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.: 107975 (FLU-LD-003)

Title: A phase II, controlled, randomized, single blind study to evaluate the immunogenicity, safety and reactogenicity of the low dose influenza vaccine adjuvanted with AS03 compared to *Fluarix*™ (GlaxoSmithKline Biologicals) administered intramuscularly in elderly ≥60 years.
Fluarix™ (Flu vaccine): GlaxoSmithKline (GSK) Biologicals' inactivated influenza split vaccine.
FluAS03: GSK Biologicals' Low dose influenza vaccine adjuvanted with AS03

Rationale: The aim of this study was to evaluate the immunogenicity in terms of humoral response and cellular mediated immune response, as well as the safety of FluAS03 vaccine compared to Flu vaccine administered intramuscularly in elderly aged 60 years old and above, using the Northern Hemisphere 2006-2007 influenza vaccine composition.

Phase: II

Study Period: 02 October 2006 to 17 November 2006

Study Design: Single-centre, randomized (1:1), single blind, controlled study with 2 parallel groups.

Centres: 1 centre in Belgium.

Indication: Immunization against influenza in male and female subjects aged 60 years and older.

Treatment: The study groups were as follows:

- FluAS03 Group: subjects received one dose of FluAS03,
- Flu Group: subjects received one dose of Flu vaccine.

All vaccines were administered intramuscularly into the deltoid region of the non-dominant arm.

Objectives: To assess the humoral immune response (anti-haemagglutinin) elicited by the low dose influenza vaccine adjuvanted with AS03 and by the Flu vaccine, with the Northern Hemisphere 2006-2007 influenza vaccine composition, 21 days after vaccination.

Primary Outcome/Efficacy Variable:
At Days 0 and 21: serum haemagglutination-inhibition (HI) antibody titre, against each of the three vaccine influenza virus strains, in each group.

Secondary Outcome/Efficacy Variable(s):
Immunogenicity
At Days 0 and 21:

- Frequency of influenza-specific CD4/CD8 T-lymphocytes per 10^6 in tests producing at least two different cytokines (IL-2, IFN-γ, TNF-α and CD40L), in each group.
- Frequency of influenza-specific CD4/CD8 cells per 10^6 in tests producing at least CD40L and another signal molecule (IL-2, IFN-γ, TNF-α), in each group.
- Frequency of influenza-specific CD4/CD8 cells per 10^6 in tests producing at least IL-2 and another signal molecule (CD40L, IFN-γ, TNF-α), in each group.
- Frequency of influenza-specific CD4/CD8 cells per 10^6 in tests producing at least TNF-α and another signal molecule (IL-2, IFN-γ, CD40L), in each group.
- Frequency of influenza-specific CD4/CD8 cells per 10^6 in tests producing at least IFN-γ and another signal molecule (CD40L, IL-2, TNF-α), in each group.

CD40L: Cluster differentiation-40L, IL-2: Interleukin-2, TNF-α: Tumour Necrosis Factor alpha, IFN-γ: Interferon-gamma.

Safety

- Occurrence, 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 in each group.
- Occurrence, intensity and relationship to vaccination of unsolicited adverse events (AEs) during a 30-day follow-up period (i.e. day of vaccination and 29 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.

Statistical Methods:
The analysis was done on the Total vaccinated cohort and the According-To-Protocol (ATP) cohort for immunogenicity.
The Total vaccinated cohort included all vaccinated subjects.
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), who received one dose of either study vaccine according to their random assignment, for whom administration site of study vaccine was known, who did not receive a vaccine forbidden in the protocol and for whom immunogenicity data were available.

Immunogenicity

The analysis was done on the ATP cohort for immunogenicity.

For the humoral immune response, for each vaccine group and each vaccine strain, geometric mean titres (GMT) with 95% confidence interval (CI) at Days 0 and 21 were tabulated together with the seroconversion* rate with exact 95% CI at Day 21, the seropositivity** and seroprotection*** rates with exact 95% CI at Days 0 and 21 and the seroconversion factor**** with 95% CI at Day 21. Antibody titres below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

* The seroconversion rate is defined as the proportion of subjects with:
  - a pre-vaccination serum HI titre <1:10 and a post-vaccination serum HI titre ≥ 1:40, or
  - a pre-vaccination serum HI titre ≥ 1:10 and a fold increase (post/pre) ≥ 4.

** A seropositive subject is a subject with antibody titre ≥1:10.

*** The seroprotection rate is defined as the proportion of subjects with a serum HI titre ≥ 1:40.

**** The seroconversion factor is defined as the fold increase in serum HI GMT on Day 21 compared to Day 0.

For the cell mediated immune (CMI) response, for each vaccine group and each vaccine strain, raw data from the frequency of influenza-specific CD4/CD8 T-cells per 10^6 producing at least 2 different cytokines (IL-2, IFN-γ, TNF-α and CD40L) were summarized at each scheduled time point. The same tabulations were done for influenza-specific CD4/CD8 T-cells per 10^6 producing

- at least IL-2 and another cytokine (IFN-γ, TNF-α and CD40L),
- at least IFN-γ and another cytokine (IL-2, TNF-α and CD40L),
- at least TNF-α and another cytokine (IL-2, IFN-γ and CD40L),
- at least CD40L and another cytokine (IL-2, IFN-γ and TNF-α).

Safety

The analysis was done on the Total vaccinated cohort.

The percentage of subjects reporting each individual solicited local and general symptom during the 7 days solicited follow-up period (Day 0–6) was tabulated with exact 95% CI. The same tabulations were done for grade 3 local and general symptoms and for general symptoms assessed by the investigator as causally related to vaccination. The percentage of subjects with at least one report of an unsolicited AE during the 30-day follow-up period (Days 0-29) after vaccination was tabulated by the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms. The total number of subjects reporting grade 3 AEs or AEs assessed by the investigator as causally related to vaccination was also tabulated. The incidence of SAEs reported during the entire study period was tabulated according to MedDRA preferred terms.

Study Population: Male or female subjects age 60 years or older at the time of the vaccination, free of obvious health problems as established by medical history and clinical examination were included in this study. Subjects having received previous vaccination against influenza within the 12 months prior to enrolment and subjects with a known history of confirmed influenza infection within the last 12 months were excluded from this study. Written informed consent was obtained from the subject prior to study participation.

Number of subjects	**FluAS03 Group**	**Flu Group**
Planned, N	75	75
Randomized, N (Total vaccinated cohort)	75	75
Completed, n (%)	75 (100)	75 (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	**FluAS03 Group**	**Flu Group**
N (Total vaccinated cohort)	75	75
Females:Males	38:37	38:37
Mean Age, years (SD)	64.4 (4.22)	64.5 (4.18)
White - Caucasian, n (%)	75 (100)	73 (97.3)

Primary Efficacy Results:

Seropositivity rates, seroprotection rate and GMTs for HI antibody titre at Day 0 and Day 21 (ATP cohort for immunogenicity)

Vaccine	**Group**	**Timing**	**N**	**≥ 1:10**	**≥ 1:40**	**GMT**

strain				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
A/New Caledonia	FluAS03	PRE	74	72	97.3	90.6	99.7	40	54.1	42.1	65.7	45.3	35.9	57.1
		PI(D21)	74	73	98.6	92.7	100	68	91.9	83.2	97.0	116.4	91.2	148.5
	Flu	PRE	74	72	97.3	90.6	99.7	54	73.0	61.4	82.6	81.1	61.5	106.8
		PI(D21)	74	74	100	95.1	100	73	98.6	92.7	100	170.9	132.7	220.3
A/Wisconsin	FluAS03	PRE	74	56	75.7	64.3	84.9	35	47.3	35.6	59.3	28.8	20.7	40.1
		PI(D21)	74	74	100	95.1	100	69	93.2	84.9	97.8	251.9	188.7	336.4
	Flu	PRE	74	60	81.1	70.3	89.3	44	59.5	47.4	70.7	41.3	29.1	58.6
		PI(D21)	74	74	100	95.1	100	71	95.9	88.6	99.2	228.4	168.5	309.6
B/Malaysia	FluAS03	PRE	74	67	90.5	81.5	96.1	28	37.8	26.8	49.9	27.1	21.8	33.6
		PI(D21)	74	74	100	95.1	100	72	97.3	90.6	99.7	161.6	131.4	198.6
	Flu	PRE	74	66	89.2	79.8	95.2	39	52.7	40.7	64.4	31.6	25.1	39.8
		PI(D21)	74	73	98.6	92.7	100	70	94.6	86.7	98.5	131.4	105.8	163.1

N = number of subjects with available results
S+ = seropositive titre (HI titre ≥ 1:10)
SPR = seroprotected titre (HI titre ≥ 1:40)
n (%) = number (percentage) of subjects in the specified category
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination at Day 0
PI(D21) = post-vaccination at Day 21

Primary Efficacy Results
Seroconversion rate (SCR) for HI antibody titre at Day 21 (ATP cohort for immunogenicity)

Vaccine strain	Group	N	SCR			
			n	%	95% CI	
					LL	UL
A/New Caledonia	FluAS03	74	21	28.4	18.5	40.1
	Flu	74	12	16.2	8.7	26.6
A/Wisconsin	FluAS03	74	52	70.3	58.5	80.3
	Flu	74	40	54.1	42.1	65.7
B/Malaysia	FluAS03	74	46	62.2	50.1	73.2
	Flu	74	31	41.9	30.5	53.9

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

Primary Efficacy Results
Seroconversion factor (SCF) for HI antibody titre at Day 21 (ATP cohort for immunogenicity)

Vaccine strain	Group	N	SCF		
			Value	95% CI	
				LL	UL
A/New Caledonia	FluAS03	74	2.6	2.0	3.3
	Flu	74	2.1	1.6	2.8
A/Wisconsin	FluAS03	74	8.7	6.3	12.1
	Flu	74	5.5	4.0	7.6
B/Malaysia	FluAS03	74	6.0	4.6	7.8
	Flu	74	4.2	3.2	5.4

SCF defined as the fold increase in serum HI GMT on Day 21 compared to Day 0.
N = number of subjects with pre- and post-vaccination results available
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Descriptive statistics on the frequency of cytokine-positive CD4 T-cells (per million CD4 T-cells) at each time point by vaccine strains (ATP cohort for immunogenicity)

Test description	Vaccine strain	Group	Timing	N	GM	SD	Median

CD4-all doubles	B/Malaysia	FluAS03	PRE	73	436.58	348.81	499.00
			PI(D21)	73	1555.92	1060.11	1572.00
		Flu	PRE	71	451.35	448.35	467.00
			PI(D21)	73	736.15	588.56	949.00
	A/New Caledonia	FluAS03	PRE	73	322.57	348.20	405.00
			PI(D21)	73	872.71	662.32	956.00
		Flu	PRE	71	370.36	408.19	429.00
			PI(D21)	73	510.86	604.98	672.00
	A/Wisconsin	FluAS03	PRE	73	37.33	155.75	63.00
			PI(D21)	73	113.74	412.68	168.00
		Flu	PRE	71	50.79	212.97	114.00
			PI(D21)	73	72.43	190.60	140.00
CD4-CD40L	B/Malaysia	FluAS03	PRE	73	424.07	328.40	477.00
			PI(D21)	73	1409.79	983.81	1432.00
		Flu	PRE	71	433.94	406.20	469.00
			PI(D21)	73	694.68	550.36	884.00
	A/New Caledonia	FluAS03	PRE	73	317.25	337.18	359.00
			PI(D21)	73	786.97	598.31	838.00
		Flu	PRE	71	354.60	399.44	392.00
			PI(D21)	73	475.96	576.45	663.00
	A/Wisconsin	FluAS03	PRE	73	36.53	145.90	65.00
			PI(D21)	73	97.23	346.59	159.00
		Flu	PRE	71	52.22	208.27	96.00
			PI(D21)	73	65.37	168.16	135.00
CD4-IFN-γ	B/Malaysia	FluAS03	PRE	73	265.46	297.90	310.00
			PI(D21)	73	1081.98	840.54	1197.00
		Flu	PRE	71	244.30	377.07	305.00
			PI(D21)	73	530.64	451.71	664.00
	A/New Caledonia	FluAS03	PRE	73	225.76	265.96	277.00
			PI(D21)	73	527.98	522.30	627.00
		Flu	PRE	71	239.78	285.26	270.00
			PI(D21)	73	407.10	492.37	460.00
	A/Wisconsin	FluAS03	PRE	73	24.45	114.69	41.00
			PI(D21)	73	83.99	365.27	103.00
		Flu	PRE	71	30.49	83.91	55.00
			PI(D21)	73	38.46	126.65	84.00
CD4-IL2	B/Malaysia	FluAS03	PRE	73	379.42	318.77	408.00
			PI(D21)	73	1297.82	880.34	1340.00
		Flu	PRE	71	382.48	378.85	430.00
			PI(D21)	73	647.93	508.83	773.00
	A/New Caledonia	FluAS03	PRE	73	256.57	307.83	317.00
			PI(D21)	73	652.75	539.89	733.00
		Flu	PRE	71	220.62	301.07	300.00
			PI(D21)	73	300.71	502.30	469.00
	A/Wisconsin	FluAS03	PRE	73	31.74	130.05	48.00
			PI(D21)	73	89.97	301.28	134.00
		Flu	PRE	71	53.93	127.47	89.00
			PI(D21)	73	53.47	148.09	107.00
CD4-TNF-α	B/Malaysia	FluAS03	PRE	73	332.83	298.11	416.00
			PI(D21)	73	1098.28	869.02	1032.00
		Flu	PRE	71	331.52	383.96	383.00
			PI(D21)	73	532.81	420.99	655.00
	A/New	FluAS03	PRE	73	219.03	276.48	307.00

	Caledonia		PI(D21)	73	582.62	506.95	657.00
		Flu	PRE	71	261.91	369.60	288.00
			PI(D21)	73	317.96	416.78	460.00
	A/Wisconsin	FluAS03	PRE	73	23.29	119.05	52.00
			PI(D21)	73	84.99	308.52	128.00
		Flu	PRE	71	36.16	190.06	71.00
			PI(D21)	73	44.97	157.29	89.00

N = number of subjects with available results
All doubles: T-cells producing at least 2 cytokines
GM = Geometric Mean
SD = Standard Deviation
PRE = pre-vaccination at Day 0
PI(D21) = post-vaccination at Day 21

Secondary Outcome Variable (s):
Descriptive Statistics on the frequency cytokine-positive CD8 T-cells (per million CD8 T-cells) at each time point by vaccine strains (ATP cohort for immunogenicity)

Test description	Vaccine strain	Group	Timing	N	GM	SD	Median
CD8-all doubles	B/Malaysia	FluAS03	PRE	72	7.91	83.49	1.00
			PI(D21)	73	7.82	95.80	1.00
		Flu	PRE	69	4.17	70.59	1.00
			PI(D21)	72	3.74	120.67	1.00
	A/New Caledonia	FluAS03	PRE	71	6.22	233.32	1.00
			PI(D21)	73	7.81	191.24	1.00
		Flu	PRE	69	7.31	112.56	1.00
			PI(D21)	70	4.40	141.07	1.00
	A/Wisconsin	FluAS03	PRE	72	3.93	82.82	1.00
			PI(D21)	73	3.35	56.70	1.00
		Flu	PRE	69	6.79	85.90	1.00
			PI(D21)	73	2.79	70.15	1.00
CD8-CD40L	B/Malaysia	FluAS03	PRE	72	2.20	34.98	1.00
			PI(D21)	73	3.66	45.91	1.00
		Flu	PRE	69	2.11	36.15	1.00
			PI(D21)	72	1.98	32.45	1.00
	A/New Caledonia	FluAS03	PRE	71	2.56	113.11	1.00
			PI(D21)	73	4.17	93.16	1.00
		Flu	PRE	69	5.34	65.09	1.00
			PI(D21)	70	2.11	51.19	1.00
	A/Wisconsin	FluAS03	PRE	72	2.15	53.59	1.00
			PI(D21)	73	2.18	39.28	1.00
		Flu	PRE	69	2.70	44.68	1.00
			PI(D21)	73	2.11	39.64	1.00
CD8-IFN-γ	B/Malaysia	FluAS03	PRE	72	4.28	56.03	1.00
			PI(D21)	73	6.24	74.51	1.00
		Flu	PRE	69	2.71	56.13	1.00
			PI(D21)	72	3.53	118.94	1.00
	A/New Caledonia	FluAS03	PRE	71	5.67	231.67	1.00
			PI(D21)	73	5.04	174.85	1.00
		Flu	PRE	69	4.34	97.73	1.00
			PI(D21)	70	3.98	133.45	1.00
	A/Wisconsin	FluAS03	PRE	72	2.84	73.55	1.00
			PI(D21)	73	2.46	44.69	1.00
		Flu	PRE	69	4.40	69.48	1.00
			PI(D21)	73	1.98	36.44	1.00

CD8-IL2	B/Malaysia	FluAS03	PRE	72	3.60	92.44	1.00
			PI(D21)	73	3.45	60.32	1.00
		Flu	PRE	69	2.12	44.04	1.00
			PI(D21)	72	2.44	32.77	1.00
	A/New Caledonia	FluAS03	PRE	71	2.48	131.52	1.00
			PI(D21)	73	4.63	125.59	1.00
		Flu	PRE	69	4.43	60.02	1.00
			PI(D21)	70	2.44	62.17	1.00
	A/Wisconsin	FluAS03	PRE	72	1.93	55.19	1.00
			PI(D21)	73	2.76	45.28	1.00
		Flu	PRE	69	3.23	61.15	1.00
			PI(D21)	73	2.55	61.31	1.00
CD8-TNF-α	B/Malaysia	FluAS03	PRE	72	8.41	83.63	1.00
			PI(D21)	73	6.25	91.95	1.00
		Flu	PRE	69	4.29	78.46	1.00
			PI(D21)	72	3.90	124.66	1.00
	A/New Caledonia	FluAS03	PRE	71	6.07	218.59	1.00
			PI(D21)	73	8.15	171.91	1.00
		Flu	PRE	69	6.05	114.14	1.00
			PI(D21)	70	5.50	128.58	1.00
	A/Wisconsin	FluAS03	PRE	72	3.12	58.61	1.00
			PI(D21)	73	2.56	49.21	1.00
		Flu	PRE	69	5.55	92.14	1.00
			PI(D21)	73	2.33	70.96	1.00

N = number of subjects with available results
GM = Geometric Mean
SD = Standard Deviation
PRE = Pre-vaccination at Day 0
PI(D21) = Post-vaccination at Day 21

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

Symptom	**Intensity**	**FluAS03 Group**					**Flu Group**				
		N	**n**	**%**	**95% CI**		**N**	**n**	**%**	**95% CI**	
					LL	**UL**				**LL**	**UL**
Ecchymosis	Any	75	1	1.3	0.0	7.2	75	1	1.3	0.0	7.2
	> 50 mm	75	1	1.3	0.0	7.2	75	0	0.0	0.0	4.8
Pain	Any	75	57	76.0	64.7	85.1	75	25	33.3	22.9	45.2
	Grade 3	75	1	1.3	0.0	7.2	75	0	0.0	0.0	4.8
Redness	Any	75	14	18.7	10.6	29.3	75	8	10.7	4.7	19.9
	> 50 mm	75	4	5.3	1.5	13.1	75	0	0.0	0.0	4.8
Swelling	Any	75	18	24.0	14.9	35.3	75	5	6.7	2.2	14.9
	> 50 mm	75	3	4.0	0.8	11.2	75	1	1.3	0.0	7.2

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 a particular symptom, regardless of intensity grade
Grade 3 Pain = pain that prevented normal activity

Secondary Outcome Variable (s):
Number/percentage of subjects reporting solicited general symptoms reported during the 7-day (Day 0-6) post-vaccination period (Total vaccinated cohort)

Symptom	**Intensity / relationship**	**FluAS03 Group**					**Flu Group**				
		N	**n**	**%**	**95% CI**		**N**	**n**	**%**	**95% CI**	
					LL	**UL**				**LL**	**UL**
Arthralgia	Any	75	12	16.0	8.6	26.3	75	8	10.7	4.7	19.9

	Grade 3	75	0	0.0	0.0	4.8	75	0	0.0	0.0	4.8
	Related	75	10	13.3	6.6	23.2	75	4	5.3	1.5	13.1
Fatigue	Any	75	30	40.0	28.9	52.0	75	13	17.3	9.6	27.8
	Grade 3	75	0	0.0	0.0	4.8	75	0	0.0	0.0	4.8
	Related	75	29	38.7	27.6	50.6	75	12	16.0	8.6	26.3
Fever (axillary)	≥ 37.5°C	75	2	2.7	0.3	9.3	75	0	0.0	0.0	4.8
	> 39.0°C	75	0	0.0	0.0	4.8	75	0	0.0	0.0	4.8
	Related	75	2	2.7	0.3	9.3	75	0	0.0	0.0	4.8
Headache	Any	75	28	37.3	26.4	49.3	75	10	13.3	6.6	23.2
	Grade 3	75	0	0.0	0.0	4.8	75	0	0.0	0.0	4.8
	Related	75	24	32.0	21.7	43.8	75	7	9.3	3.8	18.3
Muscle aches	Any	75	17	22.7	13.8	33.8	75	10	13.3	6.6	23.2
	Grade 3	75	1	1.3	0.0	7.2	75	0	0.0	0.0	4.8
	Related	75	15	20.0	11.6	30.8	75	8	10.7	4.7	19.9
Shivering	Any	75	10	13.3	6.6	23.2	75	3	4.0	0.8	11.2
	Grade 3	75	1	1.3	0.0	7.2	75	0	0.0	0.0	4.8
	Related	75	9	12.0	5.6	21.6	75	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
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = incidence of a particular symptom, regardless of intensity grade or relationship to study vaccine
Grade 3 = symptom that prevented normal activity.
Related = reasonable possibility that the vaccine contributed to the symptom.

Safety Results: Number (%) of subjects with unsolicited adverse events within the 30-day post-vaccination period (Total vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Days 0-29 following vaccination)	**FluAS03 Group N = 75**	**Flu Group N = 75**
Subjects with any AE(s), n (%)	31 (41.3)	22 (29.3)
Subjects with any grade 3* AE(s), n (%)	1 (1.3)	0 (0.0)
Subjects with any related** AE(s), n (%)	11 (14.7)	7 (9.3)
Nasopharyngitis	7 (9.3)	4 (5.3)
Influenza like illness	2 (2.7)	4 (5.3)
Pharyngolaryngeal pain	4 (5.3)	1 (1.3)
Upper respiratory tract infection	3 (4.0)	2 (2.7)
Injection site pruritus	4 (5.3)	-
Rhinitis	3 (4.0)	1 (1.3)
Dizziness	2 (2.7)	1 (1.3)
Cough	1 (1.3)	1 (1.3)
Dental caries	1 (1.3)	1 (1.3)
Injection site nodule	2 (2.7)	-
Injection site warmth	1 (1.3)	1 (1.3)
Musculoskeletal stiffness	2 (2.7)	-
Pain in extremity	1 (1.3)	1 (1.3)
Rhinorrhea	2 (2.7)	-
Lymphadenopathy	1 (1.3)	-
Abdominal pain	1 (1.3)	-
Diarrhoea	1 (1.3)	-
Gastrooesophageal reflux disease	1 (1.3)	-
Chest discomfort	1 (1.3)	-
Chills	1 (1.3)	-
Malaise	1 (1.3)	-
Oedema peripheral	1 (1.3)	-
Pyrexia	1 (1.3)	-
Lymphangitis	1 (1.3)	-
Sinusitis	1 (1.3)	-
Tooth abscess	1 (1.3)	-

Back pain	1 (1.3)	-
Myalgia	1 (1.3)	-
Headache	1 (1.3)	-
Syncope vasovagal	1 (1.3)	-
Nervousness	1 (1.3)	-
Arthropod bite	-	1 (1.3)
Axillary pain	-	1 (1.3)
Colitis	-	1 (1.3)
Coronary artery disease	-	1 (1.3)
Diverticulitis	-	1 (1.3)
Injection site anesthesia	-	1 (1.3)
Insomnia	-	1 (1.3)
Musculoskeletal pain	-	1 (1.3)
Nausea	-	1 (1.3)
Neck pain	-	1 (1.3)
Oral herpes	-	1 (1.3)
Paresthesia	-	1 (1.3)
Pharyngitis	-	1 (1.3)
Tendonitis	-	1 (1.3)
Wart excision	-	1 (1.3)
-: AE absent *Grade 3 AE: AE that prevented everyday activities **Related AE: the investigator assessed there was a reasonable possibility that the vaccine contributed to the AE		
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	**FluAS03 Group N = 75**	**Flu Group N = 75**
Subjects with any SAE(s), n (%) [n assessed by investigators as related]	0 (0.0) [0]	1 (1.3) [0]
Coronary artery disease	0 (0.0) [0]	1 (1.3) [0]
Fatal SAEs	**FluAS03 Group**	**Flu Group**
Subjects with any SAE(s), n (%) [n assessed by investigators as related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion: Before vaccination, the percentage of subjects in the FluAS03 and Flu groups who had HI antibody titres ≥1:40 against the A/New Caledonia, A/Wisconsin and B/Malaysia virus strains was 54.1% & 73.0%, 47.3% & 59.5% and 37.8 & 52.7%, respectively; at Day 21 following vaccination, the percentage of subjects in the FluAS03 and Flu groups who had HI antibody titres ≥1:40 against the A/New Caledonia, A/Wisconsin and B/Malaysia virus strains was 91.9% & 98.6%, 93.2% & 95.9% and 97.3 & 94.6%, respectively.

Across groups, pain and fatigue were the most frequently reported solicited local and general symptoms, respectively. In the FluAS03 Group, 31 (41.3%) subjects reported unsolicited AEs of which 1 was of grade 3 intensity and 11 were considered by the investigators to be related to the study vaccination. In the Flu Group, 22 (29.3%) subjects reported unsolicited AEs, none of which were of grade 3 intensity and 7 of which were considered by the investigators to be related to the study vaccination.

One SAE was reported for 1 subject in the Flu Group; it was assessed by the investigator as not related to the study vaccination. No fatal SAEs were reported throughout this study.

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