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.: 110620 (FluAS25-020)

Title: A phase II, observer-blind, multicountry, multicenter, randomized study to demonstrate the non-Inferiority of GlaxoSmithKline Biologicals' one-container AS25 adjuvanted influenza vaccine compared to GlaxoSmithKline Biologicals' two-container AS25 adjuvanted influenza vaccine in adults aged 65 years and above.
FluAS25 (Flu-1): GlaxoSmithKline (GSK) Biologicals' AS25 adjuvanted influenza vaccine.

Rationale: The trial was designed to compare the immune response of Flu-1 in 1-container versus 2-container presentation. In addition, the trial also investigated the immune response elicited by the H1N1 strain recommended for the Northern Hemisphere (NH) 2006/07 influenza season (A/New Caledonia) compared to the H1N1 strain recommended for the NH 2007/08 influenza season (A/Solomon Islands). *Fluarix*™ vaccine was used as a control.
Fluarix™ (Flu-2): GSK Biologicals' licensed influenza vaccine.

Phase: II

Study Period: 20 September 2007 to 02 November 2007.

Study Design: Multicountry, multicenter, randomized (1:1:1:1:1:1), controlled study with 6 parallel groups. The study was observer-blind between Flu-1 vaccine and Flu-2 vaccine and for Flu-1, between 1 and 2 containers; the study was blinded for the influenza season.

Centers: 6 centers: 1 in Denmark, 1 in Estonia and 4 in Norway.

Indication: Immunization against influenza in male and female subjects aged ≥ 65 years.

Treatment: The treatment groups were as follows:
A_1NC Group received 1 dose of the Flu-1 vaccine for the NH 2006/07 season presented in 1 container.
A_1SI Group received 1 dose of the Flu-1 vaccine for the NH 2007/08 season presented in 1 container.
A_2NC Group received 1 dose of the Flu-1 vaccine for the NH 2006/07 season presented in 2 containers.
A_2SI Group received 1 dose of the Flu-1 vaccine for the NH 2007/08 season presented in 2 containers.
Flu_NC Group received 1 dose of Flu-2 for the 2006-2007 season.
Flu_SI Group received 1 dose of Flu-2 for the 2007-2008 season.
The vaccines were administered by intramuscular injection in the deltoid region of the non-dominant arm.

Objectives:
To demonstrate the immunological non-inferiority [in terms of haemagglutination-inhibition (HI) antibody Geometric mean titers (GMTs)] of the 1-container presentation of the Flu-1 vaccine from the NH 2006/07 season (Flu-1-1 container NH 2006/07) versus the 2-container presentation of the Flu-1 vaccine from the NH 2006/07 season (Flu-1-2 containers NH 2006/07) 21 days after vaccination in elderly subjects ≥ 65 years old.
To demonstrate the immunological non-inferiority (in terms of HI antibody GMT) of Flu-1-1 container NH 2007/08 versus Flu-1-2 containers NH 2007/08, 21 days after vaccination in elderly subjects ≥ 65 years old.
Criterion to demonstrate the non-inferiority:
The non-inferiority was demonstrated if the upper limit of the 2-sided 95% confidence interval (CI) of the GMT ratio (Flu-1-2 containers over Flu-1-1 container) was below 1.5 in terms of anti-H1N1 antibody titers.

Primary Outcome/Efficacy Variable:
Immunogenicity
At Days 0 and 21, serum HI antibody titer, against the A/New Caledonia (H1N1) vaccine strain, in the Flu-1-1 container NH 2006/07 and Flu-1-2 containers NH 2006/07 groups.
At Days 0 and 21, serum HI antibody titer, against the A/Solomon Islands (H1N1) vaccine strain, in the Flu-1-1 container NH 2007/08 and Flu-1-2 containers NH 2007/08 groups.
Derived variable:
GMT of HI antibody titers at Days 0 and 21 for the H1N1 strain.

Secondary Outcome/Efficacy Variable(s):
Immunogenicity
At Days 0 and 21: serum HI antibody titer, against each of the 3 vaccine strains for the 2 season formulations, in each group.
Derived variables:
GMTs of HI antibody titers at Days 0 and 21, in each group.
Seroconversion rates (SCR)* at Day 21, in each group.

Seroconversion factors (SCF)** at Day 21, in each group.
Seroprotection rates (SPR)*** at Days 0 and 21, in each group.
** Seroconversion rate is defined as the percentage of vaccinees who have either a pre-vaccination titer < 1:10 and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least a 4-fold increase in post-vaccination titer.*
*** Seroconversion factor is defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.*
**** Seroprotection rate is defined as the percentage of vaccinees with a serum HI titer ≥ 1:40 that usually is accepted as indicating protection.*

Safety
Occurrence, intensity, duration and relationship to vaccination of solicited local and general signs and symptoms during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after vaccination, in each group.
Occurrence, intensity, duration* and relationship to vaccination of unsolicited adverse events (AEs) during a 21-day follow-up period (i.e. day of vaccination and 20 subsequent days) after vaccination, in each group.
Occurrence, intensity, duration* and relationship to vaccination of medically-significant conditions** prompting emergency room visits, hospitalizations or physician visits that were not routine visits for physical examination or vaccination, during a 21-day follow-up period (i.e. day of vaccination and 20 subsequent days) after vaccination, in each group.
Occurrence and relationship to vaccination of serious adverse events (SAEs) during the entire study period in each group.
* Although planned, the duration of unsolicited AEs and medically significant conditions was not analyzed.
** It was decided to analyze the medically significant conditions as all adverse events that resulted in a medically attended visit.

Statistical Methods:
The analyses were based on the Total Vaccinated Cohort and the According-To-Protocol (ATP) cohort for immunogenicity.
- The Total Vaccinated Cohort included all subjects with 1 vaccine administration documented.
- The ATP cohort for immunogenicity included all subjects who had received 1 dose of study vaccine according to their random assignment, for whom administration site of study vaccine was known, who had not received a vaccine not specified or forbidden in the protocol, for whom the randomization code had not been broken, who met all eligibility criteria, who complied with the procedures and intervals defined in the protocol, with no elimination criteria during the study and for whom data concerning immunogenicity measures were available.

Analysis of immunogenicity:
The analyses were based on the ATP cohort for immunogenicity.
Inferential analysis
To compare the immunogenicity between groups in terms of HI antibody GMT for the H1N1 results, an analysis of covariance (ANCOVA) model on the logarithm10 transformation of the titers was fitted including the H1N1 strain, the vaccine type and the strain by vaccine type interaction as fixed effects, and the pre-vaccination log-transformed titer as covariate. Regardless of the significance level of the interaction, the 95% CIs of the adjusted GMT ratios for Flu-1-2 containers NH 2006/07 over Flu-1-1 container NH 2006/07 and for Flu-1-2 containers NH 2007/08 over Flu-1-1 container NH 2007/08 were tabulated. The non-inferiority was demonstrated if the upper limit of the 2-sided 95% CI of the GMT ratio (Flu-1-2 containers over Flu-1-1 container) was below 1.5 in terms of anti-H1N1 antibody titers. The primary objective of the study was reached only if the non-inferiority was demonstrated for both NH influenza seasons vaccines.
Descriptive analysis
For each vaccine group and each vaccine strain, GMTs (with 95% CI) at Days 0 and 21, SPR (with exact 95% CI) at Days 0 and 21, seropositivity rate (with exact 95% CI) at Days 0 and 21, SCR (with exact 95% CI) at Day 21 and SCF (with 95% CI) at Day 21 were tabulated. Seropositivity rate was defined as the percentage of subjects with serum HI titers ≥ 1:10. Titers below the cut-off value were given the arbitrary value of half the cut-off.

Analysis of safety:
The analyses were based on the Total Vaccinated Cohort.
For each vaccine group, the percentage of subjects reporting each individual solicited local and general symptom during the 7-day (Day 0-6) solicited follow-up period, with exact 95% CI were tabulated. The same tabulations were done for Grade 3 solicited symptoms and for solicited general symptoms that were assessed by the investigators as causally related to the vaccination. The average number of days with solicited local and general symptoms of any grade during the 7-day (Days 0-6) post-vaccination period was tabulated per group.
The percentage of subjects with at least 1 report of medically attended event (MAE) reported up to 21 days (Days 0-20) after vaccination was tabulated per group according to Medical Dictionary for Regulatory Activities (MedDRA) preferred terms with exact 95% CI. The same tabulation was performed for Grade 3 MAEs and for MAEs assessed by the investigator as causally related to the vaccination.

The percentage of subjects with at least 1 unsolicited AE reported up to 21 days (Days 0-20) after vaccination was tabulated per group according to MedDRA preferred terms. The same tabulation was performed for Grade 3 adverse events and for adverse events assessed by the investigators as causally related to the vaccination.
SAEs during the entire study period were tabulated per group according to MedDRA preferred terms.

Study Population: Healthy male or female subjects aged 65 years or older at the time of the vaccination, free of an acute aggravation of the health status as established by clinical examination before entering into the study were enrolled. Written informed consent was obtained from each subject. Subjects who had been vaccinated against influenza since January 2007 (including the NH 2006/2007 or NH 2007/08 influenza vaccine) were excluded.

Number of subjects	**A_1NC Group**	**A_2NC Group**	**Flu_NC Group**
Planned, N	260	260	260
Randomized, N (Total Vaccinated Cohort)	269	266	264
Completed, n (%)	267 (99.3)	265 (99.6)	263 (99.6)
Total Number Subjects Withdrawn, n (%)	2 (0.7)	1 (0.4)	1 (0.4)
Withdrawn due to Adverse Events, n (%)	1 (0.4)	0 (0.0)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	1 (0.4)	1 (0.4)	1 (0.4)
Demographics	**A_1NC Group**	**A_2NC Group**	**Flu_NC Group**
N (Total Vaccinated Cohort)	269	266	264
Females: Males	151:118	149:117	150:114
Mean Age, years (SD)	73.2 (5.56)	73.0 (5.16)	72.8 (5.06)
White-Caucasian / European heritage, n (%)	267 (99.3)	265 (99.6)	264 (100)
Number of subjects	**A_1SI Group**	**A_2SI Group**	**Flu_SI Group**
Planned, N	260	260	260
Randomized, N (Total Vaccinated Cohort)	264	268	263
Completed, n (%)	264 (100)	267 (99.6)	261 (99.2)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	1 (0.4)	2 (0.8)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	1 (0.4)	1 (0.4)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	0 (0.0)	1 (0.4)
Demographics	**A_1SI Group**	**A_2SI Group**	**Flu_SI Group**
N (Total Vaccinated Cohort)	264	268	263
Females: Males	145:119	152:116	153:110
Mean Age, years (SD)	73.3 (5.86)	73.2 (5.72)	73.0 (5.20)
White-Caucasian / European heritage, n (%)	263 (99.6)	268 (100)	261 (99.2)

Primary Efficacy Results: Adjusted ratio of H1N1 vaccine strain GMTs at Day 21 between Flu-1-1 container and Flu-1-2 containers (ATP cohort for immunogenicity)

Group	**N**	**Adjusted GMT**	**Group**	**N**	**Adjusted GMT**	**Adjusted GMT ratio**			
						Ratio order	**Value**	**95% CI**	
								LL	**UL***
A_2NC	259	107.3	A_1NC	259	103.3	A_2NC / A_1NC	1.04	0.87	1.25
A_2SI	263	111.8	A_1SI	258	102.0	A_2SI / A_1SI	1.10	0.92	1.31

Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = number of subjects with both pre-and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio; LL = Lower Limit, UL = Upper Limit
*Non-inferiority criterion: UL of 95% CI < 1.5

Primary Efficacy Results: Seropositivity rates and GMTs for HI antibody titer at Days 0 and 21 (ATP cohort for immunogenicity)

Antibody	**Group**	**Timing**	**N**	**≥ 1:10**				**GMT***		
				n	**%**	**95% CI**		**value**	**95% CI**	
						LL	**UL**		**LL**	**UL**
A/New Caledonia*	A_1NC	PRE	259	228	88.0	83.4	91.7	37.9	33.1	43.3
		PI(D21)	259	257	99.2	97.2	99.9	130.8	117.0	146.3
	A_2NC	PRE	259	227	87.6	83.0	91.4	40.1	34.7	46.4
		PI(D21)	259	258	99.6	97.9	100	138.5	123.2	155.8

	Flu_NC	PRE	255	214	83.9	78.8	88.2	35.3	30.6	40.7
		PI(D21)	255	254	99.6	97.8	100	114.7	102.0	129.0
A/Solomon Islands*	A_1SI	PRE	258	112	43.4	37.3	49.7	9.4	8.4	10.5
		PI(D21)	258	250	96.9	94.0	98.7	82.0	70.9	94.8
	A_2SI	PRE	263	114	43.3	37.3	49.6	9.0	8.1	9.9
		PI(D21)	263	253	96.2	93.1	98.2	88.6	76.4	102.7
	Flu_SI	PRE	257	96	37.4	31.4	43.6	8.5	7.7	9.4
		PI(D21)	257	239	93.0	89.2	95.8	61.0	52.1	71.6
A/Wisconsin	A_1NC	PRE	259	221	85.3	80.4	89.4	47.7	39.9	57.0
		PI(D21)	259	257	99.2	97.2	99.9	379.7	328.5	439.0
	A_2NC	PRE	259	223	86.1	81.3	90.1	52.8	44.1	63.2
		PI(D21)	259	259	100	98.6	100	409.9	360.3	466.2
	Flu_NC	PRE	255	214	83.9	78.8	88.2	53.3	44.2	64.2
		PI(D21)	255	255	100	98.6	100	275.5	241.6	314.3
	A_1SI	PRE	258	228	88.4	83.8	92.0	56.7	47.7	67.5
		PI(D21)	258	258	100	98.6	100	399.9	351.4	455.1
	A_2SI	PRE	263	227	86.3	81.6	90.2	52.8	44.3	62.9
		PI(D21)	263	262	99.6	97.9	100	367.4	322.9	418.2
	Flu_SI	PRE	257	211	82.1	76.9	86.6	42.8	35.8	51.2
		PI(D21)	257	255	99.2	97.2	99.9	178.9	153.8	208.0
B/Malaysia	A_1NC	PRE	259	240	92.7	88.8	95.5	57.9	50.4	66.6
		PI(D21)	259	259	100	98.6	100	236.4	212.6	262.9
	A_2NC	PRE	259	238	91.9	87.9	94.9	59.5	51.2	69.2
		PI(D21)	259	258	99.6	97.9	100	213.8	189.7	241.0
	Flu_NC	PRE	255	231	90.6	86.3	93.9	59.6	50.9	69.7
		PI(D21)	255	254	99.6	97.8	100	193.2	170.0	219.5
	A_1SI	PRE	258	246	95.3	92.0	97.6	68.0	59.2	78.2
		PI(D21)	258	258	100	98.6	100	253.6	227.8	282.2
	A_2SI	PRE	263	243	92.4	88.5	95.3	51.6	44.8	59.6
		PI(D21)	263	263	100	98.6	100	201.9	180.0	226.6
	Flu_SI	PRE	257	232	90.3	86.0	93.6	54.3	46.5	63.5
		PI(D21)	257	255	99.2	97.2	99.9	180.5	158.5	205.7

N = number of subjects with available results
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination dose 1 (Day 0)
PI(D21) = post-vaccination dose 1 (Day 21)
* Primary Efficacy Results

Secondary Outcome Variable (s): SCR for HI antibody titer at Day 21 (ATP cohort for immunogenicity)

Vaccine strain	**Group**	**N**	**SCR**			
			n	**%**	**95% CI**	
					LL	**UL**
A/New Caledonia	A_1NC	259	104	40.2	34.1	46.4
	A_2NC	259	95	36.7	30.8	42.9
	Flu_NC	255	78	30.6	25.0	36.6
A/Solomon Islands	A_1SI	258	177	68.6	62.6	74.2
	A_2SI	263	192	73.0	67.2	78.3
	Flu_SI	257	161	62.6	56.4	68.6
A/Wisconsin	A_1NC	259	177	68.3	62.3	74.0
	A_2NC	259	188	72.6	66.7	77.9
	Flu_NC	255	128	50.2	43.9	56.5
	A_1SI	258	171	66.3	60.2	72.0
	A_2SI	263	173	65.8	59.7	71.5
	Flu_SI	257	109	42.4	36.3	48.7

B/Malaysia	A_1NC	259	110	42.5	36.4	48.7
	A_2NC	259	100	38.6	32.6	44.8
	Flu_NC	255	85	33.3	27.6	39.5
	A_1SI	258	108	41.9	35.8	48.1
	A_2SI	263	111	42.2	36.2	48.4
	Flu_SI	257	88	34.2	28.5	40.4

Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 1:40 after vaccination.
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer.
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): SCF for HI antibody titer at Day 21 (ATP cohort for immunogenicity)

Vaccine strain	**Group**	**N**	**SCF**		
			Value	**95% CI**	
				LL	**UL**
A/New Caledonia	A_1NC	259	3.5	3.0	4.0
	A_2NC	259	3.5	3.0	4.0
	Flu_NC	255	3.3	2.8	3.8
A/Solomon Islands	A_1SI	258	8.7	7.5	10.2
	A_2SI	263	9.9	8.5	11.5
	Flu_SI	257	7.2	6.1	8.4
A/Wisconsin	A_1NC	259	8.0	6.7	9.4
	A_2NC	259	7.8	6.6	9.2
	Flu_NC	255	5.2	4.3	6.3
	A_1SI	258	7.0	6.0	8.3
	A_2SI	263	7.0	5.9	8.3
	Flu_SI	257	4.2	3.5	5.0
B/Malaysia	A_1NC	259	4.1	3.5	4.7
	A_2NC	259	3.6	3.1	4.2
	Flu_NC	255	3.2	2.8	3.8
	A_1SI	258	3.7	3.2	4.3
	A_2SI	263	3.9	3.4	4.5
	Flu_SI	257	3.3	2.8	3.9

N = number of subjects with pre-and post-vaccination results available
Seroconversion factor is defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s): SPR for HI antibody titer at Days 0 and 21 (ATP cohort for immunogenicity)

Vaccine strain	**Group**	**Timing**	**N**	**SPR**			
				n	**%**	**95% CI**	
						LL	**UL**
A/New Caledonia	A_1NC	PRE	259	160	61.8	55.6	67.7
		PI(D21)	259	252	97.3	94.5	98.9
	A_2NC	PRE	259	163	62.9	56.7	68.8
		PI(D21)	259	246	95.0	91.6	97.3
	Flu_NC	PRE	255	156	61.2	54.9	67.2
		PI(D21)	255	239	93.7	90.0	96.4
A/Solomon Islands	A_1SI	PRE	258	30	11.6	8.0	16.2
		PI(D21)	258	202	78.3	72.8	83.2
	A_2SI	PRE	263	26	9.9	6.6	14.1
		PI(D21)	263	215	81.7	76.5	86.2
	Flu_SI	PRE	257	26	10.1	6.7	14.5
		PI(D21)	257	187	72.8	66.9	78.1
A/Wisconsin	A_1NC	PRE	259	169	65.3	59.1	71.0

		PI(D21)	259	252	97.3	94.5	98.9
	A_2NC	PRE	259	174	67.2	61.1	72.9
		PI(D21)	259	257	99.2	97.2	99.9
	Flu_NC	PRE	255	172	67.5	61.3	73.2
		PI(D21)	255	249	97.6	94.9	99.1
	A_1SI	PRE	258	180	69.8	63.8	75.3
		PI(D21)	258	255	98.8	96.6	99.8
	A_2SI	PRE	263	171	65.0	58.9	70.8
		PI(D21)	263	259	98.5	96.2	99.6
	Flu_SI	PRE	257	158	61.5	55.2	67.5
		PI(D21)	257	239	93.0	89.2	95.8
B/Malaysia	A_1NC	PRE	259	194	74.9	69.2	80.1
		PI(D21)	259	255	98.5	96.1	99.6
	A_2NC	PRE	259	188	72.6	66.7	77.9
		PI(D21)	259	253	97.7	95.0	99.1
	Flu_NC	PRE	255	185	72.5	66.6	77.9
		PI(D21)	255	249	97.6	94.9	99.1
	A_1SI	PRE	258	200	77.5	71.9	82.5
		PI(D21)	258	257	99.6	97.9	100
	A_2SI	PRE	263	184	70.0	64.0	75.4
		PI(D21)	263	260	98.9	96.7	99.8
	Flu_SI	PRE	257	182	70.8	64.8	76.3
		PI(D21)	257	246	95.7	92.5	97.8

N = number of subjects with available results
n (%) = number (percentage) of seroprotected subjects (HI titer ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination dose 1 (Day 0)
PI(D21) = post-vaccination dose 1 (Day 21)

Secondary Outcome Variable (s): Number (percentage) of subjects reporting solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated Cohort)

Symptom	**Intensity**	**A_1NC Group**					**A_2NC Group**					**Flu_NC Group**				
					95 % CI					**95 % CI**					**95 % CI**	
		N	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Ecchymosis	>20mm	268	4	1.5	0.4	3.8	265	4	1.5	0.4	3.8	263	6	2.3	0.8	4.9
	>100mm	268	1	0.4	0.0	2.1	265	0	0.0	0.0	1.4	263	0	0.0	0.0	1.4
Pain	Any	268	165	61.6	55.5	67.4	265	146	55.1	48.9	61.2	263	47	17.9	13.4	23.0
	Grade 3	268	0	0.0	0.0	1.4	265	2	0.8	0.1	2.7	263	0	0.0	0.0	1.4
Redness	>20mm	268	113	42.2	36.2	48.3	265	131	49.4	43.3	55.6	263	59	22.4	17.5	28.0
	>100mm	268	19	7.1	4.3	10.8	265	27	10.2	6.8	14.5	263	4	1.5	0.4	3.8
Swelling	>20mm	268	52	19.4	14.8	24.7	265	53	20.0	15.4	25.3	263	13	4.9	2.7	8.3
	>100mm	268	4	1.5	0.4	3.8	265	6	2.3	0.8	4.9	263	0	0.0	0.0	1.4
		A_1SI Group					**A_2SI Group**					**Flu_SI Group**				
Ecchymosis	>20mm	263	7	2.7	1.1	5.4	268	7	2.6	1.1	5.3	261	10	3.8	1.9	6.9
	>100mm	263	1	0.4	0.0	2.1	268	0	0.0	0.0	1.4	261	1	0.4	0.0	2.1
Pain	Any	263	148	56.3	50.0	62.4	268	144	53.7	47.6	59.8	261	37	14.2	10.2	19.0
	Grade 3	263	1	0.4	0.0	2.1	268	3	1.1	0.2	3.2	261	0	0.0	0.0	1.4
Redness	>20mm	263	108	41.1	35.1	47.3	268	120	44.8	38.7	50.9	261	51	19.5	14.9	24.9
	>100mm	263	19	7.2	4.4	11.1	268	24	9.0	5.8	13.0	261	0	0.0	0.0	1.4
Swelling	>20mm	263	53	20.2	15.5	25.5	268	49	18.3	13.8	23.4	261	18	6.9	4.1	10.7
	>100mm	263	0	0.0	0.0	1.4	268	5	1.9	0.6	4.3	261	0	0.0	0.0	1.4

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 = incidence of specific local symptom irrespective of intensity grade

Grade 3 Pain = Considerable pain at rest, pain that prevented normal everyday activities

Secondary Outcome Variable (s): Number of days with local symptoms of any grade during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated Cohort)

Solicited symptom	Group	N	Mean	Median
Ecchymosis	A_1NC	4	3.5	3.0
	A_2NC	4	4.0	4.0
	Flu_NC	5	4.8	6.0
	A_1SI	7	5.3	6.0
	A_2SI	7	3.0	3.0
	Flu_SI	10	5.1	6.0
Pain	A_1NC	165	2.6	2.0
	A_2NC	146	2.7	2.0
	Flu_NC	47	2.2	2.0
	A_1SI	148	2.7	3.0
	A_2SI	144	2.8	3.0
	Flu_SI	37	2.4	2.0
Redness	A_1NC	113	3.6	3.0
	A_2NC	131	3.8	3.0
	Flu_NC	58	3.3	3.0
	A_1SI	108	3.5	3.0
	A_2SI	120	3.9	4.0
	Flu_SI	50	2.6	2.0
Swelling	A_1NC	52	3.0	3.0
	A_2NC	53	3.2	3.0
	Flu_NC	12	2.8	2.0
	A_1SI	53	2.7	2.0
	A_2SI	49	3.3	3.0
	Flu_SI	18	2.4	2.0

N = number of subjects with the symptom and for whom complete information on duration was available

Secondary Outcome Variable (s): Number (percentage) of subjects reporting solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated Cohort)

Symptom	Intensity/ Relationship	A_1NC Group					A_2NC Group					Flu_NC Group				
					95 % CI					95 % CI					95 % CI	
		N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Arthralgia	Any	268	58	21.6	16.9	27.1	265	36	13.6	9.7	18.3	263	19	7.2	4.4	11.1
	Grade 3	268	3	1.1	0.2	3.2	265	0	0.0	0.0	1.4	263	1	0.4	0.0	2.1
	Related	268	57	21.3	16.5	26.7	265	36	13.6	9.7	18.3	263	16	6.1	3.5	9.7
Fatigue	Any	268	89	33.2	27.6	39.2	265	90	34.0	28.3	40.0	263	39	14.8	10.8	19.7
	Grade 3	268	4	1.5	0.4	3.8	265	3	1.1	0.2	3.3	263	0	0.0	0.0	1.4
	Related	268	89	33.2	27.6	39.2	265	89	33.6	27.9	39.6	263	34	12.9	9.1	17.6
Headache	Any	268	76	28.4	23.0	34.2	265	67	25.3	20.2	31.0	263	26	9.9	6.6	14.1
	Grade 3	268	6	2.2	0.8	4.8	265	3	1.1	0.2	3.3	263	0	0.0	0.0	1.4
	Related	268	73	27.2	22.0	33.0	265	64	24.2	19.1	29.8	263	23	8.7	5.6	12.8
Myalgia	Any	268	85	31.7	26.2	37.7	265	63	23.8	18.8	29.4	263	25	9.5	6.2	13.7
	Grade 3	268	1	0.4	0.0	2.1	265	0	0.0	0.0	1.4	263	1	0.4	0.0	2.1
	Related	268	83	31.0	25.5	36.9	265	63	23.8	18.8	29.4	263	22	8.4	5.3	12.4
Nausea	Any	268	22	8.2	5.2	12.2	265	25	9.4	6.2	13.6	263	14	5.3	2.9	8.8
	Grade 3	268	1	0.4	0.0	2.1	265	0	0.0	0.0	1.4	263	0	0.0	0.0	1.4
	Related	268	20	7.5	4.6	11.3	265	25	9.4	6.2	13.6	263	11	4.2	2.1	7.4
Shivering	Any	268	46	17.2	12.8	22.2	265	25	9.4	6.2	13.6	263	6	2.3	0.8	4.9
	Grade 3	268	1	0.4	0.0	2.1	265	0	0.0	0.0	1.4	263	0	0.0	0.0	1.4
	Related	268	45	16.8	12.5	21.8	265	25	9.4	6.2	13.6	263	3	1.1	0.2	3.3
Temperature (Orally)	≥38°C	268	8	3.0	1.3	5.8	265	6	2.3	0.8	4.9	263	2	0.8	0.1	2.7
	≥39°C	268	1	0.4	0.0	2.1	265	1	0.4	0.0	2.1	263	0	0.0	0.0	1.4

	Related	268	8	3.0	1.3	5.8	265	6	2.3	0.8	4.9	263	1	0.4	0.0	2.1
		A_1SI Group					**A_2SI Group**					**Flu_SI Group**				
Arthralgia	Any	264	39	14.8	10.7	19.6	267	30	11.2	7.7	15.7	261	20	7.7	4.7	11.6
	Grade 3	264	1	0.4	0.0	2.1	267	1	0.4	0.0	2.1	261	1	0.4	0.0	2.1
	Related	264	39	14.8	10.7	19.6	267	30	11.2	7.7	15.7	261	19	7.3	4.4	11.1
Fatigue	Any	264	83	31.4	25.9	37.4	267	82	30.7	25.2	36.6	261	33	12.6	8.9	17.3
	Grade 3	264	4	1.5	0.4	3.8	267	1	0.4	0.0	2.1	261	0	0.0	0.0	1.4
	Related	264	81	30.7	25.2	36.6	267	81	30.3	24.9	36.2	261	32	12.3	8.5	16.9
Headache	Any	264	62	23.5	18.5	29.1	267	58	21.7	16.9	27.2	261	27	10.3	6.9	14.7
	Grade 3	264	2	0.8	0.1	2.7	267	1	0.4	0.0	2.1	261	0	0.0	0.0	1.4
	Related	264	62	23.5	18.5	29.1	267	58	21.7	16.9	27.2	261	23	8.8	5.7	12.9
Myalgia	Any	264	75	28.4	23.0	34.3	267	77	28.8	23.5	34.7	261	29	11.1	7.6	15.6
	Grade 3	264	0	0.0	0.0	1.4	267	2	0.7	0.1	2.7	261	0	0.0	0.0	1.4
	Related	264	75	28.4	23.0	34.3	267	77	28.8	23.5	34.7	261	28	10.7	7.2	15.1
Nausea	Any	264	26	9.8	6.5	14.1	267	18	6.7	4.0	10.4	261	10	3.8	1.9	6.9
	Grade 3	264	1	0.4	0.0	2.1	267	0	0.0	0.0	1.4	261	1	0.4	0.0	2.1
	Related	264	24	9.1	5.9	13.2	267	18	6.7	4.0	10.4	261	9	3.4	1.6	6.4
Shivering	Any	264	45	17.0	12.7	22.1	267	25	9.4	6.2	13.5	261	6	2.3	0.8	4.9
	Grade 3	264	3	1.1	0.2	3.3	267	2	0.7	0.1	2.7	261	0	0.0	0.0	1.4
	Related	264	44	16.7	12.4	21.7	267	25	9.4	6.2	13.5	261	6	2.3	0.8	4.9
Temperature (Orally)	≥38°C	264	12	4.5	2.4	7.8	267	13	4.9	2.6	8.2	261	2	0.8	0.1	2.7
	≥39°C	264	1	0.4	0.0	2.1	267	1	0.4	0.0	2.1	261	0	0.0	0.0	1.4
	Related	264	12	4.5	2.4	7.8	267	13	4.9	2.6	8.2	261	1	0.4	0.0	2.1

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 = incidence of specific general symptom irrespective of intensity grade and relationship to vaccination.
Grade 3 symptom = symptom that prevented normal activity
Related = symptoms considered by the investigator to be causally related to study vaccination

Secondary Outcome Variable (s): Number of days with general symptoms of any grade during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated Cohort)

Solicited symptom	Group	N	Mean	Median
Arthralgia	A_1NC	58	2.5	2.0
	A_2NC	36	2.3	1.5
	Flu_NC	19	3.1	2.0
	A_1SI	39	2.5	2.0
	A_2SI	30	2.4	2.0
	Flu_SI	20	3.4	3.0
Fatigue	A_1NC	89	2.4	2.0
	A_2NC	90	2.1	2.0
	Flu_NC	39	2.9	2.0
	A_1SI	83	2.5	2.0
	A_2SI	82	2.2	1.0
	Flu_SI	33	2.6	2.0
Headache	A_1NC	76	2.1	1.0
	A_2NC	67	1.9	2.0
	Flu_NC	26	2.2	1.5
	A_1SI	62	2.0	1.0
	A_2SI	58	1.9	1.0
	Flu_SI	27	2.8	2.0
Myalgia	A_1NC	85	2.4	2.0
	A_2NC	63	2.2	2.0
	Flu_NC	25	2.5	2.0
	A_1SI	75	2.3	2.0

	A_2SI	77	2.6	2.0
	Flu_SI	29	2.9	2.0
Nausea	A_1NC	22	1.6	1.0
	A_2NC	25	1.8	1.0
	Flu_NC	14	2.3	1.0
	A_1SI	26	1.8	1.0
	A_2SI	18	1.4	1.0
	Flu_SI	10	1.8	1.5
Shivering	A_1NC	46	1.6	1.0
	A_2NC	25	1.2	1.0
	Flu_NC	6	2.2	1.0
	A_1SI	45	1.5	1.0
	A_2SI	25	1.4	1.0
	Flu_SI	6	1.2	1.0
Fever (≥ 38.0°C orally)	A_1NC	4	1.0	1.0
	A_2NC	4	1.0	1.0
	Flu_NC	1	3.0	3.0
	A_1SI	7	1.0	1.0
	A_2SI	9	1.4	1.0

N = number of subjects with the symptom and for whom complete information on duration was available

Secondary Outcome Variable (s): Number (percentage) of subjects reporting the occurrence of unsolicited adverse events resulting in a medically attended visit, within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated Cohort)

MAE	**A_1NC Group N = 269**				**A_2NC Group N = 266**				**Flu_NC Group N = 264**			
	n	**%**	**95% CI**		**n**	**%**	**95% CI**		**n**	**%**	**95% CI**	
			LL	**UL**			**LL**	**UL**			**LL**	**UL**
At least one MAE	7	2.6	1.1	5.3	4	1.5	0.4	3.8	11	4.2	2.1	7.3
At least one Grade 3* MAE	0	0.0	0.0	1.4	1	0.4	0.0	2.1	0	0.0	0.0	1.4
At least one Related** MAE	1	0.4	0.0	2.1	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Pneumonia	0	0.0	0.0	1.4	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Pain in extremity	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Respiratory tract infection	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Angina pectoris	2	0.7	0.1	2.7	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Influenza like illness	1	0.4	0.0	2.1	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Osteoarthritis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Otitis media	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Abdominal pain upper	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Arthritis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Bronchitis	1	0.4	0.0	2.1	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Chondrocalcinosis pyrophosphate	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Conjunctivitis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Contusion	0	0.0	0.0	1.4	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Cough	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Cystitis	0	0.0	0.0	1.4	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Diarrhea	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Dizziness	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Ecchymosis	1	0.4	0.0	2.1	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Epilepsy	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Fatigue	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Flatulence	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Gingival abscess	1	0.4	0.0	2.1	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Glaucoma	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Gout	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4

Hypertension	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Injection site warmth	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Insomnia	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Localized infection	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Nasopharyngitis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Pharyngitis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Pharyngolaryngeal pain	1	0.4	0.0	2.1	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Podagra	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Polymyalgia rheumatica	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Prostatitis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Sinusitis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Tooth infection	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Transient ischemic attack	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Upper respiratory tract infection	1	0.4	0.0	2.1	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Urinary tract infection	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Vitreous detachment	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
	A_1SI Group N = 264				**A_2SI Group N = 268**				**Flu_SI Group N = 263**			
At least one MAE	5	1.9	0.6	4.4	11	4.1	2.1	7.2	9	3.4	1.6	6.4
At least one Grade 3* MAE	1	0.4	0.0	2.1	1	0.4	0.0	2.1	1	0.4	0.0	2.1
At least one Related** MAE	0	0.0	0.0	1.4	4	1.5	0.4	3.8	2	0.8	0.1	2.7
Pneumonia	0	0.0	0.0	1.4	3	1.1	0.2	3.2	0	0.0	0.0	1.4
Pain in extremity	1	0.4	0.0	2.1	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Respiratory tract infection	0	0.0	0.0	1.4	2	0.7	0.1	2.7	1	0.4	0.0	2.1
Angina pectoris	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Influenza like illness	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Osteoarthritis	1	0.4	0.0	2.1	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Otitis media	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Abdominal pain upper	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Arthritis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Bronchitis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Chondrocalcinosis pyrophosphate	1	0.4	0.0	2.1	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Conjunctivitis	0	0.0	0.0	1.4	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Contusion	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Cough	1	0.4	0.0	2.1	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Cystitis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Diarrhea	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Dizziness	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Ecchymosis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Epilepsy	1	0.4	0.0	2.1	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Fatigue	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Flatulence	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Gingival abscess	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Glaucoma	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Gout	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Hypertension	0	0.0	0.0	1.4	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Injection site warmth	0	0.0	0.0	1.4	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Insomnia	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Localized infection	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Nasopharyngitis	0	0.0	0.0	1.4	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Pharyngitis	0	0.0	0.0	1.4	1	0.4	0.0	2.1	0	0.0	0.0	1.4
Pharyngolaryngeal pain	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Podagra	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1

Polymyalgia rheumatica	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Prostatitis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Sinusitis	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Tooth infection	0	0.0	0.0	1.4	0	0.0	0.0	1.4	1	0.4	0.0	2.1
Transient ischemic attack	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Upper respiratory tract infection	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Urinary tract infection	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4
Vitreous detachment	0	0.0	0.0	1.4	0	0.0	0.0	1.4	0	0.0	0.0	1.4

At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with the 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
* Grade 3 MAE: MAE which prevented normal, everyday activities.
** Related MAE: MAE assessed by the investigator as causally related to the study vaccination

Safety Results: Number (percentage) of subjects with unsolicited adverse events within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated Cohort)

Most frequent adverse events– On-Therapy (occurring within Days 0-20 following vaccination)	**A_1NC Group N = 269**	**A_2NC Group N = 266**	**Flu_NC Group N = 264**	**A_1SI Group N = 264**	**A_2SI Group N = 268**	**Flu_SI Group N = 263**
Subjects with any AE(s), n (%)	43 (16.0)	39 (14.7)	36 (13.6)	45 (17.0)	53 (19.8)	29 (11.0)
Subjects with any grade 3**AE(s), n (%)	2 (0.7)	1 (0.4)	0 (0.0)	3 (1.1)	2 (0.7)	1 (0.4)
Subjects with any related** AE(s), n (%)	22 (8.2)	21 (7.9)	11 (4.2)	28 (10.6)	30 (11.2)	12 (4.6)
Injection site pruritus	12 (4.5)	14 (5.3)	7 (2.7)	13 (4.9)	15 (5.6)	5 (1.9)
Nasopharyngitis	4 (1.5)	5 (1.9)	5 (1.9)	4 (1.5)	4 (1.5)	10 (3.8)
Cough	3 (1.1)	2 (0.8)	-	3 (1.1)	4 (1.5)	2 (0.8)
Diarrhea	-	-	3 (1.1)	-	5 (1.9)	-
Injection site warmth	2 (0.7)	-	-	-	4 (1.5)	-
Rhinitis	2 (0.7)	-	4 (1.5)	-	-	-
Dizziness	-	2 (0.8)	-	-	-	2 (0.8)
Hyperhidrosis	2 (0.7)	2 (0.8)	-	-	-	-
Angina pectoris	3 (1.1)	-	-	-	-	-
Headache	-	-	3 (1.1)	-	-	-
Back pain	-	2 (0.8)	-	-	-	-
Gout	-	-	-	-	-	2 (0.8)
Injection site induration	2 (0.7)	-	-	-	-	-
Injection site reaction	-	-	-	2 (0.8)	-	-
Myalgia	-	-	-	2 (0.8)	-	-
Somnolence	-	-	-	2 (0.8)	-	-
Vertigo	-	-	-	2 (0.8)	-	-

Counting rule applied: As there were more than 30 subjects per treatment group and > 3 groups, only the 5 most frequent events in each treatment group are to be listed.
-: Implies that the adverse event was not reported in the particular group or that the adverse event was reported in the particular group but did not fall within the pre-defined counting rule of 5 most frequent events for that group.
* Grade 3 AE: AE which prevented normal, everyday activities.
** Related AE: AE assessed by the investigator as causally related to the study vaccination

Safety Results: Number (%) of subjects with serious adverse events during the entire study period (Total Vaccinated Cohort)

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

All SAEs	**A_1NC Group N = 269**	**A_2NC Group N = 266**	**Flu_NC Group N = 264**	**A_1SI Group N = 264**	**A_2SI Group N = 268**	**Flu_SI Group N = 263**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	2 (0.7) [0]	0 (0.0) [0]	0 (0.0) [0]	2 (0.8) [0]	0 (0.0) [0]	1 (0.4) [0]
Dehydration	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Epilepsy	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]

Fatigue	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]
Lung cancer metastatic	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Wrist fracture	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**A_1NC Group N = 269**	**A_2NC Group N = 266**	**Flu_NC Group N = 264**	**A_1SI Group N = 264**	**A_2SI Group N = 268**	**Flu_SI Group N = 263**
Subjects with fatal SAEs, n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:
At Day 21, the adjusted GMTs of HI antibody titers were 103.3 and 107.3 for the A/ New Caledonia H1N1 strain in the A_1NC and A_2NC groups, respectively, and were 102.0 and 111.8 for the A/Solomon Islands H1N1 strain in the A_1SI and A_2SI groups, respectively.
During the 21-day post-vaccination period, unsolicited AEs were reported by 43 (16.0%), 39 (14.7%), 36 (13.6%), 45 (17.0%), 53 (19.8) and 29 (11.0%) subjects in the A_1NC, A_2NC, Flu_NC, A_1SI, A_2SI and Flu_SI groups respectively. SAEs were reported by 2 (0.7%), 2 (0.8%) and 1 (0.4%) subjects in the A_1NC, A_1SI, and Flu_SI groups respectively; all the SAEs were assessed by the investigators as not related to the study vaccination. No fatal SAEs were reported throughout the study.

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