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.: 104886 (FluAS25-003)

Title: An open, randomized phase I/II study to demonstrate the non inferiority in terms of cellular mediated immune response of GlaxoSmithKline Biologicals influenza candidate vaccines containing various adjuvants administered in elderly population (aged 65 years and older) as compared to *Fluarix*™ (known as α-Rix™ in Belgium) administered in adults (18-40 years).
Fluarix™ (α-Rix™): GlaxoSmithKline Biologicals' licensed influenza vaccine.

Rationale: The aim of this study was to demonstrate the non inferiority of the cell-mediated immune (CMI) response in elderly population immunized with adjuvanted influenza candidate vaccines as compared to the cell-mediated immune response in young adults receiving the licensed influenza vaccine. For immunogenicity and safety evaluations, 1 group of adults aged 18 to 40 years and 1 group of elderly aged 65 years and older received a dose of a licensed flu vaccine and formed respectively a control and a reference group in this trial.

Phase: I/II

Study Period: 10 October 2005 to 22 May 2006

Study Design: Single centre, open, partially randomized* controlled study with 6 groups.
*Subjects aged 18-40 years were not randomized; subjects (aged 65 years and older) were randomized (3:3:3:3:2) into 5 groups.

Centres: 1 study centre in Belgium

Indication: Immunisation against influenza disease in subjects aged 18 to 40 years and elderly aged 65 years and older.

Treatment: The study groups were as follows:

- Group 1: subjects (aged 18-40 years) received 1 dose of the licensed influenza vaccine
- Group 2: subjects (aged ≥ 65 years) received 1 dose of the licensed influenza vaccine
- Group 3: subjects (aged ≥ 65 years) received 1 dose of the adjuvanted influenza vaccine FluAS25
- Group 4: subjects (aged ≥ 65 years) received 1 dose of the adjuvanted influenza vaccine FluAS50
- Group 5: subjects (aged ≥ 65 years) received 1 dose of the adjuvanted influenza vaccine FluAS01B
- Group 6: subjects (aged ≥ 65 years) received 1 dose of the adjuvanted influenza vaccine FluAS01E

Vaccines were administered intramuscularly in the deltoid region of the non dominant arm.

Objectives: To demonstrate the non inferiority 21 days post-vaccination of the influenza adjuvanted vaccines (FluAS25, FluAS50, FluAS01B and FluAS01E) administered to elderly subjects (aged 65 years and older) as compared to the licensed influenza vaccine administered to adults (aged 18-40 years) in terms of frequency of influenza-specific CD4 T-cells producing at least 2 different cytokines (CD40L, IL-2, TNF-α or IFN-γ).

Primary Outcome/Efficacy Variable:
At Day 21: CMI response in all subjects in terms of frequency of influenza-specific CD4 T-lymphocyte per 10^6 in tests producing at least 2 different cytokines (IL-2, IFN-γ, TNF-α and CD40L).

Secondary Outcome/Efficacy Variable(s):
Immunogenicity
Observed variables:
At Days 0, 21, 90 and 180: serum haemagglutination-inhibition (HI) antibody titres, tested separately against each of the three influenza virus strains represented in the vaccine (anti-H1N1, anti-H3N2 & anti-B-antibodies).
Derived variables (with 95% confidence intervals):

- Geometric mean titres (GMTs) of serum HI antibodies pre- and post-vaccination at Days 0, 21, 90 and 180
- Seroconversion rates* at Day 21, 90 and 180
- Seroconversion factors** at Day 21, 90 and 180
- Seroprotection rates*** at Days 0 and 21, 90 and 180

* Seroconversion rates (SCR) defined as the proportion of subjects with either a pre-vaccination HI titre <1:10 and a post-vaccination titre ≥ 1:40, or a pre-vaccination titre ≥ 1:10 and a minimum 4-fold increase at post-vaccination titre.
** Seroconversion factors (SCF) defined as the fold increase in serum HI GMTs on post-vaccination compared to pre-vaccination time point.
*** Seroprotection rates (SPR) defined as the proportion of subjects with a serum HI titre ≥1:40.

Safety

- Percentage, intensity 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.
- Percentage, intensity and relationship to vaccination of unsolicited local and general signs and symptoms during a 21-day follow-up period (i.e. day of vaccination and 20 subsequent days) after vaccination.
- Occurrence of serious adverse events (SAEs) during the entire study.

Statistical Methods:

The analyses were performed on the Total Vaccinated cohort, the According-To-Protocol (ATP) cohort for immunogenicity and the ATP cohort for persistence.

- The Total Vaccinated cohort included all subjects who received the vaccine dose.
- The ATP cohort for immunogenicity 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 measures were available. This included subjects for whom assay results were available for antibodies against at least 1 study vaccine antigen component after vaccination.
- The ATP cohort for persistence included all subjects from the ATP cohort for immunogenicity who had not received any medication or vaccine forbidden by the protocol during the study period and who had available assay results for at least 1 tested antigen at the Day 90 or Day 180 time points.

Analysis of immunogenicity:

The analysis of immunogenicity was performed on the ATP cohort for immunogenicity for results at pre-vaccination and at Day 21 and on the ATP cohort for persistence for results at Days 90 and 180.

The non-inferiority was shown for each influenza adjuvanted candidate vaccine group if the Upper Limit (UL) of the two-sided 98.75% confidence interval (CI) on Geometric Mean ratio (between Group 1 and the 4 influenza adjuvanted candidate vaccine groups, i.e., Groups 3 - 6) of influenza-specific CD4 T-cells producing at least 2 cytokines on Day 21 was below 2.0.

The frequency of influenza-specific CD4 T-cells, after in vitro restimulation with pooled vaccine antigens were tabulated with the geometric mean (GM) and the standard deviation at Days 0 and 21.

Geometric mean titres (GMTs), seropositivity rates and seroprotection rates for HI antibodies were summarized at all time points with 95% confidence interval (CI). Seroconversion rates and seroconversion factor were summarized for HI antibodies at Days 21, 90 and 180 with 95%CI.

Analysis of safety:

The analysis of safety was performed on the Total Vaccinated cohort.

For each solicited local and general symptom, the percentage of subjects with the symptom reported during the 7-day (Days 0-6) follow-up period was summarized after vaccine dose. The same calculations were performed for symptoms of any intensity, those with Grade 3 intensity and for solicited general symptoms assessed by the investigator as related to vaccination.

The percentage of subjects reporting unsolicited adverse events (AEs) within 21 days (Days 0-20) following vaccination was tabulated according to the Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms. The same tabulation was performed for Grade 3 unsolicited AEs and for unsolicited AEs that were assessed by the investigators to be related to vaccination.

SAEs were tabulated according to the MedDRA Preferred Terms for each group during the entire study period.

Study Population: Male or female subjects between 18 and 40 years or aged 65 years or older at the time of the vaccination, free of obvious health problems as established by medical history and clinical examination before entering into the study. Written informed consent was obtained from the subject prior to study entry.

Number of subjects	**Group 1**	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**
Planned, N	75	50	75	75	75	75
Randomised, N (Total Vaccinated cohort)	75	50	75	75	75	75
Completed, n (%)	75 (100)	50 (100)	75 (100)	75 (100)	75 (100)	73 (97.3)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.7)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.7)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	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)	0 (0.0)	0 (0.0)
Demographics	**Group 1**	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**
N (Total Vaccinated Cohort)	75	50	75	75	75	75
Females:Males	46:29	19:31	29:46	34:41	36:39	29:46

Mean Age, years (SD)	25.9 (5.47)	69.3 (3.31)	69.2 (2.98)	69.1 (3.51)	69.5 (3.30)	69.5 (4.06)
White/Caucasian, n (%)	72 (96.0)	50 (100)	75 (100)	75 (100)	75 (100)	75 (100)

Primary Efficacy Results:
Geometric Mean ratio of influenza-specific CD4 T-cells producing at least 2 cytokines after in vitro restimulation with pooled vaccine antigens, on Day 21 (ATP cohort for immunogenicity)

Group 1		**Group 3**		**GM ratio (Group 1/ Group 3)**		
N	**GM**	**N**	**GM**	**Value**	**98.75% CI**	
					LL	**UL***
74	2974.7	70	3298.7	0.90	0.70	1.16*
Group 1		**Group 4**		**GM ratio (Group 1/ Group 4)**		
N	**GM**	**N**	**GM**	**Value**	**98. 75% CI**	
					LL	**UL***
74	2935.4	72	2784.3	1.05	0.71	1.56*
Group 1		**Group 5**		**GM ratio (Group 1/ Group 5)**		
N	**GM**	**N**	**GM**	**Value**	**98. 75% CI**	
					LL	**UL***
74	2844.8	71	2725.6	1.04	0.79	1.38*
Group 1		**Group 6**		**GM ratio (Group 1/ Group 6)**		
N	**GM**	**N**	**GM**	**Value**	**98. 75% CI**	
					LL	**UL***
74	2879.6	74	2697.0	1.07	0.79	1.44*

N: number of subjects with both pre- and post-vaccination results available
GM ratio: geometric mean ratio adjusted for baseline (pre-vaccination frequency)
98.75% CI: 98.75% confidence interval; LL: Lower limit; UL: Upper limit
* Criterion for non-inferiority: UL of the 2-sided 98.75% CI on GM ratio of influenza-specific T-cells (between Group 1 and the 4 influenza adjuvanted candidate vaccine groups) < 2.0

Primary Efficacy Results: Frequency of influenza-specific CD4 T-cells after in vitro restimulation with pooled vaccine antigens at pre-vaccination and at Day 21 (ATP cohort for immunogenicity)

Test Description	**Group**	**Timing**	**N**	**N miss**	**GM**	**SD**	**Median**
All Doubles	**Group 1**	Pre	74	1	1739.53	1190.57	1737.00
		PI(D21)*	75	0	3229.25	1643.20	3538.00
	Group 2	Pre	48	1	981.57	777.57	1153.00
		PI(D21)*	49	0	1646.05	1557.22	1637.00
	Group 3	Pre	72	2	1022.92	771.24	1131.00
		PI(D21)*	70	4	3056.06	2059.35	3123.00
	Group 4	Pre	73	2	1045.53	773.66	1066.00
		PI(D21)*	73	2	2589.31	2110.15	3002.00
	Group 5	Pre	72	3	963.82	832.87	993.00
		PI(D21)*	74	1	2454.93	1758.20	2442.00
	Group 6	Pre	75	0	992.26	846.24	1031.00
		PI(D21)*	74	1	2428.78	2693.71	2489.00
CD40L	**Group 1**	Pre	74	1	1708.23	1161.98	1716.00
		PI(D21)	75	0	3184.90	1626.38	3498.00
	Group 2	Pre	48	1	960.31	775.97	1155.00
		PI(D21)	49	0	1598.34	1557.36	1524.00
	Group 3	Pre	72	2	1009.36	757.59	1095.50
		PI(D21)	70	4	3000.48	1993.91	3104.00
	Group 4	Pre	73	2	1031.69	756.84	1060.00
		PI(D21)	73	2	2524.08	1955.70	3002.00
	Group 5	Pre	72	3	961.47	818.34	987.00
		PI(D21)	74	1	2393.11	1703.55	2444.00
	Group 6	Pre	75	0	974.67	846.51	1021.00
		PI(D21)	74	1	2344.99	2644.06	2458.50

IFN-γ	**Group 1**	Pre	74	1	1229.24	1009.93	1236.50
		PI(D21)	75	0	2231.99	1330.79	2564.00
	Group 2	Pre	48	1	536.29	569.54	694.50
		PI(D21)	49	0	993.03	1060.45	1144.00
	Group 3	Pre	72	2	636.60	589.17	720.00
		PI(D21)	70	4	1933.34	1654.67	1874.50
	Group 4	Pre	73	2	634.60	576.45	634.00
		PI(D21)	73	2	1793.56	1518.55	2015.00
	Group 5	Pre	72	3	635.47	621.59	648.00
		PI(D21)	74	1	1593.68	1170.41	1476.00
	Group 6	Pre	75	0	578.83	609.11	607.00
		PI(D21)	74	1	1568.42	1938.37	1611.00
IL2	**Group 1**	Pre	74	1	1515.11	1042.11	1538.50
		PI(D21)	75	0	2795.81	1453.94	3084.00
	Group 2	Pre	48	1	846.26	729.25	986.50
		PI(D21)	49	0	1392.14	1413.99	1513.00
	Group 3	Pre	72	2	921.13	709.03	1002.50
		PI(D21)	70	4	2568.08	1758.56	2641.00
	Group 4	Pre	73	2	940.01	704.54	1005.00
		PI(D21)	73	2	2162.63	1787.14	2633.00
	Group 5	Pre	72	3	866.08	786.16	856.50
		PI(D21)	74	1	2063.58	1529.84	2061.50
	Group 6	Pre	75	0	849.35	792.65	951.00
		PI(D21)	74	1	1953.09	2385.11	2101.50
TFN-α	**Group 1**	Pre	74	1	1139.68	1041.68	1101.50
		PI(D21)	75	0	1704.02	1145.81	1829.00
	Group 2	Pre	48	1	579.15	517.68	682.50
		PI(D21)	49	0	915.70	924.44	937.00
	Group 3	Pre	72	2	658.71	546.96	690.00
		PI(D21)	70	4	1674.13	1502.22	1642.50
	Group 4	Pre	73	2	651.02	556.42	675.00
		PI(D21)	73	2	1377.22	1348.73	1722.00
	Group 5	Pre	72	3	525.19	699.16	577.00
		PI(D21)	74	1	1317.03	1142.85	1254.00
	Group 6	Pre	75	0	605.88	612.85	612.00
		PI(D21)	74	1	1314.91	1642.87	1275.00

N: number of subjects with available results
N miss: number of subjects with missing results
GM: Geometric Mean
SD: Standard Deviation
All doubles: T-cells producing at least 2 cytokines;
CD40L: T-cells producing at least CD40L and another cytokine (IL-2, IFN-γ and TNF-α)
IFN-γ: T-cells producing at least IFN-γ and another cytokine (IL-2, CD40L and TNF-α)
IL-2: T-cells producing at least IL-2 and another cytokine (TNF-α, CD40L and IFN-γ)
TNF-α: T-cells producing at least TNF-α and another cytokine (IL-2, CD40L and IFN-γ)
Pre: pre-vaccination
PI(D21): post-vaccination blood sample at Day 21
* Primary outcome variable

Secondary Outcome Variable(s):
Seropositivity rates and GMTs for HI antibodies at pre-vaccination and at Day 21 (ATP cohort for immunogenicity)

Antibody	**Group**	**Timing**	**N**	**≥ 1:10**				**GMT**		
				n	**%**	**95% CI**			**95% CI**	
						LL	**UL**	**value**	**LL**	**UL**
A/New Caledonia	**Group 1**	Pre	75	42	56.0	44.1	67.5	20.7	14.3	30.2
		PI(D21)	75	75	100	95.2	100	728.4	549.2	966.0
	Group 2	Pre	49	38	77.6	63.4	88.2	23.5	16.2	34.1

		PI(D21)	49	48	98.0	89.1	99.9	86.5	58.7	127.4
	Group 3	Pre	74	53	71.6	59.9	81.5	23.9	17.6	32.5
		PI(D21)	74	73	98.6	92.7	100	151.9	115.1	200.5
	Group 4	Pre	75	55	73.3	61.9	82.9	24.1	18.1	32.3
		PI(D21)	75	75	100	95.2	100	223.2	170.5	292.3
	Group 5	Pre	75	62	82.7	72.2	90.4	33.9	24.5	46.9
		PI(D21)	75	75	100	95.2	100	151.4	118.4	193.6
	Group 6	Pre	75	61	81.3	70.7	89.4	33.5	24.5	45.9
		PI(D21)	75	75	100	95.2	100	166.8	130.1	213.9
A/New York	**Group 1**	Pre	75	50	66.7	54.8	77.1	16.5	12.8	21.4
		PI(D21)	75	75	100	95.2	100	151.3	119.8	191.1
	Group 2	Pre	49	27	55.1	40.2	69.3	12.0	9.2	15.6
		PI(D21)	49	46	93.9	83.1	98.7	98.9	65.1	150.3
	Group 3	Pre	74	39	52.7	40.7	64.4	13.0	10.1	16.7
		PI(D21)	74	72	97.3	90.6	99.7	249.7	186.2	334.8
	Group 4	Pre	75	44	58.7	46.7	69.9	16.0	12.1	21.2
		PI(D21)	75	73	97.3	90.7	99.7	240.3	176.0	328.0
	Group 5	Pre	75	49	65.3	53.5	76.0	15.5	12.3	19.6
		PI(D21)	75	75	100	95.2	100	202.5	157.6	260.2
	Group 6	Pre	75	48	64.0	52.1	74.8	17.2	12.9	22.9
		PI(D21)	75	73	97.3	90.7	99.7	249.3	181.7	342.0
B/Jiangsu	**Group 1**	Pre	75	57	76.0	64.7	85.1	25.2	18.9	33.6
		PI(D21)	75	75	100	95.2	100	349.5	270.7	451.2
	Group 2	Pre	49	40	81.6	68.0	91.2	31.4	21.8	45.2
		PI(D21)	49	49	100	92.7	100	134.1	100.2	179.4
	Group 3	Pre	74	58	78.4	67.3	87.1	27.7	21.1	36.5
		PI(D21)	74	74	100	95.1	100	237.1	185.1	303.8
	Group 4	Pre	75	62	82.7	72.2	90.4	38.7	27.7	54.0
		PI(D21)	75	75	100	95.2	100	293.1	234.1	366.8
	Group 5	Pre	75	66	88.0	78.4	94.4	39.2	30.2	51.0
		PI(D21)	75	75	100	95.2	100	205.4	171.3	246.2
	Group 6	Pre	75	63	84.0	73.7	91.4	30.0	23.2	38.8
		PI(D21)	75	75	100	95.2	100	202.6	161.2	254.6

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(D21): post-vaccination blood sample at Day 21

Secondary Outcome Variable(s):
Seropositivity rates and GMTs for HI antibodies at Day 90 and at Day 180 (ATP cohort for persistence)

Antibody	**Group**	**Timing**	**N**	**≥ 1:10**				**GMT**		
				n	**%**	**95% CI**			**95% CI**	
						LL	**UL**	**value**	**LL**	**UL**
A/New Caledonia	**Group 1**	PI(D90)	75	75	100	95.2	100	496.4	370.1	665.7
		PI(D180)	74	74	100	95.1	100	354.7	260.3	483.5
	Group 2	PI(D90)	49	48	98.0	89.1	99.9	76.7	54.1	108.8
		PI(D180)	49	48	98.0	89.1	99.9	62.9	45.4	87.1
	Group 3	PI(D90)	74	73	98.6	92.7	100	94.2	74.7	118.8
		PI(D180)	74	73	98.6	92.7	100	66.9	53.3	84.1
	Group 4	PI(D90)	74	74	100	95.1	100	135.3	102.4	178.7
		PI(D180)	74	74	100	95.1	100	89.1	67.2	118.2
	Group 5	PI(D90)	74	74	100	95.1	100	97.4	78.1	121.4
		PI(D180)	74	74	100	95.1	100	70.5	56.5	87.9
	Group 6	PI(D90)	74	74	100	95.1	100	105.9	84.3	133.0
		PI(D180)	73	73	100	95.1	100	81.9	65.1	103.0

A/New York	**Group 1**	PI(D90)	75	74	98.7	92.8	100	130.5	100.8	168.9
		PI(D180)	74	73	98.6	92.7	100	96.5	73.5	126.6
	Group 2	PI(D90)	49	46	93.9	83.1	98.7	60.7	41.4	89.1
		PI(D180)	49	45	91.8	80.4	97.7	43.8	30.2	63.7
	Group 3	PI(D90)	74	72	97.3	90.6	99.7	99.2	75.2	131.0
		PI(D180)	74	71	95.9	88.6	99.2	66.3	50.5	87.1
	Group 4	PI(D90)	74	73	98.6	92.7	100	116.4	88.6	153.0
		PI(D180)	74	72	97.3	90.6	99.7	71.8	55.6	92.7
	Group 5	PI(D90)	74	74	100	95.1	100	93.3	73.2	119.0
		PI(D180)	74	74	100	95.1	100	59.5	46.8	75.6
	Group 6	PI(D90)	74	71	95.9	88.6	99.2	114.8	85.1	154.8
		PI(D180)	73	70	95.9	88.5	99.1	70.4	53.0	93.4
B/Jiangsu	**Group 1**	PI(D90)	75	75	100	95.2	100	208.2	161.0	269.3
		PI(D180)	74	74	100	95.1	100	140.3	109.0	180.5
	Group 2	PI(D90)	49	49	100	92.7	100	131.3	98.1	175.8
		PI(D180)	49	49	100	92.7	100	94.5	69.2	129.0
	Group 3	PI(D90)	74	73	98.6	92.7	100	145.6	110.7	191.6
		PI(D180)	74	72	97.3	90.6	99.7	91.6	71.4	117.6
	Group 4	PI(D90)	74	74	100	95.1	100	213.0	173.0	262.1
		PI(D180)	74	74	100	95.1	100	128.0	102.6	159.8
	Group 5	PI(D90)	74	74	100	95.1	100	147.1	120.7	179.2
		PI(D180)	74	74	100	95.1	100	111.0	88.3	139.6
	Group 6	PI(D90)	74	74	100	95.1	100	144.2	116.6	178.4
		PI(D180)	73	73	100	95.1	100	91.4	74.3	112.3

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(D90) = Post-vaccination blood sample at Day 90
PI(D180) = Post-vaccination blood sample at Day 180

Secondary Outcome Variable(s):
Seroconversion rates (SCR) for HI antibodies at Day 21 (ATP cohort for immunogenicity)

Vaccine strain	**Group**	**N**	**SCR**			
			n	**%**	**95%CI**	
					LL	**UL**
A/New Caledonia	**Group 1**	75	58	77.3	66.2	86.2
	Group 2	49	15	30.6	18.3	45.4
	Group 3	74	41	55.4	43.4	67.0
	Group 4	75	56	74.7	63.3	84.0
	Group 5	75	36	48.0	36.3	59.8
	Group 6	75	39	52.0	40.2	63.7
A/New York	**Group 1**	75	57	76.0	64.7	85.1
	Group 2	49	34	69.4	54.6	81.7
	Group 3	74	67	90.5	81.5	96.1
	Group 4	75	62	82.7	72.2	90.4
	Group 5	75	64	85.3	75.3	92.4
	Group 6	75	60	80.0	69.2	88.4
B/Jiangsu	**Group 1**	75	61	81.3	70.7	89.4
	Group 2	49	22	44.9	30.7	59.8
	Group 3	74	54	73.0	61.4	82.6
	Group 4	75	50	66.7	54.8	77.1
	Group 5	75	49	65.3	53.5	76.0
	Group 6	75	53	70.7	59.0	80.6

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 available results
n (%)= number (percentage) of subjects who seroconverted
95%CI: 95% confidence interval; LL: Lower limit; UL: Upper limit

Secondary Outcome Variable(s):
Seroconversion rates (SCR) for HI antibodies at Day 90 and Day 180 (ATP cohort for persistence)

Vaccine strain	Group	Timing	N	SCR			
				n	%	95% CI	
						LL	UL
A/New Caledonia	**Group 1**	PI(D90)	75	56	74.7	63.3	84.0
		PI(D180)	74	54	73.0	61.4	82.6
	Group 2	PI(D90)	49	16	32.7	19.9	47.5
		PI(D180)	49	10	20.4	10.2	34.3
	Group 3	PI(D90)	74	32	43.2	31.8	55.3
		PI(D180)	74	20	27.0	17.4	38.6
	Group 4	PI(D90)	74	38	51.4	39.4	63.1
		PI(D180)	74	25	33.8	23.2	45.7
	Group 5	PI(D90)	74	25	33.8	23.2	45.7
		PI(D180)	74	16	21.6	12.9	32.7
	Group 6	PI(D90)	74	28	37.8	26.8	49.9
		PI(D180)	73	15	20.5	12.0	31.6
A/New York	**Group 1**	PI(D90)	75	55	73.3	61.9	82.9
		PI(D180)	74	48	64.9	52.9	75.6
	Group 2	PI(D90)	49	29	59.2	44.2	73.0
		PI(D180)	49	17	34.7	21.7	49.6
	Group 3	PI(D90)	74	56	75.7	64.3	84.9
		PI(D180)	74	40	54.1	42.1	65.7
	Group 4	PI(D90)	74	55	74.3	62.8	83.8
		PI(D180)	74	40	54.1	42.1	65.7
	Group 5	PI(D90)	74	47	63.5	51.5	74.4
		PI(D180)	74	35	47.3	35.6	59.3
	Group 6	PI(D90)	74	48	64.9	52.9	75.6
		PI(D180)	73	35	47.9	36.1	60.0
B/Jiangsu	**Group 1**	PI(D90)	75	53	70.7	59.0	80.6
		PI(D180)	74	45	60.8	48.8	72.0
	Group 2	PI(D90)	49	16	32.7	19.9	47.5
		PI(D180)	49	16	32.7	19.9	47.5
	Group 3	PI(D90)	74	38	51.4	39.4	63.1
		PI(D180)	74	28	37.8	26.8	49.9
	Group 4	PI(D90)	74	44	59.5	47.4	70.7
		PI(D180)	74	33	44.6	33.0	56.6
	Group 5	PI(D90)	74	33	44.6	33.0	56.6
		PI(D180)	74	26	35.1	24.4	47.1
	Group 6	PI(D90)	74	44	59.5	47.4	70.7
		PI(D180)	73	25	34.2	23.5	46.3

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 available results
n (%)= number (percentage) of subjects who seroconverted
95%CI: 95% confidence interval; LL: Lower limit; UL: Upper limit
PI(D90) = Post-vaccination blood sample at Day 90
PI(D180) = Post-vaccination blood sample at Day 180

Secondary Outcome Variable(s):
Seroconversion factor (SCF) for HI antibodies at post-vaccination (Day 21) (ATP cohort for immunogenicity)

Vaccine strain	Group	N	SCF

			Value	95%CI	
				LL	UL
A/New Caledonia	**Group 1**	75	35.1	21.9	56.4
	Group 2	49	3.7	2.4	5.7
	Group 3	74	6.4	4.5	9.0
	Group 4	75	9.2	6.4	13.3
	Group 5	75	4.5	3.3	6.1
	Group 6	75	5.0	3.6	6.9
A/New York	**Group 1**	75	9.2	7.1	11.8
	Group 2	49	8.2	5.7	11.8
	Group 3	74	19.2	14.6	25.3
	Group 4	75	15.0	11.2	20.2
	Group 5	75	13.1	10.0	17.1
	Group 6	75	14.5	10.4	20.2
B/Jiangsu	**Group 1**	75	13.9	10.1	19.1
	Group 2	49	4.3	3.0	6.1
	Group 3	74	8.5	6.5	11.2
	Group 4	75	7.6	5.6	10.2
	Group 5	75	5.2	4.2	6.5
	Group 6	75	6.7	5.1	8.9

N = number of subjects with available results
SCF= Fold increase in HI GMTs on post-vaccination compared to pre-vaccination time point.
95%CI: 95% confidence interval; LL: Lower limit; UL: Upper limit

Secondary Outcome Variable(s):
Seroconversion factor (SCF) for HI antibody titre at Day 90 and Day 180 (ATP cohort for persistence)

Vaccine strain	Group	Timing	N	SCF		
				Value	95% CI	
					LL	UL
A/New Caledonia	**Group 1**	PI(D90)	75	23.9	15.6	36.8
		PI(D180)	74	17.1	11.2	26.0
	Group 2	PI(D90)	49	3.3	2.3	4.7
		PI(D180)	49	2.7	1.9	3.7
	Group 3	PI(D90)	74	3.9	3.0	5.2
		PI(D180)	74	2.8	2.2	3.6
	Group 4	PI(D90)	74	5.7	4.0	8.1
		PI(D180)	74	3.7	2.6	5.4
	Group 5	PI(D90)	74	2.9	2.2	3.9
		PI(D180)	74	2.1	1.6	2.8
	Group 6	PI(D90)	74	3.1	2.3	4.1
		PI(D180)	73	2.4	1.8	3.2
A/New York	**Group 1**	PI(D90)	75	7.9	6.3	10.0
		PI(D180)	74	5.8	4.7	7.3
	Group 2	PI(D90)	49	5.1	3.7	7.0
		PI(D180)	49	3.7	2.7	4.9
	Group 3	PI(D90)	74	7.6	6.1	9.6
		PI(D180)	74	5.1	4.2	6.3
	Group 4	PI(D90)	74	7.3	5.7	9.2
		PI(D180)	74	4.5	3.5	5.8
	Group 5	PI(D90)	74	6.2	4.8	7.9
		PI(D180)	74	3.9	3.1	5.0
	Group 6	PI(D90)	74	6.6	5.0	8.6
		PI(D180)	73	4.1	3.2	5.3
B/Jiangsu	**Group 1**	PI(D90)	75	8.3	6.2	11.0
		PI(D180)	74	5.4	4.3	7.0
	Group 2	PI(D90)	49	4.2	3.0	5.9

		PI(D180)	49	3.0	2.2	4.1
	Group 3	PI(D90)	74	5.3	4.2	6.6
		PI(D180)	74	3.3	2.6	4.1
	Group 4	PI(D90)	74	5.6	4.3	7.2
		PI(D180)	74	3.3	2.6	4.3
	Group 5	PI(D90)	74	3.7	3.0	4.6
		PI(D180)	74	2.8	2.2	3.6
	Group 6	PI(D90)	74	4.8	3.7	6.1
		PI(D180)	73	3.1	2.5	3.9

N = Number of subjects with pre- and post-vaccination results available
SCF= Fold increase in HI GMTs on post-vaccination compared to pre-vaccination time point.
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D90) = Post-vaccination blood sample at Day 90
PI(D180) = Post-vaccination blood sample at Day 180

Secondary Outcome Variable(s):
Seroprotection rates (SPR) for HI antibodies at pre-vaccination and at Day 21 (ATP cohort for immunogenicity)

Vaccine strain	**Group**	**Timing**	**N**	**SPR**			
				n	**%**	**95% CI**	
						LL	**UL**
A/New Caledonia	**Group 1**	Pre	75	27	36.0	25.23	47.91
		PI(D21)	75	75	100	95.20	100
	Group 2	Pre	49	18	36.7	23.42	51.71
		PI(D21)	49	35	71.4	56.74	83.42
	Group 3	Pre	74	32	43.2	31.77	55.28
		PI(D21)	74	67	90.5	81.48	96.11
	Group 4	Pre	75	33	44.0	32.55	55.94
		PI(D21)	75	74	98.7	92.79	99.97
	Group 5	Pre	75	41	54.7	42.75	66.21
		PI(D21)	75	73	97.3	90.70	99.68
	Group 6	Pre	75	41	54.7	42.75	66.21
		PI(D21)	75	70	93.3	85.12	97.80
A/New York	**Group 1**	Pre	75	24	32.0	21.69	43.78
		PI(D21)	75	70	93.3	85.12	97.80
	Group 2	Pre	49	9	18.4	8.76	32.02
		PI(D21)	49	40	81.6	67.98	91.24
	Group 3	Pre	74	16	21.6	12.89	32.72
		PI(D21)	74	70	94.6	86.73	98.51
	Group 4	Pre	75	24	32.0	21.69	43.78
		PI(D21)	75	70	93.3	85.12	97.80
	Group 5	Pre	75	24	32.0	21.69	43.78
		PI(D21)	75	72	96.0	88.75	99.17
	Group 6	Pre	75	23	30.7	20.53	42.38
		PI(D21)	75	70	93.3	85.12	97.80
B/Jiangsu	**Group 1**	Pre	75	35	46.7	35.05	58.55
		PI(D21)	75	75	100	95.20	100
	Group 2	Pre	49	23	46.9	32.53	61.73
		PI(D21)	49	46	93.9	83.13	98.72
	Group 3	Pre	74	37	50.0	38.14	61.86
		PI(D21)	74	71	95.9	88.61	99.16
	Group 4	Pre	75	40	53.3	41.45	64.95
		PI(D21)	75	74	98.7	92.79	99.97
	Group 5	Pre	75	45	60.0	48.04	71.15
		PI(D21)	75	75	100	95.20	100
	Group 6	Pre	75	40	53.3	41.45	64.95
		PI(D21)	75	73	97.3	90.70	99.68

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
PI(D21): post-vaccination blood sample at Day 21

Secondary Outcome Variable(s):
Seroprotection rates (SPR) for HI antibody titre at Day 90 and Day 180 (ATP cohort for persistence)

Vaccine strain	Group	Timing	N	SPR			
				n	%	95% CI	
						LL	UL
A/New Caledonia	**Group 1**	PI(D90)	75	75	100	95.2	100
		PI(D180)	74	72	97.3	90.6	99.7
	Group 2	PI(D90)	49	37	75.5	61.1	86.7
		PI(D180)	49	34	69.4	54.6	81.7
	Group 3	PI(D90)	74	66	89.2	79.8	95.2
		PI(D180)	74	58	78.4	67.3	87.1
	Group 4	PI(D90)	74	68	91.9	83.2	97.0
		PI(D180)	74	62	83.8	73.4	91.3
	Group 5	PI(D90)	74	71	95.9	88.6	99.2
		PI(D180)	74	60	81.1	70.3	89.3
	Group 6	PI(D90)	74	69	93.2	84.9	97.8
		PI(D180)	73	62	84.9	74.6	92.2
A/New York	**Group 1**	PI(D90)	75	68	90.7	81.7	96.2
		PI(D180)	74	64	86.5	76.5	93.3
	Group 2	PI(D90)	49	35	71.4	56.7	83.4
		PI(D180)	49	28	57.1	42.2	71.2
	Group 3	PI(D90)	74	64	86.5	76.5	93.3
		PI(D180)	74	54	73.0	61.4	82.6
	Group 4	PI(D90)	74	67	90.5	81.5	96.1
		PI(D180)	74	58	78.4	67.3	87.1
	Group 5	PI(D90)	74	62	83.8	73.4	91.3
		PI(D180)	74	54	73.0	61.4	82.6
	Group 6	PI(D90)	74	65	87.8	78.2	94.3
		PI(D180)	73	54	74.0	62.4	83.5
B/Jiangsu	**Group 1**	PI(D90)	75	71	94.7	86.9	98.5
		PI(D180)	74	67	90.5	81.5	96.1
	Group 2	PI(D90)	49	47	95.9	86.0	99.5
		PI(D180)	49	41	83.7	70.3	92.7
	Group 3	PI(D90)	74	66	89.2	79.8	95.2
		PI(D180)	74	63	85.1	75.0	92.3
	Group 4	PI(D90)	74	72	97.3	90.6	99.7
		PI(D180)	74	70	94.6	86.7	98.5
	Group 5	PI(D90)	74	72	97.3	90.6	99.7
		PI(D180)	74	69	93.2	84.9	97.8
	Group 6	PI(D90)	74	67	90.5	81.5	96.1
		PI(D180)	73	63	86.3	76.2	93.2

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(D90) = Post-vaccination blood sample at Day 90
PI(D180) = Post-vaccination blood sample at Day 180

Secondary Outcome Variable(s):
Number and percentage of subjects reporting solicited local symptoms during the 7-day (Days 0-6) follow-up period after vaccination (Total Vaccinated cohort)

Symptom	Intensity	Group 1			Group 2			Group 3		
		n	%	95 % CI	n	%	95 % CI	n	%	95 % CI

				LL	UL			LL	UL			LL	UL
		N = 75				N = 50				N = 75			
Haematoma	Any	3	4.0	0.8	11.2	2	4.0	0.5	13.7	4	5.3	1.5	13.1
	> 50 mm	0	0.0	0.0	4.8	0	0.0	0.0	7.1	1	1.3	0.0	7.2
Pain	Any	58	77.3	66.2	86.2	8	16.0	7.2	29.1	53	70.7	59.0	80.6
	Grade 3	0	0.0	0.0	4.8	0	0.0	0.0	7.1	1	1.3	0.0	7.2
Redness	Any	12	16.0	8.6	26.3	5	10.0	3.3	21.8	11	14.7	7.6	24.7
	> 50 mm	0	0.0	0.0	4.8	0	0.0	0.0	7.1	3	4.0	0.8	11.2
Swelling	Any	9	12.0	5.6	21.6	1	2.0	0.1	10.6	14	18.7	10.6	29.3
	> 50 mm	0	0.0	0.0	4.8	0	0.0	0.0	7.1	5	6.7	2.2	14.9
		Group 4				Group 5				Group 6			
		N = 75				N = 75				N = 75			
Haematoma	Any	4	5.3	1.5	13.1	6	8.0	3.0	16.6	1	1.3	0.0	7.2
	> 50 mm	0	0.0	0.0	4.8	0	0.0	0.0	4.8	0	0.0	0.0	4.8
Pain	Any	54	72.0	60.4	81.8	51	68.0	56.2	78.3	42	56.0	44.1	67.5
	Grade 3	1	1.3	0.0	7.2	2	2.7	0.3	9.3	0	0.0	0.0	4.8
Redness	Any	22	29.3	19.4	41.0	17	22.7	13.8	33.8	11	14.7	7.6	24.7
	> 50 mm	9	12.0	5.6	21.6	5	6.7	2.2	14.9	4	5.3	1.5	13.1
Swelling	Any	15	20.0	11.6	30.8	12	16.0	8.6	26.3	9	12.0	5.6	21.6
	> 50 mm	6	8.0	3.0	16.6	4	5.3	1.5	13.1	3	4.0	0.8	11.2

N: number of subjects with the documented dose
n (%): number (percentage) of subjects reporting at least once the symptom
Any: occurrence of any local symptom regardless of intensity grade
Grade 3 pain: pain which prevented normal everyday activity
95% CI: exact 95% confidence interval; LL: lower limit, UL: upper limit

Secondary Outcome Variable(s):
Number and percentage of subjects reporting solicited general symptoms during the 7-day (Days 0-6) follow-up period after vaccination (Total Vaccinated cohort)

Symptom	**Intensity/ Relationship**	**Group 1**				**Group 2**				**Group 3**			
		n	**%**	**95 % CI**		**n**	**%**	**95 % CI**		**n**	**%**	**95 % CI**	
				LL	**UL**			**LL**	**UL**			**LL**	**UL**
		N = 75				N = 50				N = 75			
Fatigue	Any	34	45.3	33.8	57.3	7	14.0	5.8	26.7	31	41.3	30.1	53.3
	Grade 3	1	1.3	0.0	7.2	0	0.0	0.0	7.1	2	2.7	0.3	9.3
	Related	26	34.7	24.0	46.5	7	14.0	5.8	26.7	27	36.0	25.2	47.9
Fever (axillary)	≥ 37.5°C	2	2.7	0.3	9.3	0	0.0	0.0	7.1	4	5.3	1.5	13.1
	> 39°C	0	0.0	0.0	4.8	0	0.0	0.0	7.1	1	1.3	0.0	7.2
	Related	2	2.7	0.3	9.3	0	0.0	0.0	7.1	4	5.3	1.5	13.1
Headache	Any	24	32.0	21.7	43.8	12	24.0	13.1	38.2	28	37.3	26.4	49.3
	Grade 3	0	0.0	0.0	4.8	0	0.0	0.0	7.1	1	1.3	0.0	7.2
	Related	17	22.7	13.8	33.8	8	16.0	7.2	29.1	26	34.7	24.0	46.5
Joint pain	Any	5	6.7	2.2	14.9	4	8.0	2.2	19.2	19	25.3	16.0	36.7
	Grade 3	0	0.0	0.0	4.8	0	0.0	0.0	7.1	1	1.3	0.0	7.2
	Related	4	5.3	1.5	13.1	2	4.0	0.5	13.7	17	22.7	13.8	33.8
Muscle aches	Any	14	18.7	10.6	29.3	3	6.0	1.3	16.5	25	33.3	22.9	45.2
	Grade 3	0	0.0	0.0	4.8	0	0.0	0.0	7.1	1	1.3	0.0	7.2
	Related	11	14.7	7.6	24.7	2	4.0	0.5	13.7	24	32.0	21.7	43.8
Shivering	Any	6	8.0	3.0	16.6	3	6.0	1.3	16.5	18	24.0	14.9	35.3
	Grade 3	0	0.0	0.0	4.8	0	0.0	0.0	7.1	1	1.3	0.0	7.2
	Related	4	5.3	1.5	13.1	2	4.0	0.5	13.7	18	24.0	14.9	35.3
		Group 4				**Group 5**				**Group 6**			
		N = 75				N = 75				N = 75			
Fatigue	Any	34	45.3	33.8	57.3	31	41.3	30.1	53.3	22	29.3	19.4	41.0
	Grade 3	1	1.3	0.0	7.2	5	6.7	2.2	14.9	1	1.3	0.0	7.2
	Related	34	45.3	33.8	57.3	31	41.3	30.1	53.3	19	25.3	16.0	36.7

Fever (axillary)	≥ 37.5°C	6	8.0	3.0	16.6	7	9.3	3.8	18.3	4	5.3	1.5	13.1
	> 39°C	1	1.3	0.0	7.2	0	0.0	0.0	4.8	0	0.0	0.0	4.8
	Related	5	6.7	2.2	14.9	7	9.3	3.8	18.3	4	5.3	1.5	13.1
Headache	Any	27	36.0	25.2	47.9	21	28.0	18.2	39.6	14	18.7	10.6	29.3
	Grade 3	1	1.3	0.0	7.2	1	1.3	0.0	7.2	0	0.0	0.0	4.8
	Related	25	33.3	22.9	45.2	20	26.7	17.1	38.1	14	18.7	10.6	29.3
Joint pain	Any	13	17.3	9.6	27.8	23	30.7	20.5	42.4	17	22.7	13.8	33.8
	Grade 3	0	0.0	0.0	4.8	1	1.3	0.0	7.2	1	1.3	0.0	7.2
	Related	12	16.0	8.6	26.3	20	26.7	17.1	38.1	14	18.7	10.6	29.3
Muscle aches	Any	25	33.3	22.9	45.2	26	34.7	24.0	46.5	21	28.0	18.2	39.6
	Grade 3	1	1.3	0.0	7.2	3	4.0	0.8	11.2	2	2.7	0.3	9.3
	Related	25	33.3	22.9	45.2	25	33.3	22.9	45.2	18	24.0	14.9	35.3
Shivering	Any	21	28.0	18.2	39.6	27	36.0	25.2	47.9	13	17.3	9.6	27.8
	Grade 3	2	2.7	0.3	9.3	3	4.0	0.8	11.2	2	2.7	0.3	9.3
	Related	20	26.7	17.1	38.1	27	36.0	25.2	47.9	13	17.3	9.6	27.8

N: number of subjects with the documented dose
n (%): number (percentage) of subjects reporting at least once the symptom
Any: occurrence of any general symptom regardless of intensity grade and relationship to vaccination
Grade 3: symptoms that prevented normal activity
Related: general symptom assessed by the investigator as causally related to the study vaccination
95% CI: exact 95% confidence interval; LL: lower limit, UL: upper limit

Safety Results: Number (%) of subjects with unsolicited Adverse Events (AEs) within the 21-day post-vaccination period (Total Vaccinated cohort)

All Adverse Events - On-Therapy (occurring within Days 0-20 following vaccination)	**Group 1 N = 75**	**Group 2 N = 50**	**Group 3 N = 75**	**Group 4 N = 75**	**Group 5 N = 75**	**Group 6 N = 75**
Subjects with any AE(s), n (%)	37 (49.3)	6 (12.0)	27 (36.0)	26 (34.7)	31 (41.3)	24 (32.0)
Subjects with Grade 3 AEs, n (%)	1 (1.3)	0 (0.0)	4 (5.3)	6 (8.0)	4 (5.3)	3 (4.0)
Subjects with related AEs, n (%)	11 (14.7)	2 (4.0)	9 (12.0)	14 (18.7)	18 (24.0)	5 (6.7)
Lymphadenitis	-	-	1 (1.3)	-	-	-
Coronary artery disease	-	-	-	-	1 (1.3)	-
Tinnitus	-	-	-	-	1 (1.3)	-
Vertigo	-	-	1 (1.3)	-	2 (2.7)	-
Conjunctivitis	-	-	-	1 (1.3)	-	-
Abdominal pain upper	3 (4.0)	-	-	-	-	-
Cheilitis	-	-	-	-	1 (1.3)	-
Diarrhoea	-	-	1 (1.3)	-	-	4 (5.3)
Dyspepsia	-	-	-	1 (1.3)	-	-
Enteritis	-	-	-	-	1 (1.3)	-
Gastrointestinal disorder	-	-	1 (1.3)	-	-	-
Nausea	2 (2.7)	-	1 (1.3)	2 (2.7)	2 (2.7)	1 (1.3)
Toothache	-	-	1 (1.3)	-	-	1 (1.3)
Vomiting	-	-	-	-	1 (1.3)	-
Asthenia	1 (1.3)	-	-	-	-	-
Chills	-	-	-	1 (1.3)	-	-
Fatigue	-	-	-	1 (1.3)	-	-
Feeling hot	-	-	-	1 (1.3)	-	-
Influenza like illness	3 (4.0)	1 (2.0)	1 (1.3)	-	4 (5.3)	2 (2.7)
Injection site discolouration	-	-	1 (1.3)	-	1 (1.3)	-
Injection site induration	-	-	1 (1.3)	-	1 (1.3)	-
Injection site irritation	-	-	-	1 (1.3)	-	-
Injection site pruritus	1 (1.3)	1 (2.0)	-	-	1 (1.3)	-
Injection site reaction	2 (2.7)	1 (2.0)	1 (1.3)	-	2 (2.7)	-
Injection site warmth	-	-	-	1 (1.3)	1 (1.3)	-
Malaise	1 (1.3)	-	-	2 (2.7)	1 (1.3)	1 (1.3)

Oedema peripheral	-	-	1 (1.3)	-	-	-
Pain	-	-	-	1 (1.3)	-	-
Hypersensitivity	-	-	-	1 (1.3)	-	-
Bronchitis	-	1 (2.0)	-	-	3 (4.0)	-
Campylobacter infection	1 (1.3)	-	-	-	-	-
Cystitis	-	-	-	-	1 (1.3)	-
Gastroenteritis	-	-	1 (1.3)	-	-	-
Herpes simplex	1 (1.3)	-	1 (1.3)	1 (1.3)	-	1 (1.3)
Herpes zoster	-	-	-	1 (1.3)	-	-
Nasopharyngitis	5 (6.7)	1 (2.0)	3 (4.0)	2 (2.7)	3 (4.0)	2 (2.7)
Oral candidiasis	-	-	1 (1.3)	-	-	-
Pharyngitis	1 (1.3)	-	-	1 (1.3)	-	1 (1.3)
Rhinitis	2 (2.7)	2 (4.0)	2 (2.7)	1 (1.3)	1 (1.3)	-
Sinusitis	1 (1.3)	-	1 (1.3)	-	-	-
Upper respiratory tract infection	1 (1.3)	-	2 (2.7)	3 (4.0)	1 (1.3)	1 (1.3)
Urinary tract infection	-	-	-	1 (1.3)	-	-
Arthropod bite	-	-	1 (1.3)	-	-	-
Fall	-	-	1 (1.3)	-	-	-
Joint injury	-	-	-	-	-	1 (1.3)
Anorexia	-	-	1 (1.3)	-	-	-
Hypercholesterolaemia	-	-	1 (1.3)	-	-	-
Hyperglycaemia	-	-	-	1 (1.3)	-	-
Arthralgia	-	-	1 (1.3)	-	-	-
Back pain	1 (1.3)	-	-	-	-	1 (1.3)
Chest wall pain	-	-	1 (1.3)	-	-	-
Gouty arthritis	-	-	1 (1.3)	-	-	-
Joint effusion	-	-	-	-	-	1 (1.3)
Muscle spasms	-	-	-	-	1 (1.3)	-
Musculoskeletal stiffness	2 (2.7)	-	-	1 (1.3)	1 (1.3)	-
Myalgia	2 (2.7)	-	1 (1.3)	-	-	1 (1.3)
Neck pain	-	-	1 (1.3)	-	-	-
Pain in extremity	-	-	1 (1.3)	1 (1.3)	1 (1.3)	1 (1.3)
Pain in jaw	1 (1.3)	-	-	-	-	-
Tendonitis	2 (2.7)	-	1 (1.3)	-	-	-
Dysaesthesia	-	-	-	1 (1.3)	-	-
Headache	10 (13.3)	-	1 (1.3)	-	1 (1.3)	3 (4.0)
Migraine	-	-	-	-	1 (1.3)	-
Paraesthesia	-	-	-	2 (2.7)	1 (1.3)	-
Syncope	-	-	-	1 (1.3)	-	-
Insomnia	-	-	1 (1.3)	-	2 (2.7)	-
Listless	-	-	1 (1.3)	1 (1.3)	-	-
Renal colic	-	-	-	1 (1.3)	-	-
Dysmenorrhoea	4 (5.3)	-	-	-	-	-
Scrotal ulcer	-	-	-	-	-	1 (1.3)
Cough	2 (2.7)	-	1 (1.3)	-	-	1 (1.3)
Dysphonia	-	-	-	1 (1.3)	-	1 (1.3)
Increased upper airway secretion	-	-	-	-	-	1 (1.3)
Pharyngolaryngeal pain	3 (4.0)	-	1 (1.3)	1 (1.3)	-	1 (1.3)
Pleuritic pain	-	-	-	-	1 (1.3)	-
Cold sweat	-	-	1 (1.3)	-	-	-
Eczema	-	-	1 (1.3)	-	-	-
Hyperhidrosis	-	-	-	-	2 (2.7)	-
Rash	1 (1.3)	-	-	-	-	-
Flushing	-	-	-	1 (1.3)	1 (1.3)	-
Hypertension	-	-	2 (2.7)	1 (1.3)	-	-

-: AE absent
Grade 3 =event that prevented normal everyday activity
Related = event assessed by the investigator as causally related to the study vaccination

Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) 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	**Group 1 N = 75**	**Group 2 N = 50**	**Group 3 N = 75**	**Group 4 N = 75**	**Group 5 N = 75**	**Group 6 N = 75**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	3 (6.0) [0]	5 (6.7) [0]	6 (8.0) [0]	4 (5.3) [0]	6 (8.0) [0]
Colon cancer	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	1 (1.3) [0]	0 (0.0) [0]	1 (1.3) [0]
Coronary artery disease	0 (0.0) [0]	1 (2.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	1 (1.3) [0]
Atrial fibrillation	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]
Cholecystitis acute	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	2 (2.7) [0]
Inguinal hernia	0 (0.0) [0]	1 (2.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]
Calculus urinary	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Cardiac failure	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]
Cerebrovascular accident	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Diabetes mellitus inadequate control	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]
Diverticulum	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]
Dyspnoea	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]
Fibula fracture	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]
Head injury	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]
Intestinal obstruction	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]
Ligament rupture	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]
Lumbar radiculopathy	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]
Malaise	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]
Myocardial infarction	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]
Oedema peripheral	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]
Osteoarthritis	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]
Prostate cancer	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Syncope	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]
Transient ischemic attack	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]	0 (0.0) [0]	0 (0.0) [0]
Urinary retention	0 (0.0) [0]	1 (2.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**Group 1 N = 75**	**Group 2 N = 50**	**Group 3 N = 75**	**Group 4 N = 75**	**Group 5 N = 75**	**Group 6 N = 75**
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]
Myocardial infarction	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.3) [0]

Conclusion: The frequency of influenza-specific T-cells (per 10^6 T-cells) producing at least 2 cytokines in elderly subjects measured as GM (geometric means) on Day 21 was 3229.25, 1646.05, 3056.06 , 2589.31, 2454.93 and 2428.78 in groups 1 to 6, respectively.
Unsolicited AEs were reported by 37 (49.3%), 6 (12.0%), 27 (36.0%), 26 (34.7%), 31 (41.3%) and 24 (32.0%) subjects in groups 1 to 6, respectively. During the course of the study, SAEs were reported in 3 (6.0%) subjects in Group 2, 5 (6.7%) in Group 3, 6 (8.0%) in Group 4, 4 (5.3%) in Group 5 and 6 (8.0%) in Group 6. One fatal SAE occurred in Group 6. The reported SAEs were all assessed by the investigators as not related to the study vaccination.

Date updated: 08-July-2014