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.: 113459 (FLU D-PAN H1N1-008)

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

Rationale: The aim of the study was to assess the immunogenicity and safety of Flu vaccine administered following a 1- or 2- dose schedule.

Phase: III

Study Period:
08 September 2009 to
- 7 October 2009 (Day 21)
- 28 October 2009 (Day 42)
- 29 March 2010 (Day 182)
- 23 September 2010 (Day 364)

Study Design: Open, randomized (1:1) study with 2 parallel groups.
Enrolment was age-stratified, with 2 age strata (18-60 years and >60 years, in 1:1 ratio).

Centres: 1 centre in Belgium.

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

Treatment: Study groups were as follows:
- 1 dose Group: subjects received a single dose of Flu vaccine at Day 0.
- 2 doses Group: subjects received 2 doses of Flu vaccine, one at Day 0 and one at Day 21.

Vaccine was given intramuscularly in the deltoid region of the non-dominant arm at Day 0 and of the dominant arm at Day 21 (for the 2 doses Group).

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 (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 vaccination in adults within the 18 to 60 years and above 60 years age strata.

Primary Outcome/Efficacy Variable:
Humoral immune response in terms of HI antibodies
In subjects receiving two doses of 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*** (also called seroconversion factor [SCF]) 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 estimated for SCR was > 40% in subjects 18 to 60 years of age or > 30% for subjects > 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 > 60 years of age.
***GMFR of the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination reciprocal HI titre for the vaccine virus. The Committee for Medicinal Products for Human Use (CHMP) criterion was fulfilled if the point estimate for GMFR was > 2.5 in subjects 18 to 60 years of age or > 2 for subjects > 60 years of age.

Secondary Outcome/Efficacy Variable(s):
Humoral immune response in terms of HI antibodies
In subjects receiving 1 or 2 dose(s) of Flu vaccine:

- Geometric Mean Titres (GMTs) and seropositivity rates at Day 0, 21, 42, 182 and 364
- SCR* at Day 21, 182 and 364
- SPR* at Day 0, 21, 182 and 364
- GMFR* at Day 21, 182 and 364

*Criteria for evaluation were the same as that for the primary outcome variables for each age stratum.

Humoral immune response in terms of neutralising antibodies
In a subset of subjects against A/California/7/2009 (H1N1)v-like[$]:

- GMTs at Day 0, 21, 42, 182 and 364[#]
- SCR** at Day 21, 42, 182 and 364[#]

**SCR was defined as the percentage of vaccinees that have a four-fold increase between pre- and post-vaccination titres. The cut-off value for microneutralisation titres was 1:8.
[$]The neutralising antibodies were assayed using the A/Netherlands/602/9 H1N1v strain.
[#] As across the different trials of the H1N1 pandemic vaccine the vaccine homologous neutralising antibody response has paralleled the homologous HI response and has provided little additional insight (if any) in the humoral response profile, neutralising antibody testing at Day 364 was cancelled.

Safety

- 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
- Occurrence, intensity and relationship to vaccination of unsolicited adverse events (AEs) within 21 or 84 days after the first vaccination and 63 days after the second vaccination (Day 0 - Day 20, Day 0 - Day 84 and Day 21- Day 84), according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence and relationship to vaccination of adverse events of specific interest (AESIs), which included autoimmune diseases and other immune mediated inflammatory disorders, during the entire study period (up to Day 364).
- Occurrence and relationship to vaccination of serious adverse events (SAEs) during the entire study period (up to Day 364).

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 and Day 364.

Statistical Methods:
Analyses were performed on the Total Vaccinated cohort, the According-To-Protocol (ATP) cohort for immunogenicity at Day 42, the ATP cohort for persistence at Month 6 and the ATP cohort for persistence at Month 12.

- The Total Vaccinated cohort included all vaccinated subjects.
- The ATP cohort for immunogenicity at Day 42 included all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study), who complied with the procedures and intervals defined in the protocol, who did not meet any of the criteria for elimination from an ATP analysis during the study, who did not receive a product leading to exclusion from an ATP analysis, who did not present with a medical condition leading to exclusion from an ATP analysis, for whom 1 dose was administered and assay result was available for antibodies against H1N1 antigen for the blood sample taken 42 days after the first vaccine dose and for whom 2 doses were administered and assay result was available for antibodies against H1N1 antigen for the blood sample taken 21 days after second vaccine dose.
- The ATP cohort for persistence at Month 6 included all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study) for whom data concerning immunogenicity outcome measures were available. This included subject for whom assay results were available for antibodies against the study vaccine antigen component at Month 6.
- The ATP cohort for persistence at Month 12 included all evaluable subjects (i.e. those meeting all eligibility criteria; complying with the procedures defined in the protocol, with no elimination criteria during the study) for whom data concerning immunogenicity outcome measures were available. This cohort included subjects for whom assay results were available for antibodies against the study vaccine antigen component at Month 12.

Analysis of immunogenicity:
The analysis was based on the ATP cohort for immunogenicity at Day 42, the ATP cohort for persistence at Month 6, the ATP cohort for persistence at Month 12 and Total Vaccinated cohort.
The HI immune response to the vaccine-homologous virus was described, by estimating the following parameters (with 95% confidence intervals [CI]): GMT and SPR on Days 0, 21, 42, 182 and 364, SCR, GMRF and SCF on Days 21, 42, 182 and 364 in the pooled group for analysis at Day 21 and in both groups and both age strata for the next time point analyses.
For the humoral immune response in terms of neutralising antibodies to A/Netherlands/602/9 (H1N1)v strain, in a subset of subjects receiving one or two doses, the following parameters were calculated with 95% CIs: seropositivity rates, GMTs and SCRs.

Analysis of safety:
The analysis was based on the Total Vaccinated cohort.
The incidence of solicited local and general symptoms occurring during the 7 days after the first vaccination was tabulated with exact 95% CI for the pooled groups and per age stratum. The incidence of solicited local and general symptoms occurring during the 7 days after each vaccination was tabulated with exact 95% CI for the 2 doses group and per age stratum. The same calculation was performed for symptoms of any intensity, those with intensity of grade 3, as well as for solicited general symptoms assessed by the investigator as related to the study vaccination. Moreover, the duration of each local and general symptom was summarised.
The percentage of subjects with at least one report of an unsolicited AE classified by MedDRA Preferred Term within 21 or 84 days after the first vaccination and 63 days after the second vaccination (Day 0 - Day 20, Day 0 - Day 84 and Day 21- Day 84) was tabulated. The same tabulation was performed for Grade 3 unsolicited AEs and for unsolicited AEs that were assessed by the investigator as causally related to vaccination.
SAEs and AESIs were collected and summarized up to Day 364 by MedDRA Preferred Term.
The number and proportion of subjects with normal or abnormal values for each haematological and biochemical parameter were tabulated per group at Days 0, 21, 42, 182 and 364.

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

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

Interim analysis Day 21*	**Pooled Group***	
Number of subjects	**18y-60y**	**>60y**
Planned N	240	
Randomized, N (Total Vaccinated cohort)	120	120
Completed, n (%)	120 (100)	120 (100)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	0 (0.0)
Demographics	**18y-60y**	**>60y**
N (Total Vaccinated cohort)	120	120
Females:Males	65:55	52:68
Mean Age, years (SD)	39.7 (13.90)	69.1 (6.12)
White - Caucasian / European heritage, n (%)	120 (100)	120 (100)

* At Day 21 all subjects had received 1 dose of Flu vaccine and therefore no distinction was made between groups for the Day 21 analysis.

Analysis Day 42	**1 dose Group**		**2 doses Group**	
Number of subjects	**18y-60y**	**>60y**	**18y-60y**	**>60y**
Planned, N	120		120	
Randomized, N (Total Vaccinated cohort)	52	50	68	70
Completed at Day 42, n (%)	52 (100)	50 (100)	68 (100)	70 (100)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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 (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Analysis Day 182	**1 dose Group**		**2 dose Group**	
Number of subjects	**18y-60y**	**>60y**	**18y-60y**	**>60y**
Planned, N	120		120	
Randomised, N (Total Vaccinated cohort)	52	50	68	70
Completed at Day 182, n (%)	52 (100)	50 (100)	67 (98.5)	69 (98.6)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)	1 (1.5)	1 (1.4)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)
Analysis Day 364	**1 dose Group**		**2 dose Group**	
Number of subjects	**18y-60y**	**>60y**	**18y-60y**	**>60y**
Planned, N	120		120	
Randomised, N (Total Vaccinated cohort)	52	50	68	70
Completed at Day 364, n (%)	52 (100)	50 (100)	67 (98.5)	68 (97.1)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)	1 (1.5)	2 (2.9)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.9)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)
Demographics	**1 dose Group**		**2 doses Group**	
	18y-60y	**>60y**	**18y-60y**	**>60y**
N (Total Vaccinated cohort)	52	50	68	70
Females:Males	26:26	23:27	39:29	29:41
Mean Age, years (SD)	39.0 (13.76)	68.8 (5.76)	40.2 (14.09)	69.4 (6.40)
White - Caucasian / European heritage, n (%)	52 (100)	50 (100)	68 (100)	70 (100)

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years

Primary Efficacy Results: SCR for HI antibody titre (Total Vaccinated cohort) – *Interim analysis posted at Day 21*

					SCR			
							95% CI	
Vaccine strain	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/2009	Pooled	18y-60y	PI(21)	120	114	95.0	89.4	98.1
		>60y	PI(21)	120	95	79.2	70.8	86.0

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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(21)=Post dose 1 Day 21
Note: This interim analysis is superseded by the final analysis.

Primary Efficacy Results: SCR for HI antibodies against Flu A/CAL/7/2009 in **2 doses Group** (ATP cohort for immunogenicity at Day 42) – *Final analysis*

				SCR			
						95% CI	
Antibodies against	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/2009	18y-60y	PI(21)*	66	63	95.5	87.3	99.1
		PII(D42)	66	65	98.5	91.8	100
	>60y	PI(21)*	67	53	79.1	67.4	88.1

		PII(D42)	67	63	94.0	85.4	98.3

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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(21)= post-dose 1 Day 21
PII(D42)= post-dose 2 Day 42
* Primary outcome variable

Primary Efficacy Results: SPR for HI antibodies against Flu A/CAL/09 (Total Vaccinated cohort) – *Interim analysis posted at Day 21*

					SPR			
							95% CI	
Strain	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/2009	Pooled	18y-60y	PRE	120	10	8.3	4.1	14.8
			PI(21)	120	117	97.5	92.9	99.5
		>60y	PRE	120	11	9.2	4.7	15.8
			PI(21)	120	105	87.5	80.2	92.8

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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= Day 0
PI(21)=Post dose 1 Day 21
Note: This interim analysis is superseded by the final analysis.

Primary Efficacy Results: SPR for HI antibodies against Flu A/CAL/7/2009 in **2 doses Group** (ATP cohort for immunogenicity at Day 42) – *Final analysis*

				SPR			
						95% CI	
Antibodies against	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/2009	18y-60y	PRE	66	6	9.1	3.4	18.7
		PI(21)*	66	65	98.5	91.8	100
		PII(D42)	66	66	100	94.6	100
	>60y	PRE	67	6	9.0	3.4	18.5
		PI(21)*	67	59	88.1	77.8	94.7
		PII(D42)	67	66	98.5	92.0	100

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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(21)= Post-dose 1 Day 21
PII(D42)= Post-dose 2 Day 42
* Primary outcome variable

Primary Efficacy Results: GMFR for HI antibody titre (Total Vaccinated cohort) – *Interim analysis posted at Day 21*

					GMFR		
						95% CI	
Vaccine strain	**Group**	**Sub-group**	**Timing**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/2009	Pooled	18y-60y	PI(21)	120	42.15	33.43	53.16
		>60y	PI(21)	120	13.66	10.88	17.14

18y-60y = Subject aged between and including 18 years to 60 years

>60y = Subjects aged more than 60 years
N = Number of subjects with pre- and post-vaccination results available
GMFR = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(21)=Post dose 1 D21
Note: This interim analysis is superseded by the final analysis.

Primary Efficacy Results: GMFR for HI antibodies against Flu A/CAL/7/2009 in **2 doses Group** (ATP cohort for immunogenicity at Day 42) – *Final analysis*

					GMFR		
						95% CI	
Antibodies against	**Group**	**Sub-group**	**Timing**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/2009	2 doses	18y-60y	PI(21)*	66	38.71	29.10	51.51
			PII(D42)	66	69.70	53.79	90.32
		>60y	PI(21)*	67	13.86	10.29	18.65
			PII(D42)	67	33.57	24.87	45.31

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
N = Number of subjects with pre- and post-vaccination results available
GMFR = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(21)= Post-dose 1 Day 21
PII(D42)= Post-dose 2 Day 42
* Primary outcome variable

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/09 (Total Vaccinated cohort) – *Interim analysis posted at Day 21*

					≥ 1:10				**GMT**		
							95% CI			**95% CI**	
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/2009	Pooled	18y-60y	PRE	120	44	36.7	28.1	45.9	8.52	7.32	9.92
			PI(21)	120	120	100	97.0	100	359.25	287.18	449.40
		>60y	PRE	120	51	42.5	33.5	51.9	9.99	8.21	12.15
			PI(21)	120	118	98.3	94.1	99.8	136.44	110.52	168.43

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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
PI(21)=Post dose 1 Day 21
Note: This interim analysis is superseded by the final analysis.

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/2009 in **2 doses Group** (ATP cohort for immunogenicity at Day 42) – *Final analysis*

				≥ 1:10				**≥ 1:40**				**GMT**		
						95% CI				**95% CI**			**95% CI**	
Antibodies against	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/2009	18y-60y	PRE	66	24	36.4	24.9	49.1	6	9.1	3.4	18.7	8.8	7.0	10.9
		PI(21)	66	66	100	94.6	100	65	98.5	91.8	100	339.1	258.6	444.8
		PII(D42)	66	66	100	94.6	100	66	100	94.6	100	610.6	507.9	734.0
	>60y	PRE	67	28	41.8	29.8	54.5	6	9.0	3.4	18.5	10.3	7.7	13.7
		PI(21)	67	67	100	94.6	100	59	88.1	77.8	94.7	142.7	108.5	187.8
		PII(D42)	67	67	100	94.6	100	66	98.5	92.0	100	345.8	278.0	430.1

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
Seroprotection = Flu A/CAL/7/2009 antibody titre ≥ 1:40
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(21)= Post-dose 1 Day 21
PII(D42)= Post-dose 2 Day 42

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/2009 in **1 dose Group** (ATP cohort for immunogenicity at Day 42) – *Final analysis*

				≥ 1:10				≥ 1:40				GMT		
						95% CI				95% CI			95% CI	
Antibodies against	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/2009	18y-60y	PRE	50	20	40.0	26.4	54.8	4	8.0	2.2	19.2	8.6	6.8	10.8
		PI(21)	50	50	100	92.9	100	48	96.0	86.3	99.5	388.6	262.0	576.2
		PI(D42)	50	50	100	92.9	100	47	94.0	83.5	98.7	331.2	220.7	497.1
	>60y	PRE	49	21	42.9	28.8	57.8	5	10.2	3.4	22.2	9.7	7.3	13.0
		PI(21)	49	47	95.9	86.0	99.5	42	85.7	72.8	94.1	129.3	89.9	186.0
		PI(D42)	49	48	98.0	89.1	99.9	43	87.8	75.2	95.4	117.1	82.4	166.4

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
Seroprotection = Flu A/CAL/7/2009 antibody titre ≥ 1:40
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(21)= Post-dose 1 Day 21
PI(D42)= Post-dose 1 Day 42

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/2009 Day 182 (ATP cohort for persistence at Month 6) – *Final analysis*

					≥ 1:10				≥ 1:40				GMT		
							95% CI				95% CI			95% CI	
Antibodies against	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/2009	2 doses Group	18y-60y	PII(D182)	67	67	100	94.6	100	65	97.0	89.6	99.6	214.8	169.8	271.8
		>60y	PII(D182)	68	68	100	94.7	100	61	89.7	79.9	95.8	108.7	85.7	137.8
	1 dose Group	18y-60y	PI(D182)	51	51	100	93.0	100	44	86.3	73.7	94.3	143.5	96.6	213.0
		>60y	PI(D182)	50	46	92.0	80.8	97.8	28	56.0	41.3	70.0	51.6	34.9	76.5

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
Seroprotection = Flu A/CAL/7/2009 antibody titre ≥ 1:40
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PI(D182)= Post-dose 1 Day 182
PII(D182)= Post-dose 2 Day 182

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/2009 at Day 364 (ATP cohort for persistence at Month 12) – *Final analysis*

					≥ 1:10				GMT		
							95% CI			95% CI	
Antibodies against	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/CAL/7/09	2 doses Group	18y-60y	PII(D364)	67	67	100	94.6	100	90.5	69.4	118.1
		>60y	PII(D364)	68	65	95.6	87.6	99.1	42.3	32.6	54.8
	1 dose Group	18y-60y	PI(D364)	52	44	84.6	71.9	93.1	64.2	41.3	99.7
		>60y	PI(D364)	50	41	82.0	68.6	91.4	28.1	19.4	40.6

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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
PI(D364)= Post-dose 1 Day 364
PII(D364)= Post-dose 2 Day 364

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/2009 in **1 dose Group** (ATP cohort for immunogenicity at Day 42) – *Final analysis*

				SCR			
						95% CI	
Antibodies against	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/2009	18y-60y	PI(21)	50	47	94.0	83.5	98.7
		PI(D42)	50	46	92.0	80.8	97.8
	>60y	PI(21)	49	38	77.6	63.4	88.2
		PI(D42)	49	39	79.6	65.7	89.8

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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(21)= Post-dose 1 Day 21
PI(D42)= Post-dose 1 Day 42

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/2009 at Day 182 (ATP cohort for persistence at Month 6) – *Final analysis*

				SCR			
						95% CI	
Antibodies against	**Group**	**Sub-group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/2009	2 doses Group	18y-60y	67	63	94.0	85.4	98.3
		>60y	68	52	76.5	64.6	85.9
	1 dose Group	18y-60y	51	42	82.4	69.1	91.6
		>60y	50	21	42.0	28.2	56.8

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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

Secondary Outcome Variable(s): SCR for HI antibodies against Flu A/CAL/7/2009 at Day 364 (ATP cohort for persistence at Month 12) – *Final analysis*

				SCR			
						95% CI	
Antibodies against	**Group**	**Sub-group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/2009	2 doses Group	18y-60y	67	50	74.6	62.5	84.5
		>60y	68	28	41.2	29.4	53.8
	1 dose Group	18y-60y	52	32	61.5	47.0	74.7
		>60y	50	15	30.0	17.9	44.6

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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

Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/2009 in **1 dose Group** (ATP cohort for immunogenicity at Day 42) – *Final analysis*

				SPR			
						95% CI	
Antibodies against	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/2009	18y-60y	PRE	50	4	8.0	2.2	19.2
		PI(21)	50	48	96.0	86.3	99.5
		PI(D42)	50	47	94.0	83.5	98.7
	>60y	PRE	49	5	10.2	3.4	22.2
		PI(21)	49	42	85.7	72.8	94.1
		PI(D42)	49	43	87.8	75.2	95.4

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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(21)= Post-dose 1 Day 21
PI(D42)= Post-dose 1 Day 42

Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/2009 at Day 182 (ATP cohort for persistence at Month 6) – *Final analysis*

					SPR			
							95% CI	
Antibodies against	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/2009	2 doses Group	18y-60y	PII(D182)	67	65	97.0	89.6	99.6
		>60y	PII(D182)	68	61	89.7	79.9	95.8
	1 dose Group	18y-60y	PI(D182)	51	44	86.3	73.7	94.3
		>60y	PI(D182)	50	28	56.0	41.3	70.0

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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
PI(D182)= Post-dose 1 Day 182
PII(D182)= Post-dose 2 Day 182

Secondary Outcome Variable(s): SPR for HI antibodies against Flu A/CAL/7/2009 at Day 364 (ATP cohort for persistence at Month 12) – *Final analysis*

				SPR			
						95% CI	
Antibodies against	**Group**	**Sub-group**	**N**	**n**	**%**	**LL**	**UL**

Flu A/CAL/7/2009	2 doses Group	18y-60y	67	53	79.1	67.4	88.1
		>60y	68	37	54.4	41.9	66.5
	1 dose Group	18y-60y	52	34	65.4	50.9	78.0
		>60y	50	22	44.0	30.0	58.7

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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): GMFR for HI antibodies against Flu A/CAL/7/2009 in **1 dose Group** (ATP cohort for immunogenicity at Day 42) – *Final analysis*

				GMFR		
					95% CI	
Antibodies against	**Sub-group**	**Timing**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/2009	18y-60y	PI(21)	50	45.30	30.32	67.68
		PI(D42)	50	38.62	25.96	57.45
	>60y	PI(21)	49	13.32	9.04	19.61
		PI(D42)	49	12.06	8.39	17.33

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
N = Number of subjects with pre- and post-vaccination results available
GMFR = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(21)= Post-dose 1 Day 21
PI(D42)= Post-dose 1 Day 42

Secondary Outcome Variable(s): GMFR for HI antibodies against Flu A/CAL/7/2009 at Day 182 (ATP cohort for persistence at Month 6) – *Final analysis*

				GMFR		
					95% CI	
Antibodies against	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/2009	2 doses Group	18y-60y	67	24.73	19.31	31.67
		>60y	68	10.45	8.24	13.24
	1 dose Group	18y-60y	51	17.14	11.83	24.84
		>60y	50	5.31	3.73	7.56

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
N = Number of subjects with pre- and post-vaccination results available
GMFR = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): GMFR for HI antibodies against Flu A/CAL/7/2009 at Day 364 (ATP cohort for persistence at Month 12) – *Final analysis*

				GMFR		
					95% CI	
Antibodies against	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/2009	2 doses Group	18y-60y	67	10.4	8.1	13.4
		>60y	68	4.3	3.5	5.2
	1 dose Group	18y-60y	52	7.6	5.1	11.5
		>60y	50	2.9	2.1	4.0

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
N = Number of subjects with pre- and post-vaccination results available
GMFR = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre

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

Secondary Outcome Variable(s): Seropositivity rates and GMTs for neutralising antibodies against Flu A/Neth/602/09– for subjects aged 18y-60y years, more than 60 years and overall (ATP cohort for persistence at Month 6)

					≥ 1:8				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/Neth/602/09	2 doses Group	18y-60y	PRE	22	16	72.7	49.8	89.3	11.9	8.0	17.8
			PI(D21)	22	21	95.5	77.2	99.9	199.8	94.1	424.2
			PII(D42)	22	22	100	84.6	100	326.8	183.0	583.3
			PII(D182)	22	21	95.5	77.2	99.9	128.7	73.5	225.2
		>60y	PRE	22	17	77.3	54.6	92.2	16.9	10.1	28.1
			PI(D21)	22	22	100	84.6	100	169.7	85.6	336.5
			PII(D42)	22	22	100	84.6	100	309.5	189.3	505.9
			PII(D182)	22	22	100	84.6	100	96.7	59.3	157.5
		Overall	PRE	44	33	75.0	59.7	86.8	14.2	10.3	19.4
			PI(D21)	44	43	97.7	88.0	99.9	184.2	113.0	300.1
			PII(D42)	44	44	100	92.0	100	318.0	220.9	457.7
			PII(D182)	44	43	97.7	88.0	99.9	111.5	77.9	159.6
	1 dose Group	18y-60y	PRE	17	11	64.7	38.3	85.8	12.6	6.7	23.9
			PI(D21)	17	17	100	80.5	100	199.1	92.3	429.7
			PI(D42)	17	17	100	80.5	100	136.7	64.8	288.6
			PI(D182)	17	16	94.1	71.3	99.9	55.2	24.7	123.3
		>60y	PRE	18	12	66.7	41.0	86.7	21.3	10.1	44.9
			PI(D21)	18	18	100	81.5	100	83.5	38.8	179.4
			PI(D42)	18	18	100	81.5	100	86.7	48.0	156.7
			PI(D182)	18	16	88.9	65.3	98.6	65.3	30.8	138.4
		Overall	PRE	35	23	65.7	47.8	80.9	16.5	10.3	26.6
			PI(D21)	35	35	100	90.0	100	127.3	74.5	217.5
			PI(D42)	35	35	100	90.0	100	108.2	68.6	170.5
			PI(D182)	35	32	91.4	76.9	98.2	60.2	35.7	101.3

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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
PRE= Pre-vaccination Day 0
PI(21) = Post-dose 1 Day 21
PI(D42) = Post-dose 1 Day 42
PII(D42) = Post-dose 2 Day 42
PI(D182) = Post-dose 1 Day 182
PII(D182) = Post-dose 2 Day 182

Secondary Outcome Variable(s): SCR for neutralising antibodies against Flu A/Neth/602/09 at Day 21, Day 42 and Day 182 – (ATP cohort persistence at Month 6)

					SCR			
							95% CI	
Strain	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Neth/602/09	2 doses Group	18y-60y	PI(21)	22	15	68.2	45.1	86.1
			PII(D42)	22	20	90.9	70.8	98.9
			PII(D182)	22	18	81.8	59.7	94.8
		>60y	PI(21)	22	15	68.2	45.1	86.1
			PII(D42)	22	19	86.4	65.1	97.1
			PII(D182)	22	14	63.6	40.7	82.8
		Overall	PI(21)	44	30	68.2	52.4	81.4

			PII(D42)	44	39	88.6	75.4	96.2
			PII(D182)	44	32	72.7	57.2	85.0
	1 dose Group	18y-60y	PI(21)	17	12	70.6	44.0	89.7
			PI(D42)	17	11	64.7	38.3	85.8
			PI(D182)	17	6	35.3	14.2	61.7
		>60y	PI(21)	18	6	33.3	13.3	59.0
			PI(D42)	18	5	27.8	9.7	53.5
			PI(D182)	18	7	38.9	17.3	64.3
		Overall	PI(21)	35	18	51.4	34.0	68.6
			PI(D42)	35	16	45.7	28.8	63.4
			PI(D182)	35	13	37.1	21.5	55.1

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
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
PI(21) = Post-dose 1 Day 21
PI(D42) = Post-dose 1 Day 42
PII(D42) = Post-dose 2 Day 42
PI(D182) = Post-dose 1 Day 182
PII(D182) = Post-dose 2 Day 182

Secondary Outcome Variable(s): Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-dose 1 vaccination period – **Pooled Group** (Total Vaccinated cohort)

		Pooled Group									
		18y-60y					**>60y**				
					95 % CI					**95 % CI**	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Pain	Any	120	105	87.5	80.2	92.8	120	78	65.0	55.8	73.5
	Grade 3	120	0	0.0	0.0	3.0	120	0	0.0	0.0	3.0
Redness	Any	120	1	0.8	0.0	4.6	120	9	7.5	3.5	13.8
	> 100 mm	120	0	0.0	0.0	3.0	120	0	0.0	0.0	3.0
Swelling	Any	120	11	9.2	4.7	15.8	120	12	10.0	5.3	16.8
	> 100 mm	120	0	0.0	0.0	3.0	120	0	0.0	0.0	3.0

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
N= number of subjects with at least one administered dose
n (%)= number (percentage) of subjects reporting at least once the symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Any= occurrence of any local symptom regardless of intensity grade
Grade 3 pain= pain that prevented normal activity

Secondary Outcome Variable(s): Number of days with any local symptoms during the solicited post-dose 1 vaccination period – **Pooled Group** (Total Vaccinated cohort)

Solicited symptom	**Dose**	**Group**	**Sub-group**	**N**	**Mean**	**Median**
Pain	Dose 1	Pooled	18y-60y	105	3.1	3.0
			>60y	78	2.8	2.5
Redness	Dose 1	Pooled	18y-60y	1	1.0	1.0
			>60y	9	2.0	2.0
Swelling	Dose 1	Pooled	18y-60y	11	2.2	2.0
			>60y	12	2.2	2.0

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
N = number of subjects with the symptom

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, for subjects who received 2 doses of Flu vaccine (**2 doses Group**) (Total Vaccinated cohort)

		2 doses Group									
		18y-60y					>60y				
					95 % CI					95 % CI	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Pain	Any	68	57	83.8	72.9	91.6	70	46	65.7	53.4	76.7
	Grade 3	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
Redness	Any	68	0	0.0	0.0	5.3	70	3	4.3	0.9	12.0
	>100 mm	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
Swelling	Any	68	5	7.4	2.4	16.3	70	4	5.7	1.6	14.0
	>100 mm	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
Dose 2											
Pain	Any	68	51	75.0	63.0	84.7	70	42	60.0	47.6	71.5
	Grade 3	68	2	2.9	0.4	10.2	70	0	0.0	0.0	5.1
Redness	Any	68	1	1.5	0.0	7.9	70	5	7.1	2.4	15.9
	>100 mm	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
Swelling	Any	68	3	4.4	0.9	12.4	70	3	4.3	0.9	12.0
	>100 mm	68	0	0.0	0.0	5.3	70	1	1.4	0.0	7.7
Across doses											
Pain	Any	68	61	89.7	79.9	95.8	70	52	74.3	62.4	84.0
	Grade 3	68	2	2.9	0.4	10.2	70	0	0.0	0.0	5.1
Redness	Any	68	1	1.5	0.0	7.9	70	6	8.6	3.2	17.7
	>100 mm	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
Swelling	Any	68	7	10.3	4.2	20.1	70	6	8.6	3.2	17.7
	>100 mm	68	0	0.0	0.0	5.3	70	1	1.4	0.0	7.7

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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 symptom regardless of intensity grade
Grade 3 pain= pain that prevented normal activity

Secondary Outcome Variable(s): Number of days with solicited local symptoms during the 7-day post-vaccination period for subjects who received 2 doses of Flu vaccine (**2 doses Group**) (Total Vaccinated cohort)

Solicited symptom	**Dose**	**Sub-group**	**N**	**Mean**	**Median**
Pain	Dose 1	18y-60y	57	3.0	3.0
		>60y	46	2.7	2.0
	Dose 2	18y-60y	51	3.0	3.0
		>60y	42	2.5	2.0
	Overall/dose	18y-60y	108	3.0	3.0
		>60y	88	2.6	2.0
Redness	Dose 1	18y-60y	0	0.0	0.0
		>60y	3	1.7	1.0
	Dose 2	18y-60y	1	1.0	1.0
		>60y	5	1.8	2.0
	Overall/dose	18y-60y	1	1.0	1.0
		>60y	8	1.8	1.5
Swelling	Dose 1	18y-60y	5	2.0	2.0
		>60y	4	2.0	2.0
	Dose 2	18y-60y	3	2.3	2.0
		>60y	3	1.0	1.0
	Overall/dose	18y-60y	8	2.1	2.0
		>60y	7	1.6	1.0

18y-60y = Subject aged between and including 18 years to 60 years

>60y = 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-dose 1 vaccination period – **Pooled Group** (Total Vaccinated cohort)

		Pooled Group									
		18y-60y					**>60y**				
					95 % CI					**95 % CI**	
Symptom	**Intensity/ Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Fatigue	Any	120	43	35.8	27.3	45.1	120	26	21.7	14.7	30.1
	Grade 3	120	2	1.7	0.2	5.9	120	1	0.8	0.0	4.6
	Related	120	40	33.3	25.0	42.5	120	24	20.0	13.3	28.3
Headache	Any	120	44	36.7	28.1	45.9	120	22	18.3	11.9	26.4
	Grade 3	120	1	0.8	0.0	4.6	120	0	0.0	0.0	3.0
	Related	120	43	35.8	27.3	45.1	120	21	17.5	11.2	25.5
Joint pain at other location	Any	120	19	15.8	9.8	23.6	120	17	14.2	8.5	21.7
	Grade 3	120	0	0.0	0.0	3.0	120	1	0.8	0.0	4.6
	Related	120	17	14.2	8.5	21.7	120	14	11.7	6.5	18.8
Muscle aches	Any	120	29	24.2	16.8	32.8	120	25	20.8	14.0	29.2
	Grade 3	120	2	1.7	0.2	5.9	120	1	0.8	0.0	4.6
	Related	120	25	20.8	14.0	29.2	120	23	19.2	12.6	27.4
Shivering	Any	120	23	19.2	12.6	27.4	120	7	5.8	2.4	11.6
	Grade 3	120	0	0.0	0.0	3.0	120	0	0.0	0.0	3.0
	Related	120	22	18.3	11.9	26.4	120	7	5.8	2.4	11.6
Sweating	Any	120	19	15.8	9.8	23.6	120	6	5.0	1.9	10.6
	Grade 3	120	1	0.8	0.0	4.6	120	0	0.0	0.0	3.0
	Related	120	17	14.2	8.5	21.7	120	6	5.0	1.9	10.6
Temperature/ (Axillary)	>37.5 °C	120	1	0.8	0.0	4.6	120	0	0.0	0.0	3.0
	≥ 39 °C	120	0	0.0	0.0	3.0	120	0	0.0	0.0	3.0
	Related	120	1	0.8	0.0	4.6	120	0	0.0	0.0	3.0

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
N= number of subjects with at least one administered dose
n (%)= number (percentage) of subjects reporting at least once the symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = occurrence of any general symptom regardless of intensity grade and relationship to vaccination
Grade 3 = event that prevented normal everyday activities as assessed by inability to attend/do work or school, or required intervention of a physician/healthcare provider
Related = general symptom assessed by the investigator as causally related to the study vaccination

Secondary Outcome Variable(s): Number of days with any general symptoms during the solicited post-dose 1 vaccination period – **Pooled Group** (Total Vaccinated cohort)

Solicited symptom	**Dose**	**Sub-group**	**N**	**Mean**	**Median**
Fatigue	Dose 1	18y-60y	43	2.7	2.0
		>60y	26	2.2	1.5
Headache	Dose 1	18y-60y	44	1.9	1.0
		>60y	22	2.4	2.0
Joint pain at other location	Dose 1	18y-60y	19	2.5	2.0
		>60y	17	2.8	2.0
Muscle aches	Dose 1	18y-60y	29	2.6	2.0
		>60y	25	3.0	3.0
Shivering	Dose 1	18y-60y	23	1.7	1.0
		>60y	7	1.9	1.0
Sweating	Dose 1	18y-60y	19	1.7	2.0
		>60y	6	1.7	1.5
Temperature	Dose 1	18y-60y	1	1.0	1.0

		>60y	0	0.0	0.0	

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
N = number of subjects 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 overall, for subjects who received 2 doses of Flu vaccine (**2 doses Group**) (Total Vaccinated cohort)

		2 doses Group									
		18y-60y					**>60y**				
					95 % CI					**95 % CI**	
Symptom	**Intensity/ Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Fatigue	Any	68	24	35.3	24.1	47.8	70	15	21.4	12.5	32.9
	Grade 3	68	2	2.9	0.4	10.2	70	0	0.0	0.0	5.1
	Related	68	21	30.9	20.2	43.3	70	14	20.0	11.4	31.3
Headache	Any	68	23	33.8	22.8	46.3	70	12	17.1	9.2	28.0
	Grade 3	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
	Related	68	22	32.4	21.5	44.8	70	11	15.7	8.1	26.4
Joint pain at other location	Any	68	12	17.6	9.5	28.8	70	9	12.9	6.1	23.0
	Grade 3	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
	Related	68	10	14.7	7.3	25.4	70	6	8.6	3.2	17.7
Muscle aches	Any	68	19	27.9	17.7	40.1	70	12	17.1	9.2	28.0
	Grade 3	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
	Related	68	15	22.1	12.9	33.8	70	10	14.3	7.1	24.7
Shivering	Any	68	14	20.6	11.7	32.1	70	2	2.9	0.3	9.9
	Grade 3	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
	Related	68	13	19.1	10.6	30.5	70	2	2.9	0.3	9.9
Sweating	Any	68	12	17.6	9.5	28.8	70	5	7.1	2.4	15.9
	Grade 3	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
	Related	68	11	16.2	8.4	27.1	70	5	7.1	2.4	15.9
Temperature (Axillary)	>37.5°C	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
	≥ 39.0°C	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
	Related	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
Dose 2											
Fatigue	Any	68	19	27.9	17.7	40.1	70	15	21.4	12.5	32.9
	Grade 3	68	2	2.9	0.4	10.2	70	0	0.0	0.0	5.1
	Related	68	19	27.9	17.7	40.1	70	15	21.4	12.5	32.9
Headache	Any	68	15	22.1	12.9	33.8	70	12	17.1	9.2	28.0
	Grade 3	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
	Related	68	15	22.1	12.9	33.8	70	12	17.1	9.2	28.0
Joint pain at other location	Any	68	11	16.2	8.4	27.1	70	13	18.6	10.3	29.7
	Grade 3	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
	Related	68	11	16.2	8.4	27.1	70	13	18.6	10.3	29.7
Muscle aches	Any	68	15	22.1	12.9	33.8	70	13	18.6	10.3	29.7
	Grade 3	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
	Related	68	15	22.1	12.9	33.8	70	13	18.6	10.3	29.7
Shivering	Any	68	18	26.5	16.5	38.6	70	5	7.1	2.4	15.9
	Grade 3	68	2	2.9	0.4	10.2	70	1	1.4	0.0	7.7
	Related	68	18	26.5	16.5	38.6	70	5	7.1	2.4	15.9
Sweating	Any	68	11	16.2	8.4	27.1	70	5	7.1	2.4	15.9
	Grade 3	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
	Related	68	11	16.2	8.4	27.1	70	5	7.1	2.4	15.9
Temperature	>37.5°C	68	2	2.9	0.4	10.2	70	0	0.0	0.0	5.1

(Axillary)	≥ 39.0°C	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
	Related	68	2	2.9	0.4	10.2	70	0	0.0	0.0	5.1
Across doses											
Fatigue	Any	68	29	42.6	30.7	55.2	70	26	37.1	25.9	49.5
	Grade 3	68	3	4.4	0.9	12.4	70	0	0.0	0.0	5.1
	Related	68	27	39.7	28.0	52.3	70	25	35.7	24.6	48.1
Headache	Any	68	29	42.6	30.7	55.2	70	20	28.6	18.4	40.6
	Grade 3	68	2	2.9	0.4	10.2	70	0	0.0	0.0	5.1
	Related	68	28	41.2	29.4	53.8	70	19	27.1	17.2	39.1
Joint pain at other location	Any	68	16	23.5	14.1	35.4	70	18	25.7	16.0	37.6
	Grade 3	68	1	1.5	0.0	7.9	70	0	0.0	0.0	5.1
	Related	68	15	22.1	12.9	33.8	70	16	22.9	13.7	34.4
Muscle aches	Any	68	26	38.2	26.7	50.8	70	22	31.4	20.9	43.6
	Grade 3	68	2	2.9	0.4	10.2	70	0	0.0	0.0	5.1
	Related	68	23	33.8	22.8	46.3	70	20	28.6	18.4	40.6
Shivering	Any	68	22	32.4	21.5	44.8	70	7	10.0	4.1	19.5
	Grade 3	68	2	2.9	0.4	10.2	70	1	1.4	0.0	7.7
	Related	68	21	30.9	20.2	43.3	70	7	10.0	4.1	19.5
Sweating	Any	68	19	27.9	17.7	40.1	70	9	12.9	6.1	23.0
	Grade 3	68	2	2.9	0.4	10.2	70	0	0.0	0.0	5.1
	Related	68	18	26.5	16.5	38.6	70	9	12.9	6.1	23.0
Temperature (Axillary)	>37.5°C	68	3	4.4	0.9	12.4	70	0	0.0	0.0	5.1
	≥ 39.0°C	68	0	0.0	0.0	5.3	70	0	0.0	0.0	5.1
	Related	68	3	4.4	0.9	12.4	70	0	0.0	0.0	5.1

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
N= number of subjects with at least one administered dose
n (%)= number (percentage) of subjects reporting at least once the symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = occurrence of any general symptom regardless of intensity grade and relationship to vaccination
Grade 3 = event 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 solicited general symptoms during the 7-day post-vaccination period, for subjects who received 2 doses of Flu vaccine (**2 doses Group**) (Total Vaccinated cohort)

Solicited symptom	**Dose**	**Sub-group**	**N**	**Mean**	**Median**
Fatigue	Dose 1	18y-60y	24	2.9	2.0
		>60y	15	1.4	1.0
	Dose 2	18y-60y	19	2.7	2.0
		>60y	15	1.4	1.0
	Overall/dose	18y-60y	43	2.8	2.0
		>60y	30	1.4	1.0
Headache	Dose 1	18y-60y	23	1.7	1.0
		>60y	12	2.1	2.0
	Dose 2	18y-60y	15	1.7	1.0
		>60y	12	1.6	1.0
	Overall/dose	18y-60y	38	1.7	1.0
		>60y	24	1.8	1.5
Joint pain at other location	Dose 1	18y-60y	12	2.4	2.0
		>60y	9	2.4	1.0
	Dose 2	18y-60y	11	2.0	2.0
		>60y	13	1.6	1.0
	Overall/dose	18y-60y	23	2.2	2.0
		>60y	22	2.0	1.0

Muscle aches	Dose 1	18y-60y	19	2.7	2.0
		>60y	12	2.8	2.5
	Dose 2	18y-60y	15	2.4	2.0
		>60y	13	2.3	1.0
	Overall/dose	18y-60y	34	2.6	2.0
		>60y	25	2.5	1.0
Sweating	Dose 1	18y-60y	12	1.8	2.0
		>60y	5	1.4	1.0
	Dose 2	18y-60y	11	2.2	2.0
		>60y	5	1.2	1.0
	Overall/dose	18y-60y	23	2.0	2.0
		>60y	10	1.3	1.0
Shivering	Dose 1	18y-60y	14	1.6	1.0
		>60y	2	1.0	1.0
	Dose 2	18y-60y	18	1.6	1.0
		>60y	5	1.0	1.0
	Overall/dose	18y-60y	32	1.6	1.0
		>60y	7	1.0	1.0
Temperature	Dose 1	18y-60y	1	1.0	1.0
		>60y	0	0.0	0.0
	Dose 2	18y-60y	2	2.0	2.0
		>60y	0	0.0	0.0
	Overall/dose	18y-60y	3	1.7	2.0
		>60y	0	0.0	0.0

18y-60y = Subject aged between and including 18 years to 60 years
>60y = 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 up to Day 21 (Total Vaccinated cohort)

	Pooled Group	
Most frequent adverse events of specific interest - On-Therapy (occurring within Day 0-20 following vaccination)	**18y-60y N = 120**	**>60y N = 120**
Subjects with any AESI(s), n (%)	0 (0.0)	0 (0.0)

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years

Secondary Outcome Variable(s): Number (%) of subjects with adverse events of specific interest up to Day 42 (Total Vaccinated cohort)

Most frequent adverse events of specific interest - On-Therapy (occurring within Day 0-41 following vaccination)	**1 dose Group**		**2 doses Group**	
	18y-60y N = 52	**>60y N = 50**	**18y-60y N = 68**	**>60y N = 70**
Subjects with any AESI(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

8y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years

Secondary Outcome Variable(s): Number (%) of subjects with adverse events of specific interest up to Day 182 (Total Vaccinated cohort)

Most frequent adverse events of specific interest (occurring within Day 0-181 following vaccination)	**1 dose Group**		**2 doses Group**	
	18y-60y N = 52	**>60y N = 50**	**18y-60y N = 68**	**>60y N = 70**
Subjects with any AESI(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years

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

Most frequent adverse events of specific interest	1 dose Group		2 doses Group	
	18y-60y N = 52	>60y N = 50	18y-60y N = 68	>60y N = 70
Subjects with any AESI(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years

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

		2 doses Group																	
		18y-60y N = 68									>60y N = 70								
			Unknown		Below		Within		Above			Unknown		Below		Within		Above	
Laboratory parameter	Timing	N	n	%	n	%	n	%	n	%	N	n	%	n	%	n	%	n	%
ALAT	PRE	68	0	0.0	0	0.0	56	82.4	12	17.6	70	0	0.0	0	0.0	66	94.3	4	5.7
	PI(21)	68	0	0.0	0	0.0	56	82.4	12	17.6	70	0	0.0	0	0.0	65	92.9	5	7.1
	PII(D42)	68	0	0.0	0	0.0	57	83.8	11	16.2	70	0	0.0	0	0.0	68	97.1	2	2.9
	PII(D182)	67	0	0.0	0	0.0	57	85.1	10	14.9	69	0	0.0	0	0.0	63	91.3	6	8.7
	PII(D364)	67	0	0.0	0	0.0	58	86.6	9	13.4	68	0	0.0	0	0.0	65	95.6	3	4.4
AP	PRE	68	0	0.0	0	0.0	67	98.5	1	1.5	70	0	0.0	0	0.0	70	100	0	0.0
	PI(21)	68	0	0.0	0	0.0	67	98.5	1	1.5	70	0	0.0	0	0.0	69	98.6	1	1.4
	PII(D42)	68	0	0.0	0	0.0	66	97.1	2	2.9	70	0	0.0	0	0.0	68	97.1	2	2.9
	PII(D182)	67	0	0.0	0	0.0	65	97.0	2	3.0	69	0	0.0	0	0.0	66	95.7	3	4.3
	PII(D364)	67	0	0.0	0	0.0	63	94.0	4	6.0	68	0	0.0	0	0.0	67	98.5	1	1.5
ASAT	PRE	68	0	0.0	0	0.0	63	92.6	5	7.4	70	0	0.0	0	0.0	66	94.3	4	5.7
	PI(21)	68	0	0.0	0	0.0	67	98.5	1	1.5	70	0	0.0	0	0.0	67	95.7	3	4.3
	PII(D42)	68	0	0.0	0	0.0	63	92.6	5	7.4	70	0	0.0	0	0.0	66	94.3	4	5.7
	PII(D182)	67	0	0.0	0	0.0	62	92.5	5	7.5	69	0	0.0	0	0.0	64	92.8	5	7.2
	PII(D364)	67	0	0.0	0	0.0	63	94.0	4	6.0	68	0	0.0	0	0.0	65	95.6	3	4.4
Total Bilirubin	PRE	68	0	0.0	0	0.0	64	94.1	4	5.9	70	0	0.0	0	0.0	68	97.1	2	2.9
	PI(21)	68	0	0.0	0	0.0	64	94.1	4	5.9	70	0	0.0	0	0.0	66	94.3	4	5.7
	PII(D42)	68	0	0.0	0	0.0	64	94.1	4	5.9	70	0	0.0	0	0.0	67	95.7	3	4.3
	PII(D182)	67	0	0.0	0	0.0	65	97.0	2	3.0	69	0	0.0	0	0.0	68	98.6	1	1.4
	PII(D364)	67	0	0.0	0	0.0	59	88.1	8	11.9	68	0	0.0	0	0.0	64	94.1	4	5.9
Creatinine	PRE	68	0	0.0	0	0.0	59	86.8	9	13.2	70	0	0.0	0	0.0	52	74.3	18	25.7
	PI(21)	68	0	0.0	0	0.0	60	88.2	8	11.8	70	0	0.0	0	0.0	51	72.9	19	27.1
	PII(D42)	68	0	0.0	0	0.0	60	88.2	8	11.8	70	0	0.0	0	0.0	54	77.1	16	22.9
	PII(D182)	67	0	0.0	0	0.0	57	85.1	10	14.9	69	0	0.0	0	0.0	51	73.9	18	26.1
	PII(D364)	67	0	0.0	0	0.0	63	94.0	4	6.0	68	0	0.0	0	0.0	60	88.2	8	11.8
BUN	PRE	68	0	0.0	0	0.0	66	97.1	2	2.9	70	0	0.0	0	0.0	58	82.9	12	17.1
	PI(21)	68	0	0.0	0	0.0	66	97.1	2	2.9	70	0	0.0	0	0.0	59	84.3	11	15.7
	PII(D42)	68	0	0.0	0	0.0	64	94.1	4	5.9	70	0	0.0	0	0.0	57	81.4	13	18.6
	PII(D182)	67	0	0.0	0	0.0	67	100	0	0.0	69	0	0.0	0	0.0	59	85.5	10	14.5
	PII(D364)	67	0	0.0	0	0.0	67	100	0	0.0	68	0	0.0	0	0.0	60	88.2	8	11.8
		1 dose Group																	
		18y-60y N = 52									>60y N = 50								
			Unknown		Below		Within		Above			Unknown		Below		Within		Above	
Laboratory parameter	Timing	N	n	%	n	%	n	%	n	%	N	n	%	n	%	n	%	n	%
ALAT	PRE	52	0	0.0	0	0.0	44	84.6	8	15.4	50	0	0.0	0	0.0	48	96.0	2	4.0
	PI(21)	52	0	0.0	0	0.0	45	86.5	7	13.5	50	0	0.0	0	0.0	46	92.0	4	8.0
	PI(D42)	52	0	0.0	0	0.0	46	88.5	6	11.5	50	0	0.0	0	0.0	44	88.0	6	12.0
	PI(D182)	52	0	0.0	0	0.0	47	90.4	5	9.6	50	0	0.0	0	0.0	48	96.0	2	4.0

	PI(D364)	52	0	0.0	0	0.0	47	90.4	5	9.6	50	0	0.0	0	0.0	47	94.0	3	6.0
AP	PRE	52	0	0.0	0	0.0	51	98.1	1	1.9	50	0	0.0	0	0.0	45	90.0	5	10.0
	PI(21)	52	0	0.0	0	0.0	52	100	0	0.0	50	0	0.0	0	0.0	46	92.0	4	8.0
	PI(D42)	52	0	0.0	0	0.0	52	100	0	0.0	50	0	0.0	0	0.0	44	88.0	6	12.0
	PI(D182)	52	0	0.0	0	0.0	51	98.1	1	1.9	50	0	0.0	0	0.0	45	90.0	5	10.0
	PI(D364)	52	0	0.0	0	0.0	51	98.1	1	1.9	50	0	0.0	0	0.0	47	94.0	3	6.0
ASAT	PRE	52	0	0.0	0	0.0	47	90.4	5	9.6	50	0	0.0	0	0.0	48	96.0	2	4.0
	PI(21)	52	0	0.0	0	0.0	49	94.2	3	5.8	50	0	0.0	0	0.0	48	96.0	2	4.0
	PI(D42)	52	0	0.0	0	0.0	45	86.5	7	13.5	50	0	0.0	0	0.0	48	96.0	2	4.0
	PI(D182)	52	0	0.0	0	0.0	47	90.4	5	9.6	50	0	0.0	0	0.0	48	96.0	2	4.0
	PI(D364)	52	0	0.0	0	0.0	49	94.2	3	5.8	50	0	0.0	0	0.0	48	96.0	2	4.0
Total Bilirubin	PRE	52	0	0.0	0	0.0	49	94.2	3	5.8	50	0	0.0	0	0.0	48	96.0	2	4.0
	PI(21)	52	0	0.0	0	0.0	49	94.2	3	5.8	50	0	0.0	0	0.0	49	98.0	1	2.0
	PI(D42)	52	0	0.0	0	0.0	50	96.2	2	3.8	50	0	0.0	0	0.0	49	98.0	1	2.0
	PI(D182)	52	0	0.0	0	0.0	51	98.1	1	1.9	50	0	0.0	0	0.0	50	100	0	0.0
	PI(D364)	52	0	0.0	0	0.0	46	88.5	6	11.5	50	0	0.0	0	0.0	49	98.0	1	2.0
Creatinine	PRE	52	0	0.0	0	0.0	50	96.2	2	3.8	50	0	0.0	0	0.0	42	84.0	8	16.0
	PI(21)	52	0	0.0	0	0.0	49	94.2	3	5.8	50	0	0.0	0	0.0	41	82.0	9	18.0
	PI(D42)	52	0	0.0	0	0.0	51	98.1	1	1.9	50	0	0.0	0	0.0	41	82.0	9	18.0
	PI(D182)	52	0	0.0	0	0.0	50	96.2	2	3.8	50	0	0.0	0	0.0	41	82.0	9	18.0
	PI(D364)	52	0	0.0	0	0.0	52	100	0	0.0	50	0	0.0	0	0.0	45	90.0	5	10.0
BUN	PRE	52	0	0.0	0	0.0	51	98.1	1	1.9	50	0	0.0	0	0.0	47	94.0	3	6.0
	PI(21)	52	0	0.0	0	0.0	51	98.1	1	1.9	50	0	0.0	0	0.0	42	84.0	8	16.0
	PI(D42)	52	0	0.0	0	0.0	51	98.1	1	1.9	50	0	0.0	0	0.0	43	86.0	7	14.0
	PI(D182)	52	0	0.0	0	0.0	50	96.2	2	3.8	50	0	0.0	0	0.0	43	86.0	7	14.0
	PI(D364)	52	0	0.0	0	0.0	52	100	0	0.0	50	0	0.0	0	0.0	45	90.0	5	10.0

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
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(21) = Post-dose 1 Day 21
PI(D42) = Post-dose 1 Day 42
PII(D42) = Post-dose 2 Day 42
PI(D182) = Post-dose 1 Day 182
PII(D182) = Post-dose 2 Day 182
PI(D364) = Post-dose 1 Day 364
PII(D364) = Post-dose 2 Day 364

Safety results: Number (%) of subjects with unsolicited adverse events within 21 Days (0-20) (Total Vaccinated cohort)

	Pooled Group	
Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)	**18y-60y N = 120**	**>60y N = 120**
Subjects with any AE(s), n (%)	53 (44.2)	31 (25.8)
Subjects with grade 3 AE(s), n (%)	10 (8.3)	1 (0.8)
Subjects with related AE(s), n (%)	24 (20.0)	14 (11.7)
Nasopharyngitis	15 (12.5)	3 (2.5)
----------*	4 (3.3)	6 (5.0)

Headache	5 (4.2)	2 (1.7)
Oropharyngeal pain	4 (3.3)	2 (1.7)
Ecchymosis	2 (1.7)	2 (1.7)
Upper respiratory tract infection	2 (1.7)	2 (1.7)
Influenza like illness	3 (2.5)	-
Abdominal pain	2 (1.7)	-
Back pain	-	2 (1.7)
Cough	-	2 (1.7)
Diarrhoea	-	2 (1.7)
Gastroenteritis	2 (1.7)	-
Haematoma	-	2 (1.7)
Injection site pruritus	-	2 (1.7)
Malaise	-	2 (1.7)
Nausea	2 (1.7)	-
Renal impairment	-	2 (1.7)

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects aged more than 60 years
- : Adverse event absent or not meeting the selected rule: > 30 subjects per treatment group and ≤ 3 groups: display the most frequent 10 events in each group
* AE not yet classified by MedDRA Preferred Term
Grade 3 = event that prevented normal everyday activities
Related = event assessed by the investigator as causally related to the study vaccination

Safety results: Number (%) of subjects with unsolicited adverse events during the 42-days (Day 0-41) follow-up period after the first vaccination and 21 days (Day 21-42) follow-up period after the second vaccination (Total Vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-41 following the first vaccination and within Day (21-42 following the second vaccination)	**1 dose Group**		**2 doses Group**	
	18y-60y N = 52	**>60y N = 50**	**18y-60y N = 68**	**>60y N = 70**
Subjects with any AE(s), n (%)	29 (55.8)	17 (34.0)	30 (44.1)	31 (44.3)
Subjects with grade 3 AE(s), n (%)	3 (5.8)	2 (4.0)	8 (11.8)	4 (5.7)
Subjects with related AE(s), n (%)	9 (17.3)	7 (14.0)	16 (23.5)	10 (14.3)
Abdominal pain	3 (5.8)	-	-	-
Diarrhoea	2 (3.8)	-	-	2 (2.9)
Nausea	-	-	3 (4.4)	-
Fatigue	-	-	2 (2.9)	-
Influenza like illness	-	-	4 (5.9)	-
Injection site pruritus	-	2 (4.0)	-	-
Malaise	-	-	-	2 (2.9)
Gastroenteritis	-	-	2 (2.9)	-
Laryngitis	2 (3.8)	-	-	-
Nasopharyngitis	9 (17.3)	3 (6.0)	10 (14.7)	4 (5.7)
Rhinitis	-	2 (4.0)	-	-
Upper respiratory tract infection	-	-	2 (2.9)	2 (2.9)
Back pain	-	2 (4.0)	-	2 (2.9)
Tendonitis	-	2 (4.0)	-	-
Headache	4 (7.7)	-	3 (4.4)	3 (4.3)
Renal impairment	-	-	-	2 (2.9)
Cough	-	-	-	2 (2.9)
Oropharyngeal pain	3 (5.8)	-	-	3 (4.3)
Erythema	-	-	-	2 (2.9)

18y-60y = Subject aged between and including 18 years to 60 years
>60y = Subjects 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 everyday activities

Related= event assessed by the investigator as causally related to the study vaccination				
Safety results: Number (%) of subjects with unsolicited adverse events within 84 days follow-up after the first vaccination and 63 days follow-up after the second vaccination (Total Vaccinated cohort)				
Most frequent adverse events - On-Therapy (occurring within 84 days follow-up after the first vaccination and 63 days follow-up after the second vaccination)	**2 doses Group**		**1 dose Group**	
	18y-60y N = 68	**>60y N = 70**	**18y-60y N = 52**	**>60y N = 50**
Subjects with any AE(s), n (%)	45 (66.2)	46 (65.7)	39 (75.0)	30 (60.0)
Subjects with grade 3 AE(s), n (%)	13 (19.1)	9 (12.9)	10 (19.2)	7 (14.0)
Subjects with related AE(s), n (%)	15 (22.1)	10 (14.3)	9 (17.3)	7 (14.0)
Nasopharyngitis	19 (27.9)	15 (21.4)	13 (25.0)	7 (14.0)
Headache	6 (8.8)	3 (4.3)	4 (7.7)	4 (8.0)
Upper respiratory tract infection	3 (4.4)	-	4 (7.7)	3 (6.0)
Diarrhoea	-	3 (4.3)	4 (7.7)	-
Influenza like illness	4 (5.9)	-	3 (5.8)	-
Back pain	-	-	-	3 (6.0)
Oropharyngeal pain	-	3 (4.3)	3 (5.8)	-
Cough	-	3 (4.3)	3 (5.8)	-
Gastroenteritis	5 (7.4)	-	-	-
Bronchitis	-	-	-	3 (6.0)
Abdominal pain	-	-	3 (5.8)	-
Nausea	3 (4.4)	-	-	-
Pain in extremity	-	-	-	3 (6.0)
Sinusitis	3 (4.4)	-	-	-
18y-60y = Subject aged between and including 18 years to 60 years >60y = Subjects 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 everyday activities Related= event assessed by the investigator as causally related to the study vaccination				
Safety results: Number (%) of subjects with serious adverse events up to Day 21 (Total Vaccinated cohort)				
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]				
	Pooled Group			
All SAEs	**18y-60y N = 120**	**>60y N = 120**		
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]		
Fatal SAEs	**18y-60y N = 120**	**>60y N = 120**		
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]		
18y-60y = Subject aged between and including 18 years to 60 years >60y = Subjects aged more than 60 years				
Safety results: Number (%) of subjects with serious adverse events up to Day 42 (Total Vaccinated cohort)				
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]				
All SAEs	**1 dose Group**		**2 doses Group**	
	18y-60y N = 52	**>60y N = 50**	**18y-60y N = 68**	**>60y N = 70**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	1 (2.0) [0]	0 (0.0) [0]	2 (2.9) [0]
Atrial fibrillation	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.4) [0]
Intervertebral disc disorder	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.4) [0]
Headache	0 (0.0) [0]	1 (2.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**1 dose Group**		**2 doses Group**	
	18y-60y N = 52	**>60y N = 50**	**18y-60y N = 68**	**>60y N = 70**
Subjects with fatal SAE(s), n (%) [n assessed by	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

investigator as related]				
18y-60y = Subject aged between and including 18 years to 60 years >60y = Subjects aged more than 60 years				
Safety results: Number (%) of subjects with serious adverse events up to Day 182 (Total Vaccinated cohort)				
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]				
All SAEs	**2 doses Group**		**1 dose Group**	
	18y-60y N = 68	**>60y N = 70**	**18y-60y N = 52**	**>60y N = 50**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	8 (11.4) [0]	1 (1.9) [0]	2 (4.0) [0]
Atrial fibrillation	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Breast cancer	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cerebrovascular accident	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cholecystitis acute	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Concussion	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Contusion	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cystitis	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Deep vein thrombosis	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Hand fracture	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Headache	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (2.0) [0]
Intervertebral disc disorder	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Non-hodgkin's lymphoma unspecified histology indolent	0 (0.0) [0]	0 (0.0) [0]	1 (1.9) [0]	0 (0.0) [0]
Tibia fracture	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (2.0) [0]
Transient ischaemic attack	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**2 doses Group**		**1 dose Group**	
	18y-60y N = 68	**>60y N = 70**	**18y-60y N = 52**	**>60y N = 50**
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
18y-60y = Subject aged between and including 18 years to 60 years >60y = Subjects aged more than 60 years				
Safety results: Number (%) of subjects with serious adverse events up to Day 364 (Total Vaccinated cohort)				
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]				
All SAEs	**2 doses Group**		**1 dose Group**	
	18y-60y N = 68	**>60y N = 70**	**18y-60y N = 52**	**>60y N = 50**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	10 (14.3) [0]	3 (5.8) [0]	3 (6.0) [0]
Aortic stenosis	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Arrhythmia	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Arterial thrombosis limb	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Atrial fibrillation	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Benign prostatic hyperplasia	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Breast cancer	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cerebrovascular accident	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cervical root pain	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (2.0) [0]
Cholecystitis acute	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cholelithiasis	0 (0.0) [0]	0 (0.0) [0]	1 (1.9) [0]	0 (0.0) [0]
Concussion	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Contusion	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cystitis	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Deep vein thrombosis	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Drug hypersensitivity	0 (0.0) [0]	0 (0.0) [0]	1 (1.9) [0]	0 (0.0) [0]

Hand fracture	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Headache	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (2.0) [0]
Intervertebral disc disorder	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Intervertebral disc protrusion	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (2.0) [0]
Multiple fractures	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Pneumothorax	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Post procedural haemorrhage	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Splenic marginal zone lymphoma	0 (0.0) [0]	0 (0.0) [0]	1 (1.9) [0]	0 (0.0) [0]
Subdural haematoma	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Syncope	0 (0.0) [0]	0 (0.0) [0]	1 (1.9) [0]	0 (0.0) [0]
Tibia fracture	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (2.0) [0]
Transient ischaemic attack	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Urethral stenosis	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**2 doses Group N = 138**		**1 dose Group N = 102**	
	18y-60y N = 68	**>60y N = 70**	**18y-60y N = 52**	**>60y N = 50**
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
18y-60y = Subject aged between and including 18 years to 60 years >60y = Subjects aged more than 60 years				

Conclusion: At 21 days after the first vaccine dose, in the 2 doses Group, seroconversion and seroprotection rates were 95.5% and 98.5% in the 18y-60y subgroup and 79.1% and 88.1% in the >60y subgroup, respectively. Seroconversion factor value was 38.71 in the 18y-60y subgroup and 13.86 in the >60y subgroup.
Up to Day 42, at least one unsolicited AE was reported by 29 (55.8%) subjects of 1 dose Group (18y-60y), 17 (34.0%) subjects of 1 dose Group (>60y), 30 (44.1%) subjects of 2 doses Group (18y-60y) and 31 (44.3%) subjects of 2 doses Group (>60y).
Up to Day 83, at least one unsolicited AE was reported by 45 (66.2%), 46 (65.7%), 39 (75.0%) and 30 (60.0%) subjects in the 2 doses Group (18y-60y), 2 doses Group (>60y), 1 dose Group (18y-60y) and 1 dose Group (>60y), respectively.
Up to Day 364, SAEs were reported by 10 (14.3%), 3 (5.8%) and 3 (6.0%) subjects in 2 doses Group (>60y), 1 dose Group (18y-60y) and 1 dose Group (>60y), respectively. None of the SAEs were assessed by the investigator as causally related to the study vaccination. No fatal SAEs were reported up to Day 364.
Please also refer to the publication citations.

Date updated: 10-November-2014