	2.1	1.0
Shivering	Pooled Groups	18-60	31	1.4	1.0
		>60	18	1.9	1.0
Temperature	Pooled Groups	18-60	3	1.3	1.0
		>60	3	1.0	1.0

N = number of doses with the symptom

Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Number of subjects with 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) - *Interim analysis posted at Day 42*

		Flu D21 Group									
		18-60 years					>60 years				
					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	30	32.6	23.2	43.2	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	13	14.1	7.7	23.0	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	9	9.8	4.6	17.8	90	6	6.7	2.5	13.9
Temperature/ (Axillary)	≥37.5°C	92	1	1.1	0.0	5.9	90	1	1.1	0.0	6.0
	≥ 39.0°C	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	90	48	53.3	42.5	63.9	84	27	32.1	22.4	43.2
	Grade 3	90	3	3.3	0.7	9.4	84	1	1.2	0.0	6.5
	Related	90	41	45.6	35.0	56.4	84	18	21.4	13.2	31.7
Headache	Any	90	41	45.6	35.0	56.4	84	19	22.6	14.2	33.0
	Grade 3	90	1	1.1	0.0	6.0	84	1	1.2	0.0	6.5
	Related	90	36	40.0	29.8	50.9	84	12	14.3	7.6	23.6
Joint pain at other location	Any	90	17	18.9	11.4	28.5	84	21	25.0	16.2	35.6
	Grade 3	90	0	0.0	0.0	4.0	84	0	0.0	0.0	4.3
	Related	90	13	14.4	7.9	23.4	84	17	20.2	12.3	30.4
Muscle aches	Any	90	38	42.2	31.9	53.1	84	25	29.8	20.3	40.7
	Grade 3	90	0	0.0	0.0	4.0	84	0	0.0	0.0	4.3
	Related	90	31	34.4	24.7	45.2	84	19	22.6	14.2	33.0
Shivering	Any	90	26	28.9	19.8	39.4	84	13	15.5	8.5	25.0
	Grade 3	90	1	1.1	0.0	6.0	84	1	1.2	0.0	6.5
	Related	90	24	26.7	17.9	37.0	84	9	10.7	5.0	19.4
Sweating	Any	90	19	21.1	13.2	31.0	84	13	15.5	8.5	25.0
	Grade 3	90	1	1.1	0.0	6.0	84	0	0.0	0.0	4.3
	Related	90	17	18.9	11.4	28.5	84	8	9.5	4.2	17.9
Temperature/ (Axillary)	≥37.5°C	90	6	6.7	2.5	13.9	84	5	6.0	2.0	13.3
	≥ 39.0°C	90	0	0.0	0.0	4.0	84	2	2.4	0.3	8.3
	Related	90	5	5.6	1.8	12.5	84	4	4.8	1.3	11.7
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	53	57.6	46.9	67.9	90	30	33.3	23.7	44.1
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	46	50.0	39.4	60.6	90	23	25.6	16.9	35.8
Joint pain at other location	Any	92	26	28.3	19.4	38.6	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	21	22.8	14.7	32.8	90	22	24.4	16.0	34.6
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	29	32.2	22.8	42.9
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	29	31.5	22.2	42.0	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	19	20.7	12.9	30.4	90	13	14.4	7.9	23.4
Temperature/ (Axillary)	≥37.5°C	92	7	7.6	3.1	15.1	90	5	5.6	1.8	12.5
	≥ 39.0°C	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

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= 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
Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Number of days with general symptoms during the solicited post-vaccination period following each dose and overall (Total Vaccinated cohort – Flu D21 Group) - *Interim analysis posted at Day 42*

Solicited symptom	Dose	Group	Sub-group	N	Mean	Median
Fatigue	Dose 1	Flu D21 Group	18-60	40	2.2	2.0
			>60	26	2.5	2.0
	Dose 2	Flu D21 Group	18-60	48	2.1	2.0
			>60	27	2.8	2.0
	Overall/dose	Flu D21 Group	18-60	88	2.2	2.0
			>60	53	2.7	2.0
Headache	Dose 1	Flu D21 Group	18-60	34	1.5	1.0
			>60	20	2.0	1.0
	Dose 2	Flu D21 Group	18-60	41	2.2	2.0
			>60	19	2.2	2.0
	Overall/dose	Flu D21 Group	18-60	75	1.9	1.0
			>60	39	2.1	2.0
Joint pain at other location	Dose 1	Flu D21 Group	18-60	21	2.0	2.0
			>60	19	2.9	2.0
	Dose 2	Flu D21 Group	18-60	17	2.2	2.0
			>60	21	2.6	2.0
	Overall/dose	Flu D21 Group	18-60	38	2.1	2.0
			>60	40	2.7	2.0
Muscle aches	Dose 1	Flu D21 Group	18-60	43	2.1	2.0
			>60	26	2.4	2.0
	Dose 2	Flu D21 Group	18-60	38	2.2	2.0
			>60	25	2.6	2.0

	Overall/dose	Flu D21 Group	18-60	81	2.2	2.0
			>60	51	2.5	2.0
Sweating	Dose 1	Flu D21 Group	18-60	12	1.8	1.5
			>60	10	2.4	2.0
	Dose 2	Flu D21 Group	18-60	19	2.1	2.0
			>60	13	1.9	1.0
	Overall/dose	Flu D21 Group	18-60	31	2.0	2.0
			>60	23	2.1	2.0
Shivering	Dose 1	Flu D21 Group	18-60	17	1.3	1.0
			>60	12	2.1	1.0
	Dose 2	Flu D21 Group	18-60	26	1.5	1.0
			>60	13	1.6	2.0
	Overall/dose	Flu D21 Group	18-60	43	1.4	1.0
			>60	25	1.8	1.0
Temperature	Dose 1	Flu D21 Group	18-60	1	1.0	1.0
			>60	1	1.0	1.0
	Dose 2	Flu D21 Group	18-60	6	1.5	1.0
			>60	5	1.0	1.0
	Overall/dose	Flu D21 Group	18-60	7	1.4	1.0
			>60	6	1.0	1.0

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
Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Percentage of subjects with 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 years					**>60 years**				
					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
Temperature (Axillary)	≥ 37.5°C	92	1	1.1	0.0	5.9	90	1	1.1	0.0	6.0
	≥ 39.0°C	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
Temperature (Axillary)	≥ 37.5°C	91	6	6.6	2.5	13.8	85	5	5.9	1.9	13.2
	≥ 39.0°C	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
Temperature (Axillary)	≥ 37.5°C	92	7	7.6	3.1	15.1	90	5	5.6	1.8	12.5
	≥ 39.0°C	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 years					**>60 years**				
					95% CI					**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
Temperature (Axillary)	≥ 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
Temperature (Axillary)	≥ 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
Temperature (Axillary)	≥ 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

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
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
			>60	0	0	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 (pIMDs) reporting until Day 42 (Total Vaccinated cohort) – *Interim analysis posted at Day 42*

Adverse events of specific interest or pIMDs (occurring within Days 0-41 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, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Number (%) of subjects with adverse events of specific interest or potential immune-mediated diseases (pIMDs) and adverse events of special interest reporting up to Day 203 (Total Vaccinated Cohort) – *Interim analysis posted at Day 182/203*

Adverse events of specific interest or pIMDs and AES of special interest (occurring up to Day 203)	**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)

Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Number (%) of subjects with adverse events of specific interest or potential immune-mediated diseases reporting up to Day 364 (Total Vaccinated Cohort)

Adverse events of specific interest or pIMDs [occurring up to Day 364 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), n (%)	1 (1.1)	0 (0.0)	1 (1.4)	0 (0.0)
Subjects with related AESI(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ankylosing spondylitis	1 (1.1)	-	-	-
Multiple sclerosis	-	-	1 (1.4)	-

-: Adverse event absent

Secondary Outcome Variable(s): Number (%) of subjects with adverse events of specific interest or potential immune-mediated diseases reporting up to Day 546 (Total Vaccinated Cohort)

Most frequent adverse events - On-Therapy [occurring up to Day 546 following vaccination]	**Flu M6 Group**	
	18-60 years N = 70	**>60 years N = 52**
Subjects with any AESI(s), n (%)	1 (1.4)	0 (0.0)

Subjects with related AESI(s), n (%)	0 (0.0)	0 (0.0)
Multiple sclerosis	1 (1.4)	-

-: Adverse event absent

Secondary Outcome Variable(s): Number (%) of subjects with adverse events of special interest reporting up to Day 364 (Total Vaccinated Cohort)

Most frequent adverse events - On-Therapy [occurring up to Day 364 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 AE(s) of special interest, n (%)	0 (0.0)	1 (1.1)	1 (1.4)	0 (0.0)
Subjects with related AESI(s), n (%)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
Urticaria	-	1 (1.1)	-	-
Multiple sclerosis	-	-	1 (1.4)	-

-: Adverse event absent

Secondary Outcome Variable(s): Number (%) of subjects with adverse events of special interest reported up to Day 546 (Total Vaccinated Cohort)

Most frequent adverse events - On-Therapy [occurring up to Day 546 following vaccination]	**Flu M6 Group**	
	18-60 years N = 70	**>60 years N = 52**
Subjects with any AE(s) of special interest, n (%)	1 (1.4)	0 (0.0)
Subjects with related AE(s) of special interest, n (%)	0 (0.0)	0 (0.0)
Multiple sclerosis	1 (1.4)	-

-: Adverse event absent

Secondary Outcome Variable(s): Distribution of haematology and biochemistry with respect to normal laboratory ranges (Total Vaccinated cohort – Pooled Groups) - *Interim analysis posted at Day 42*

		Pooled Groups																	
		18-60 years N = 163									**>60 years N = 143**								
			Unknown		**Below**		**Within**		**Above**			**Unknown**		**Below**		**Within**		**Above**	
Laboratory parameter	**Timing**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
ALAT	PRE	163	0	0.0	4	2.5	144	88.3	13	8.0	143	2	1.4	0	0.0	129	90.2	12	8.4
	PI(D21)	161	1	0.6	3	1.9	143	88.8	12	7.5	140	0	0.0	0	0.0	123	87.9	14	10.0
AP	PRE	163	1	0.6	7	4.3	150	92.0	3	1.8	143	0	0.0	5	3.5	135	94.4	3	2.1
	PI(D21)	161	0	0.0	8	5.0	149	92.5	2	1.2	140	0	0.0	5	3.6	128	91.4	4	2.9
ASAT	PRE	163	0	0.0	2	1.2	149	91.4	10	6.1	143	2	1.4	1	0.7	130	90.9	10	7.0
	PI(D21)	161	1	0.6	0	0.0	147	91.3	11	6.8	140	1	0.7	1	0.7	125	89.3	10	7.1
Bilirubin	PRE	163	1	0.6	0	0.0	153	93.9	7	4.3	143	2	1.4	0	0.0	137	95.8	4	2.8
	PI(D21)	161	1	0.6	0	0.0	151	93.8	7	4.3	140	0	0.0	0	0.0	132	94.3	5	3.6
Creatinine	PRE	163	0	0.0	5	3.1	149	91.4	7	4.3	143	0	0.0	2	1.4	120	83.9	21	14.7
	PI(D21)	161	0	0.0	5	3.1	146	90.7	8	5.0	140	0	0.0	3	2.1	119	85.0	15	10.7
BUN	PRE	163	2	1.2	1	0.6	153	93.9	5	3.1	143	1	0.7	3	2.1	110	76.9	29	20.3
	PI(D21)	161	0	0.0	0	0.0	152	94.4	7	4.3	140	0	0.0	2	1.4	102	72.9	33	23.6

N = number of subjects with laboratory results for the specified time point and laboratory parameter
n/% = number/percentage of subjects in a given category
Unknown = value unknown for the specified time point and laboratory parameter
Below = value below the laboratory reference range defined for the specified time point and laboratory parameter
Within = value within the laboratory reference range defined for the specified time point and laboratory parameter
Above = value above the laboratory reference range defined for the specified time point and laboratory parameter
ALAT= Alanine aminotransferase
AP= Alkaline phosphatase
ASAT=Aspartate aminotransferase
BUN= Blood urea nitrogen
Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Distribution of haematology and biochemistry with respect to normal laboratory ranges (Total Vaccinated cohort – Flu D21 Group) - *Interim analysis posted at Day 42*

		Flu D21 Group																	
		18-60 years N = 93									>60 years 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	6	6.6
	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	11	12.5
	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
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	3	3.3
	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	4	4.5
	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
ASAT	PRE	93	0	0.0	1	1.1	87	93.5	3	3.2	91	2	2.2	1	1.1	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	1	1.1	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
Bilirubin	PRE	93	0	0.0	0	0.0	86	92.5	5	5.4	91	2	2.2	0	0.0	88	96.7	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	83	94.3	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
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	15	16.5
	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	12	13.6
	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
BUN	PRE	93	2	2.2	1	1.1	87	93.5	1	1.1	91	1	1.1	1	1.1	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	1	1.1	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

N = number of subjects with laboratory results for the specified time point and laboratory parameter
n/% = number/percentage of subjects in a given category
Unknown = value unknown for the specified time point and laboratory parameter
Below = value below the laboratory reference range defined for the specified time point and laboratory parameter
Within = value within the laboratory reference range defined for the specified time point and laboratory parameter
Above = value above the laboratory reference range defined for the specified time point and laboratory parameter
ALAT= Alanine aminotransferase
AP= Alkaline phosphatase
ASAT=Aspartate aminotransferase
BUN= Blood urea nitrogen
Note: This interim analysis is superseded by the final analysis.

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

		Flu D21 Group																	
		18-60 years N = 93									>60 years 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 years N = 70									**>60 years 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
	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
ASAT	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
	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
Bilirubin	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
	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
Creatinine	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
	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

N = number of subjects with laboratory results for the specified time point and laboratory parameter
n/% = number/percentage of subjects in a given category
Unknown = value unknown for the specified time point and laboratory parameter
Below = value below the laboratory reference range defined for the specified time point and laboratory parameter

Within = value within the laboratory reference range defined for the specified time point and laboratory parameter
Above = value above the laboratory reference range defined for the specified time point and laboratory parameter
ALAT= Alanine aminotransferase
AP= Alkaline phosphatase
ASAT=Aspartate aminotransferase
BUN= Blood urea nitrogen
PRE = Pre-vaccination, Day 0
PI (D21) = Post dose 1, Day 21
PII (D42) = Post dose 2, Day 42
PII (D182) = Post dose 2, Day 182
PII (D203) = Post dose 2, Day 203 (only for Group B)

Secondary Outcome Variable(s): Distribution of haematology and biochemistry with respect to normal laboratory ranges at Day 364 (Total Vaccinated Cohort)

	Flu D21 Group																	
	18-60 years N = 93									**>60 years N = 91**								
		Unknown		**Below**		**Within**		**Above**			**Unknown**		**Below**		**Within**		**Above**	
Laboratory parameter	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
ALAT	85	0	0.0	2	2.4	79	92.9	4	4.7	83	1	1.2	0	0.0	77	92.8	5	6.0
AP	85	0	0.0	3	3.5	82	96.5	0	0.0	83	0	0.0	0	0.0	82	98.8	1	1.2
ASAT	85	0	0.0	1	1.2	81	95.3	3	3.5	83	0	0.0	0	0.0	77	92.8	6	7.2
Total Bilirubin	85	1	1.2	0	0.0	81	95.3	3	3.5	83	0	0.0	0	0.0	82	98.8	1	1.2
Creatinine	85	0	0.0	2	2.4	82	96.5	1	1.2	83	1	1.2	0	0.0	75	90.4	7	8.4
BUN	85	1	1.2	0	0.0	84	98.8	0	0.0	83	0	0.0	0	0.0	65	78.3	18	21.7
	Flu M6 Group																	
	18-60 years N = 70									**>60 years N = 52**								
		Unknown		**Below**		**Within**		**Above**			**Unknown**		**Below**		**Within**		**Above**	
Laboratory parameter	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
ALAT	62	0	0.0	0	0.0	57	91.9	5	8.1	47	0	0.0	0	0.0	45	95.7	2	4.3
AP	62	0	0.0	0	0.0	62	100	0	0.0	47	0	0.0	2	4.3	45	95.7	0	0.0
ASAT	62	0	0.0	5	8.1	55	88.7	2	3.2	47	0	0.0	0	0.0	46	97.9	1	2.1
Total Bilirubin	62	0	0.0	0	0.0	59	95.2	3	4.8	47	0	0.0	0	0.0	44	93.6	3	6.4
Creatinine	62	0	0.0	4	6.5	56	90.3	2	3.2	47	0	0.0	2	4.3	41	87.2	4	8.5
BUN	62	1	1.6	2	3.2	57	91.9	2	3.2	47	2	4.3	1	2.1	37	78.7	7	14.9

N = number of subjects with laboratory results for the laboratory parameter
n/% = number/percentage of subjects in a given category
Unknown = value unknown for the laboratory parameter
Below = value below the laboratory reference range defined for the laboratory parameter
Within = value within the laboratory reference range defined for the laboratory parameter
Above = value above the laboratory reference range defined for the 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 42-day (Days 0-41) post vaccination period (Total Vaccinated cohort) *Interim analysis posted at Day 42*

Most frequent adverse events - On-Therapy (occurring within Days 0-41 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 AE(s), n (%)	40 (43.0)	38 (41.8)	27 (38.6)	11 (21.2)
Subjects with Grade 3 AE(s), n (%)	6 (6.5)	6 (6.6)	6 (8.6)	1 (1.9)

Subjects with related AE(s), n (%)	11 (11.8)	15 (16.5)	5 (7.1)	2 (3.8)
Lymphadenopathy	-	-	-	1 (1.9)
Vertigo	3 (3.2)	-	-	-
Conjunctivitis	-	-	-	1 (1.9)
Abdominal pain	-	2 (2.2)	-	1 (1.9)
Diarrhoea	4 (4.3)	-	-	1 (1.9)
Fatigue	-	-	-	1 (1.9)
Influenza like illness	-	-	-	1 (1.9)
Injection site joint pain	-	-	-	1 (1.9)
Injection site pruritus	-	2 (2.2)	-	-
Bronchitis	-	2 (2.2)	-	-
Nasopharyngitis	9 (9.7)	3 (3.3)	2 (2.9)	1 (1.9)
Rhinitis	9 (9.7)	7 (7.7)	4 (5.7)	-
Joint injury	-	-	-	1 (1.9)
Joint sprain	-	-	-	1 (1.9)
Hepatic enzyme increased	-	2 (2.2)	-	-
Liver function test abnormal	-	2 (2.2)	-	-
Arthralgia	-	-	2 (2.9)	1 (1.9)
Back pain	-	3 (3.3)	-	1 (1.9)
Hypercreatinaemia	-	2 (2.2)	-	-
Headache	-	-	2 (2.9)	1 (1.9)
Sciatica	-	-	-	1 (1.9)
Cough	-	-	-	1 (1.9)
Oropharyngeal pain	3 (3.2)	-	3 (4.3)	-
Dermatitis contact	-	-	-	1 (1.9)
Haematoma	-	-	-	1 (1.9)

*In Flu Day 21 Group: after 2 vaccine doses
**In Flu M6 Group: after 1 vaccine dose
-: 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
Note: This interim analysis is superseded by the final analysis.

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

Most frequent adverse events - On-Therapy (occurring within 21 days post-Dose 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 years N = 93	**>60 years N = 91**	**18-60 years N = 70**	**>60 years N = 52**
Subjects with any AE(s), n (%)	52 (55.9)	53 (58.2)	30 (42.9)	15 (28.8)
Subjects with Grade 3 AE(s), n (%)	10 (10.8)	9 (9.9)	6 (8.6)	2 (3.8)
Subjects with related AE(s), n (%)	12 (12.9)	15 (16.5)	10 (14.3)	5 (9.6)
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)

-: 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 after Dose 2 for Flu M6 Group at the time of writing this summary, the remaining 9 days will be added when data are available
Note: This interim analysis is superseded by the final analysis.

Safety results: Number (%) of subjects with unsolicited adverse events within the 21-days post-vaccination Dose 1 (Days 0-20; both groups) and either 63 days post-vaccination Dose 2 (Days 21-84; Flu D21 Group) or 30 days post-vaccination Dose 2 (Days 182-212; Flu M6 Group) (Total Vaccinated Cohort)

Most frequent adverse events - On-Therapy (occurring within Days 0-21 post-Dose 1 for both groups and 0-62 post-Dose 2 for Flu D21 Group ; 0-29 post-Dose 2 for Flu M6 Group)	**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 AE(s), n (%)	52 (55.9)	53 (58.2)	35 (50.0)	16 (30.8)
Subjects with Grade 3 AE(s), n (%)	10 (10.8)	9 (9.9)	6 (8.6)	2 (3.8)
Subjects with related AE(s), n (%)	12 (12.9)	15 (16.5)	13 (18.6)	5 (9.6)
Nasopharyngitis	12 (12.9)	7 (7.7)	6 (8.6)	2 (3.8)
Rhinitis	10 (10.8)	10 (11.0)	5 (7.1)	1 (1.9)
Headache	8 (8.6)	6 (6.6)	5 (7.1)	1 (1.9)
Back pain	-	4 (4.4)	2 (2.9)	1 (1.9)
Diarrhoea	5 (5.4)	-	-	1 (1.9)
Bronchitis	-	-	2 (2.9)	3 (5.8)
Oropharyngeal pain	-	-	2 (2.9)	1 (1.9)
Rhinotracheitis	-	-	-	2 (3.8)
Vertigo	5 (5.4)	-	-	-
Migraine	-	3 (3.3)	-	-
Arthralgia	-	-	2 (2.9)	1 (1.9)
Azotaemia	-	-	2 (2.9)	1 (1.9)
Conjunctivitis	-	-	-	2 (3.8)
Cytologic hepatitis	-	-	2 (2.9)	-
Gastroenteritis	-	-	2 (2.9)	-
Lymphadenopathy	-	-	-	1 (1.9)
Eye irritation	-	-	-	1 (1.9)
Abdominal pain	-	-	-	1 (1.9)
Gastritis	-	-	-	1 (1.9)
Injection site joint pain	-	-	-	1 (1.9)
Post procedural infection	-	-	-	1 (1.9)
Epicondylitis	-	-	-	1 (1.9)
Joint injury	-	-	-	1 (1.9)
Migraine with aura	-	-	-	1 (1.9)

Presyncope	-	-	-	1 (1.9)
Rhinorrhea	-	-	-	1 (1.9)
Dermatitis contact	-	-	-	1 (1.9)
Hematoma	-	-	-	1 (1.9)

-: 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

Safety results: Number (%) of subjects with serious adverse events until Day 42 (Total Vaccinated cohort) - *Interim analysis posted at Day 42*

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]	0 (0.0) [0]	2 (2.2) [1]	0 (0.0) [0]	0 (0.0) [0]
Hepatic enzyme increased	0 (0.0) [0]	1 (1.1) [1]	0 (0.0) [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]
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]

Note: This interim analysis is superseded by the final analysis.

Safety results: Number (%) of subjects with SAEs up to Day 203 (Total Vaccinated Cohort) *Interim analysis posted at Day 182/203*

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]

Note: This interim analysis is superseded by the final analysis.

Safety results: Number (%) of subjects with SAEs up to Day 364 (Total Vaccinated Cohort)

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

All SAEs	**Flu 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]	4 (4.3) [0]	7 (7.7) [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]
Lung neoplasm malignant	0 (0.0) [0]	1 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]
Metastases to ovary	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]
Ovarian cyst	1 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Pneumonia	0 (0.0) [0]	1 (1.1) [0]	0 (0.0) [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]
Suicide attempt	1 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Uterine leiomyoma	1 (1.1) [0]	0 (0.0) [0]	0 (0.0) [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]

Note: 1 fatal SAE occurred in the Flu M6 Group before the Day 364 data lock point but was reported at Day 546 phone contact only; therefore it was part of the Day 546 analysis and is tabulated in the next safety table.

Safety results: Number (%) of subjects with SAEs up to Day 546 (Total Vaccinated Cohort)

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

All SAEs	**Flu M6 Group**	
	18-60 years N = 70	**>60 years N = 52**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	4 (5.7) [1]	4 (7.7) [0]
Acute coronary syndrome	0 (0.0) [0]	1 (1.9) [0]
Breast cancer	0 (0.0) [0]	1 (1.9) [0]
Cervix carcinoma	1 (1.4) [0]	0 (0.0) [0]
Coronary artery disease	0 (0.0) [0]	1 (1.9) [0]
Herpes zoster	1 (1.4) [1]	0 (0.0) [0]
Intervertebral disc disorder	1 (1.4) [0]	0 (0.0) [0]
Nephrolithiasis	1 (1.4) [0]	0 (0.0) [0]
Pancreatic carcinoma	0 (0.0) [0]	1 (1.9) [0]
Post procedural infection	0 (0.0) [0]	1 (1.9) [0]
Pyelonephritis	1 (1.4) [0]	0 (0.0) [0]
Spinal fracture	1 (1.4) [0]	0 (0.0) [0]
Fatal SAEs	**Flu M6 Group**	
	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]	1 (1.9) [0]
Pancreatic carcinoma	0 (0.0) [0]	1 (1.9) [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 > 60 years. At the same time point, SPR was of 97.5% for subjects aged 18-60 years and 91.9% in subjects > 60 years, and SCF was 45.0 in subjects aged 18-60 years and 23.4 in subjects > 60 years.

Within the 21 days post-Dose 1 vaccination (Days 0-20; for both groups) and either 63 days post-Dose 2 vaccination (Days 21-84; for Flu D21 Group) or 30 days post-Dose 2 vaccination (Days 182-212; for Flu M6 Group), at least one unsolicited adverse event was reported for 52 (55.9%) subjects aged 18-60 years and 53 (58.2%) subjects aged > 60 years in the Flu D21 Group and for 35 (50.0%) subjects aged 18-60 years and 16 (30.8%) subjects aged > 60 years in the Flu M6 Group.
Up to Day 364, SAEs were reported for 4 (4.3%) subjects from the Flu D21 (18-60 years) Group, 7 (7.7%) subjects from the Flu D21 (>60 years) Group. In the Flu D21 (> 60 years) Group, one of the SAEs was assessed by the investigator as related to the study vaccination.
Up to Day 546, SAEs were reported for 4 (5.7%) subjects from the Flu M6 (18-60 years) Group and 4 (7.7%) subjects from the Flu M6 (>60 years) Group. In the Flu M6 (18-60 years) Group, one of the SAEs was assessed by the investigator as related to the study vaccination.
During the entire study period, one fatal SAE was reported for one subject in the Flu M6 (>60 years) Group; it was assessed by the investigator as not related to the study vaccination.

Date updated: 04-September-2014