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.: 107973 (FluAS25-014)

Title: A phase II, open, controlled study to evaluate the reactogenicity and the immunogenicity of GlaxoSmithKline Biologicals AS25 adjuvanted influenza vaccine (FluAS25) in elderly adults (≥ 67 years) previously vaccinated in the FluAS25-002 clinical trial with the same candidate vaccine. Fluarix™ (known as α-Rix™ in Belgium) will be used as a reference.
FluAS25 (Flu-1): GlaxoSmithKline (GSK) Biologicals' AS25 adjuvanted influenza vaccine.
Fluarix™ (Flu-2): GSK Biologicals' licensed influenza vaccine.

Rationale: The aim of this study was to evaluate the safety and immunogenicity of a re-vaccination dose of the Flu-1 vaccine (2006-2007 season) compared to that of the Flu-2 vaccine (2006-2007 season) after 2 previous vaccine administrations in adults aged 67 years or older.
Subjects participating in this study had received the same vaccine in the FluAS25-001 (104887) and the FluAS25-002 (104540) studies.

Phase: II

Study Period: 16 October 2006 to 14 November 2006

Study Design: Open, controlled study with 2 parallel groups (1:1).

Centres: 1 study centre in Belgium.

Indication: Immunisation against influenza disease in an elderly population aged over 65 years.

Treatment: The study groups were as follows:

- Flu-1 Group: subjects received 1 dose of Flu-1 vaccine at Day 0
- Flu-2 Group: subjects received 1 dose of Flu-2 vaccine at Day 0

All vaccines were administered intramuscularly into the deltoid region of the non-dominant arm. All subjects had received 2 previous administrations of the same vaccine, a first one 24 months and another one 12 months before this study dose.

Objectives: To evaluate the safety of repeated revaccination with Flu-1 vaccine during the 21 days following the intramuscular administration of the vaccine. Flu-2 was used as reference.

Primary Outcome/Efficacy Variable:
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.

Secondary Outcome/Efficacy Variable(s):
Immunogenicity
Humoral immune response
Observed variable:

- At Days 0 and 21: serum haemagglutination-inhibition (HI) antibody titre, against each of the 3 vaccine strains

Derived variables:

- Geometric mean titres (GMTs) of HI antibody titres at Days 0 and 21
- Seroconversion rates* (SCR) at Day 21
- Seroconversion factors** (SCF) at Day 21
- Seroprotection rates*** (SPR) at Days 0 and 21

* Seroconversion rate was defined as the percentage of vaccinees who had either a HI pre-vaccination titre < 1:10 and post-vaccination titre ≥ 1:40 or a HI pre-vaccination titre ≥ 1:10 and at least a four-fold increase in post-vaccination titre.
**Seroconversion factor was defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.
***Seroprotection rate was defined as the percentage of vaccinees with a serum HI titre ≥ 1:40 that usually is accepted as indicating protection.
Anti-3-deacylated monophosphoryl lipid A (Anti-*MPL) response*
Observed variables:

- At Days 0 and 21: anti-MPL antibody concentrations

Derived variables:

- Geometric mean concentrations (GMCs) of serum anti-MPL antibodies pre- and post-vaccination

Cell-mediated immune (CMI) response

Observed variables:

- At Days 0 and 21: analysis of CMI for each sample collected at each stimulation dose used *in vitro*.

Derived variables:

- Frequency of cytokine-positive cluster of differentiation 4/8 (CD4/CD8) cells per million (10^6) in tests producing at least 2 different cytokines among cluster of differentiation 40 Ligand, Interleukin-2, Tumour Necrosis alpha and Interferon-gamma (CD40L, IL-2, TNF-α, IFN-γ).
- Frequency of cytokine-positive CD4/CD8 cells per 10^6 in tests producing at least CD40L and another signal molecule (IL-2, IFN-γ, TNF-α).
- Frequency of cytokine-positive CD4/CD8 cells per 10^6 in tests producing at least IL-2 and another signal molecule (CD40L, IFN-γ, TNF-α).
- Frequency of cytokine-positive CD4/CD8 cells per 10^6 in tests producing at least IFN-γ and another signal molecule (IL2, CD40L, TNF-α).
- Frequency of cytokine-positive CD4/CD8 cells per 10^6 in tests producing at least TNF-α and another signal molecule (IL2, CD40L, IFN-γ).

Statistical Methods:

Analyses were performed on the Total Vaccinated cohort and on the According-To-Protocol (ATP) cohort for immunogenicity.

The Total Vaccinated cohort included all vaccinated subjects for whom data were available.

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 immunogenicity data were available.

Analysis of immunogenicity

The analysis was performed on the ATP cohort for immunogenicity.

For each treatment group, the following parameters were calculated with 95% confidence intervals (CIs):

- Seropositivity rates and GMTs of HI antibody titres at Days 0 and 21
- SCR at Day 21
- SCF at Day 21
- SPR at Days 0 and 21
- GMC of anti-MPL antibodies at Days 0 and 21.

Descriptive statistics of the frequency of influenza-specific cytokine-positive CD4/CD8 T-lymphocytes were also tabulated for each treatment group at Days 0 and 21 and each strain.

Analysis of safety

The analysis was performed on the Total Vaccinated cohort.

The percentages of subjects reporting each individual solicited local symptom and general symptom during the 7-day (Days 0-6) solicited follow-up period were tabulated with exact 95% CI. The same tabulation was done for grade 3 symptom and general symptom assessed by the investigator as causally related to vaccination.

The percentage of subjects with at least one report of an unsolicited symptom classified by the Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term within the 21 days (Days 0-20) after vaccination was tabulated. The same tabulation was done for unsolicited grade 3 AEs and unsolicited AEs that were assessed by the investigator as causally related to vaccination.

SAEs occurring during the entire study period were summarized according to MedDRA preferred terms.

Study Population: Male or female subjects aged 67 years or older at the time of revaccination, who previously received either Flu-1 (for subjects of the Flu-1 Group) or Flu-2 (for subjects of the Flu-2 Group) vaccine during FluAS25-002 clinical trial and who were free of any acute aggravation of the health status as established by clinical examination before entering the study. Subjects with a history of confirmed influenza infection since the date of previous vaccination, a history of hypersensitivity to a previous dose of influenza vaccine and/or a previous vaccination with influenza vaccine season 2006/2007 were excluded from the study. Written informed consent was obtained from the subjects before study enrolment.

Number of subjects	**Flu-1 Group**	**Flu-2 Group**
Planned, N	38	45
Randomised, N (Total Vaccinated cohort)	36	38

Completed, n (%)	36 (100)	38 (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	**Flu-1 Group**	**Flu-2 Group**
N (Total Vaccinated cohort)	36	38
Females:Males	21:15	22:16
Mean Age, years (SD)	72.5 (4.93)	72.7 (5.56)
White - Caucasian, n (%)	36 (100)	38 (100)

Primary Efficacy Results: Percentage of subjects reporting solicited local symptoms during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort)

Symptom	**Intensity**	**Flu-1 Group**					**Flu-2 Group**				
		N	**n**	**%**	**95% CI**		**N**	**n**	**%**	**95% CI**	
					LL	**UL**				**LL**	**UL**
Ecchymosis	Any	36	0	0.0	0.0	9.7	38	0	0.0	0.0	9.3
	> 50 mm	36	0	0.0	0.0	9.7	38	0	0.0	0.0	9.3
Pain	Any	36	24	66.7	49.0	81.4	38	10	26.3	13.4	43.1
	Grade 3	36	0	0.0	0.0	9.7	38	0	0.0	0.0	9.3
Redness	Any	36	6	16.7	6.4	32.8	38	2	5.3	0.6	17.7
	> 50 mm	36	3	8.3	1.8	22.5	38	0	0.0	0.0	9.3
Swelling	Any	36	6	16.7	6.4	32.8	38	2	5.3	0.6	17.7
	> 50 mm	36	1	2.8	0.1	14.5	38	0	0.0	0.0	9.3

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
Any = incidence of a particular symptom regardless of intensity grade
Grade 3 pain = pain that prevented normal activity

Primary Efficacy Results: Percentage of subjects reporting solicited general symptoms during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort)

Symptom	**Intensity/ Relationship**	**Flu-1 Group**					**Flu-2 Group**				
		N	**n**	**%**	**95% CI**		**N**	**n**	**%**	**95% CI**	
					LL	**UL**				**LL**	**UL**
Arthralgia	Any	36	12	33.3	18.6	51.0	38	3	7.9	1.7	21.4
	Grade 3	36	0	0.0	0.0	9.7	38	0	0.0	0.0	9.3
	Related	36	10	27.8	14.2	45.2	38	1	2.6	0.1	13.8
Fatigue	Any	36	18	50.0	32.9	67.1	38	6	15.8	6.0	31.3
	Grade 3	36	0	0.0	0.0	9.7	38	1	2.6	0.1	13.8
	Related	36	15	41.7	25.5	59.2	38	3	7.9	1.7	21.4
Fever (axillary)	≥ 37.5°C	36	3	8.3	1.8	22.5	38	0	0.0	0.0	9.3
	> 39°C	36	0	0.0	0.0	9.7	38	0	0.0	0.0	9.3
	Related	36	3	8.3	1.8	22.5	38	0	0.0	0.0	9.3
Headache	Any	36	12	33.3	18.6	51.0	38	4	10.5	2.9	24.8
	Grade 3	36	1	2.8	0.1	14.5	38	0	0.0	0.0	9.3
	Related	36	11	30.6	16.3	48.1	38	1	2.6	0.1	13.8
Myalgia	Any	36	13	36.1	20.8	53.8	38	5	13.2	4.4	28.1
	Grade 3	36	1	2.8	0.1	14.5	38	0	0.0	0.0	9.3
	Related	36	12	33.3	18.6	51.0	38	2	5.3	0.6	17.7
Shivering	Any	36	13	36.1	20.8	53.8	38	1	2.6	0.1	13.8
	Grade 3	36	1	2.8	0.1	14.5	38	0	0.0	0.0	9.3
	Related	36	13	36.1	20.8	53.8	38	0	0.0	0.0	9.3

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
Any = incidence of a particular symptom regardless of intensity grade or relationship to vaccination

Grade 3 symptom = symptom that prevented normal everyday activities
Related = symptoms assessed by the investigator as causally related to vaccination

Primary Efficacy Results: For results about unsolicited adverse events and serious adverse events, please refer to the safety section of this CTRS

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibody titre at Day 0 and Day 21 (ATP cohort for immunogenicity)

Antibody against	Group	Timing	N	≥ 1:10				GMT		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
A/New Caledonia	Flu-1	PRE	36	36	100	90.3	100	63.5	48.4	83.4
		PI(D21)	36	36	100	90.3	100	117.7	92.7	149.4
	Flu-2	PRE	38	37	97.4	86.2	99.9	52.6	36.7	75.4
		PI(D21)	38	37	97.4	86.2	99.9	90.1	62.3	130.3
A/Wisconsin	Flu-1	PRE	36	35	97.2	85.5	99.9	76.9	50.7	116.8
		PI(D21)	36	36	100	90.3	100	538.2	372.4	777.8
	Flu-2	PRE	38	35	92.1	78.6	98.3	63.1	43.8	91.0
		PI(D21)	38	38	100	90.7	100	222.2	163.8	301.6
B/Malaysia	Flu-1	PRE	36	36	100	90.3	100	40.3	29.7	54.8
		PI(D21)	36	36	100	90.3	100	188.5	140.0	253.7
	Flu-2	PRE	38	38	100	90.7	100	45.9	35.3	59.6
		PI(D21)	38	38	100	90.7	100	169.1	125.6	227.7

GMT = geometric mean antibody titre
N = number of subjects with available results
n (%) = number (percentage) of seropositive subjects (HI titre ≥ 1:10)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination Dose 1 at Day 0
PI(D21) = post-vaccination Dose 1 at Day 21

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

Antibody against	Group	SCR				
		N	n	%	95% CI	
					LL	UL
A/New Caledonia	Flu-1	36	6	16.7	6.4	32.8
	Flu-2	38	6	15.8	6.0	31.3
A/Wisconsin	Flu-1	36	26	72.2	54.8	85.8
	Flu-2	38	13	34.2	19.6	51.4
B/Malaysia	Flu-1	36	24	66.7	49.0	81.4
	Flu-2	38	16	42.1	26.3	59.2

Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n (%) = number (percentage) of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): Seroconversion factor (SCF) for HI antibody titre at Day 21 (ATP cohort for immunogenicity)

Antibody against	Group	N	SCF		
			Value	95% CI	
				LL	UL
A/New Caledonia	Flu-1	36	1.9	1.5	2.2
	Flu-2	38	1.7	1.2	2.5
A/Wisconsin	Flu-1	36	7.0	4.7	10.3
	Flu-2	38	3.5	2.5	5.0
B/Malaysia	Flu-1	36	4.7	3.5	6.2
	Flu-2	38	3.7	2.6	5.2

SCF = seroconversion factor of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal

HI titre
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): Seroprotection rates (SPR) for HI antibody titre at Day 0 and Day 21 (ATP cohort for immunogenicity)

Antibody against	Group	Timing	SPR				
			N	n	%	95% CI	
						LL	UL
A/New Caledonia	Flu-1	PRE	36	28	77.8	60.8	89.9
		PI(D21)	36	35	97.2	85.5	99.9
	Flu-2	PRE	38	27	71.1	54.1	84.6
		PI(D21)	38	34	89.5	75.2	97.1
A/Wisconsin	Flu-1	PRE	36	27	75.0	57.8	87.9
		PI(D21)	36	35	97.2	85.5	99.9
	Flu-2	PRE	38	31	81.6	65.7	92.3
		PI(D21)	38	37	97.4	86.2	99.9
B/Malaysia	Flu-1	PRE	36	20	55.6	38.1	72.1
		PI(D21)	36	36	100	90.3	100
	Flu-2	PRE	38	26	68.4	51.3	82.5
		PI(D21)	38	38	100	90.7	100

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

Secondary Outcome Variable(s): Percentage of subjects with anti-MPL antibody concentrations ≥ the limit of quantitation level and GMCs at Day 0 and Day 21 (ATP cohort for immunogenicity)

Group	Timing	N	≥ 59 EL.U/mL				GMC (EL.U/mL)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
Flu-1	PRE	36	31	86.1	70.5	95.3	198.2	143.5	273.8
	PI(D21)	36	34	94.4	81.3	99.3	594.8	417.9	846.7
Flu-2	PRE	37	18	48.6	31.9	65.6	74.6	52.0	106.9
	PI(D21)	38	25	65.8	48.6	80.4	125.1	82.6	189.4

GMC = geometric mean antibody concentration
N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody concentration ≥ 59 EL.U/mL
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination Dose 1 at Day 0
PI(D21) = post-vaccination Dose 1 a t Day 21

Secondary Outcome Variable(s): Descriptive statistics on the frequency of cytokine-positive CD4 T-cells (per million CD4 T-cells) for each strain at Day 0 and Day 21 (ATP cohort for immunogenicity)

Immune marker	Stimulating antigen	Group	Timing	N	Nmiss	GM	SD	Median
CD4. All doubles	A/New Caledonia	Flu-1	PRE	35	1	825.00	619.49	1056.00
			PI(D21)	35	1	1666.81	916.01	1705.00
		Flu-2	PRE	35	3	576.96	483.69	538.00
			PI(D21)	36	2	920.49	756.25	817.50
	A/Wisconsin	Flu-1	PRE	35	1	372.06	314.43	446.00
			PI(D21)	35	1	498.86	509.52	608.00
		Flu-2	PRE	35	3	148.51	192.35	216.00
			PI(D21)	36	2	319.52	398.33	338.50
	B/Malaysia	Flu-1	PRE	35	1	961.89	486.85	1180.00
			PI(D21)	35	1	1867.22	902.97	1807.00
		Flu-2	PRE	35	3	751.70	437.63	876.00

			PI(D21)	36	2	1117.70	682.45	1130.00
	Pooled strains	Flu-1	PRE	35	1	2104.77	1043.04	2412.00
			PI(D21)	35	1	4176.85	1978.54	4188.00
		Flu-2	PRE	35	3	1602.29	937.48	1576.00
			PI(D21)	36	2	2464.81	1396.53	2547.00
CD4. CD40L	A/New Caledonia	Flu-1	PRE	35	1	723.20	582.31	985.00
			PI(D21)	35	1	1471.77	819.74	1539.00
		Flu-2	PRE	35	3	507.74	456.89	471.00
			PI(D21)	36	2	781.48	676.91	711.50
	A/Wisconsin	Flu-1	PRE	35	1	264.30	295.86	429.00
			PI(D21)	35	1	394.56	468.73	491.00
		Flu-2	PRE	35	3	97.45	157.66	167.00
			PI(D21)	36	2	235.63	362.36	260.50
	B/Malaysia	Flu-1	PRE	35	1	726.46	467.40	956.00
			PI(D21)	35	1	1575.63	817.80	1632.00
		Flu-2	PRE	35	3	638.66	393.60	618.00
			PI(D21)	36	2	948.84	567.54	966.00
	Pooled strains	Flu-1	PRE	35	1	1848.49	949.66	2145.00
			PI(D21)	35	1	3630.08	1822.09	3850.00
		Flu-2	PRE	35	3	1393.13	852.22	1470.00
			PI(D21)	36	2	2125.84	1236.49	2241.00
CD4. IFN-γ	A/New Caledonia	Flu-1	PRE	35	1	546.48	480.07	651.00
			PI(D21)	35	1	1007.72	644.51	1161.00
		Flu-2	PRE	35	3	262.08	312.05	323.00
			PI(D21)	36	2	440.25	520.69	459.00
	A/Wisconsin	Flu-1	PRE	35	1	175.08	213.54	210.00
			PI(D21)	35	1	365.26	383.10	434.00
		Flu-2	PRE	35	3	54.70	99.28	109.00
			PI(D21)	36	2	185.43	239.54	191.50
	B/Malaysia	Flu-1	PRE	35	1	515.60	385.49	622.00
			PI(D21)	35	1	1178.39	713.74	1313.00
		Flu-2	PRE	35	3	306.37	337.90	320.00
			PI(D21)	36	2	484.69	506.99	617.50
	Pooled strains	Flu-1	PRE	35	1	1176.07	810.60	1335.00
			PI(D21)	35	1	2633.52	1354.87	2836.00
		Flu-2	PRE	35	3	748.52	623.12	788.00
			PI(D21)	36	2	1282.71	854.58	1495.00
CD4. IL-2	A/New Caledonia	Flu-1	PRE	35	1	742.50	539.78	904.00
			PI(D21)	35	1	1464.45	808.31	1472.00
		Flu-2	PRE	35	3	497.40	424.03	541.00
			PI(D21)	36	2	793.27	682.87	731.50
	A/Wisconsin	Flu-1	PRE	35	1	318.33	268.73	340.00
			PI(D21)	35	1	409.91	421.98	446.00
		Flu-2	PRE	35	3	130.21	176.16	176.00
			PI(D21)	36	2	276.52	350.26	271.50
	B/Malaysia	Flu-1	PRE	35	1	838.59	438.83	1015.00
			PI(D21)	35	1	1593.12	799.39	1596.00
		Flu-2	PRE	35	3	631.04	390.90	659.00
			PI(D21)	36	2	977.32	627.69	1006.50
	Pooled strains	Flu-1	PRE	35	1	1800.98	970.46	2019.00
			PI(D21)	35	1	3605.58	1748.74	3602.00
		Flu-2	PRE	35	3	1366.11	843.79	1451.00
			PI(D21)	36	2	2104.25	1229.21	2137.00
CD4. TNF-α	A/New Caledonia	Flu-1	PRE	35	1	666.85	554.47	809.00
			PI(D21)	35	1	1312.45	744.43	1402.00

		Flu-2	PRE	35	3	445.25	418.83	503.00
			PI(D21)	36	2	676.62	603.96	650.50
	A/Wisconsin	Flu-1	PRE	35	1	244.02	284.28	352.00
			PI(D21)	35	1	378.70	426.23	530.00
		Flu-2	PRE	35	3	100.78	176.19	157.00
			PI(D21)	36	2	229.28	322.18	240.00
	B/Malaysia	Flu-1	PRE	35	1	762.05	410.29	873.00
			PI(D21)	35	1	1386.45	730.64	1496.00
		Flu-2	PRE	35	3	596.87	378.99	610.00
			PI(D21)	36	2	839.27	550.60	926.00
	Pooled strains	Flu-1	PRE	35	1	1725.85	917.29	2054.00
			PI(D21)	35	1	3253.24	1459.71	3277.00
		Flu-2	PRE	35	3	1272.70	833.25	1359.00
			PI(D21)	36	2	1903.06	1140.51	1931.50

N = number of subjects with available results
GM= Geometric Mean
SD = Standard Deviation
Nmiss = number of subjects with missing results
CD4. All doubles: T-cells producing at least 2 cytokines
CD4. CD40L = T-cells producing at least CD40L and another cytokine
CD4. IL2 = T-cells producing at least IL2 and another cytokine
CD4. INFγ = T-cells producing at least INFγ and another cytokine
CD4. TNFα = T-cells producing at least TNFα and another cytokine
PRE = pre-vaccination Dose 1 at Day 0
PI(D21) = post-vaccination Dose 1 at Day 21

Secondary Outcome Variable(s): Descriptive statistics on the frequency of cytokine-positive CD8 T-cells (per million CD8 T-cells) for each strain at Day 0 and Day 21 (ATP cohort for immunogenicity)

Immune marker	**Stimulating antigen**	**Group**	**Timing**	**N**	**Nmiss**	**GM**	**SD**	**Median**
CD8. All doubles	A/New Caledonia	Flu-1	PRE	34	2	8.92	187.49	1.00
			PI(D21)	35	1	9.55	240.50	1.00
		Flu-2	PRE	35	3	11.30	197.38	3.00
			PI(D21)	36	2	13.48	177.88	35.00
	A/Wisconsin	Flu-1	PRE	35	1	13.13	120.47	67.00
			PI(D21)	35	1	5.34	92.96	1.00
		Flu-2	PRE	35	3	8.98	57.91	1.00
			PI(D21)	36	2	5.74	50.79	1.00
	B/Malaysia	Flu-1	PRE	35	1	28.01	175.78	75.00
			PI(D21)	35	1	17.11	200.83	72.00
		Flu-2	PRE	35	3	9.20	108.45	1.00
			PI(D21)	36	2	6.49	64.20	1.00
	Pooled strains	Flu-1	PRE	34	2	21.49	266.71	74.00
			PI(D21)	35	1	44.29	283.36	145.00
		Flu-2	PRE	35	3	30.46	212.21	93.00
			PI(D21)	36	2	13.17	243.54	4.00
CD8. CD40L	A/New Caledonia	Flu-1	PRE	34	2	1.30	19.74	1.00
			PI(D21)	35	1	1.84	25.10	1.00
		Flu-2	PRE	35	3	1.63	23.38	1.00
			PI(D21)	36	2	1.61	22.57	1.00
	A/Wisconsin	Flu-1	PRE	35	1	5.12	75.34	1.00
			PI(D21)	35	1	1.93	54.05	1.00
		Flu-2	PRE	35	3	2.45	40.04	1.00
			PI(D21)	36	2	1.64	22.27	1.00
	B/Malaysia	Flu-1	PRE	35	1	3.82	80.68	1.00
			PI(D21)	35	1	2.41	113.96	1.00

		Flu-2	PRE	35	3	2.54	46.64	1.00
			PI(D21)	36	2	2.13	34.03	1.00
	Pooled strains	Flu-1	PRE	34	2	3.10	108.03	1.00
			PI(D21)	35	1	5.07	105.88	1.00
		Flu-2	PRE	35	3	1.94	42.49	1.00
			PI(D21)	36	2	1.85	32.41	1.00
CD8. IFN-γ	A/New Caledonia	Flu-1	PRE	34	2	6.11	190.75	1.00
			PI(D21)	35	1	7.45	243.05	1.00
		Flu-2	PRE	35	3	7.41	192.90	1.00
			PI(D21)	36	2	10.81	177.11	1.50
	A/Wisconsin	Flu-1	PRE	35	1	3.77	61.72	1.00
			PI(D21)	35	1	3.99	72.14	1.00
		Flu-2	PRE	35	3	2.20	28.09	1.00
			PI(D21)	36	2	2.40	40.26	1.00
	B/Malaysia	Flu-1	PRE	35	1	9.22	91.98	1.00
			PI(D21)	35	1	12.02	133.42	67.00
		Flu-2	PRE	35	3	3.80	79.64	1.00
			PI(D21)	36	2	4.51	47.43	1.00
	Pooled strains	Flu-1	PRE	34	2	8.71	237.11	1.00
			PI(D21)	35	1	12.86	291.36	1.00
		Flu-2	PRE	35	3	12.04	209.40	5.00
			PI(D21)	36	2	13.33	217.86	38.50
CD8. IL-2	A/New Caledonia	Flu-1	PRE	34	2	5.00	117.21	1.00
			PI(D21)	35	1	4.26	105.25	1.00
		Flu-2	PRE	35	3	8.49	79.44	1.00
			PI(D21)	36	2	4.17	102.57	1.00
	A/Wisconsin	Flu-1	PRE	35	1	9.63	116.27	1.00
			PI(D21)	35	1	4.62	84.54	1.00
		Flu-2	PRE	35	3	8.78	55.39	1.00
			PI(D21)	36	2	4.53	50.46	1.00
	B/Malaysia	Flu-1	PRE	35	1	16.87	172.06	74.00
			PI(D21)	35	1	9.17	181.07	1.00
		Flu-2	PRE	35	3	4.79	69.40	1.00
			PI(D21)	36	2	3.33	50.43	1.00
	Pooled strains	Flu-1	PRE	34	2	13.88	239.55	8.50
			PI(D21)	35	1	35.72	187.69	134.00
		Flu-2	PRE	35	3	13.80	118.45	75.00
			PI(D21)	36	2	6.03	94.53	1.00
CD8. TNF-α	A/New Caledonia	Flu-1	PRE	34	2	7.55	165.15	1.00
			PI(D21)	35	1	6.49	250.57	1.00
		Flu-2	PRE	35	3	6.70	195.35	1.00
			PI(D21)	36	2	11.57	166.56	2.50
	A/Wisconsin	Flu-1	PRE	35	1	7.73	75.97	1.00
			PI(D21)	35	1	4.33	53.80	1.00
		Flu-2	PRE	35	3	4.77	56.68	1.00
			PI(D21)	36	2	4.34	43.52	1.00
	B/Malaysia	Flu-1	PRE	35	1	15.17	130.56	67.00
			PI(D21)	35	1	17.45	152.72	73.00
		Flu-2	PRE	35	3	7.22	87.99	1.00
			PI(D21)	36	2	6.01	57.59	1.00
	Pooled strains	Flu-1	PRE	34	2	12.25	206.95	9.50
			PI(D21)	35	1	27.48	258.14	72.00
		Flu-2	PRE	35	3	20.36	206.20	86.00
			PI(D21)	36	2	10.01	214.64	2.50
N = number of subjects with available results								

GM= Geometric Mean
SD = Standard Deviation
Nmiss = number of subjects with missing results
CD8. All doubles: T-cells producing at least 2 cytokines
CD8. CD40L = T-cells producing at least CD40L and another cytokine
CD8. IL2 = T-cells producing at least IL2 and another cytokine
CD8. INFγ = T-cells producing at least INFγ and another cytokine
CD8. TNFα = T-cells producing at least TNFα and another cytokine
PRE = pre-vaccination Dose 1 at Day 0
PI(D21) = post-vaccination Dose 1 at Day 21

Safety Results: Number (%) of subjects with unsolicited adverse events (AEs) reported during the 21-day follow-up period (Total Vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Days 0-20 following vaccination)	**Flu-1 Group N = 36**	**Flu-2 Group N = 38**
Subjects with any AE(s), n (%)	8 (22.2)	11 (28.9)
Subjects with Grade 3* AE(s)	3 (8.3)	0 (0.0)
Subjects with related **AE(s)	2 (5.6)	1 (2.6)
Nasopharyngitis	1 (2.8)	3 (7.9)
Chills	2 (5.6)	1 (2.6)
Upper respiratory tract infection	1 (2.8)	2 (5.3)
Listlessness	1 (2.8)	1 (2.6)
Arthritis	-	1 (2.6)
Diarrhoea	-	1 (2.6)
Emotional disorder	-	1 (2.6)
Gastroenteritis	-	1 (2.6)
Headache	1 (2.8)	-
Herpes zoster	1 (2.8)	-
Nausea	1 (2.8)	-
Nervousness	1 (2.8)	-
Pharyngolaryngeal pain	-	1 (2.6)
Pyrexia	1 (2.8)	-
Rhinitis	-	1 (2.6)
Sensation of heaviness	1 (2.8)	-
Tooth abscess	1 (2.8)	-
Vertigo	1 (2.8)	-

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

Safety Results: Number (%) of subjects with serious adverse events (SAEs) throughout the study (Total Vaccinated cohort)

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

All SAEs	**Flu-1 Group N = 36**	**Flu-2 Group N = 38**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**Flu-1 Group N = 36**	**Flu-2 Group N = 38**
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:
During the 7-day post-vaccination period, across groups, pain was the most frequently reported solicited local symptom with 24 (66.7%) and 10 (26.3%) subjects in the Flu-1 and the Flu-2 groups, respectively. In the Flu-2 Group, no grade 3 local symptoms were reported. In the Flu-1 Group, 3 subjects reported redness above 50 mm and 1 subject reported swelling above 50 mm.
During the same period, the most frequently reported solicited general symptom was fatigue for 18 (50.0%) and 6 (15.8%) subjects in the Flu-1 and Flu-2 groups, respectively. Among all the general symptoms assessed, related symptoms were reported in at least 8.3% of the subjects in the Flu-1 Group and 2.6% of the subjects in the Flu-2 Group.

Grade 3 headache, myalgia and shivering in the Flu-1 Group and Grade 3 fatigue in the Flu-2 Group were each reported in 1 subject.
Within the 21-day follow-up period, at least one unsolicited AE was reported by 8 (22.2%) and 11 (28.9%) subjects in the Flu-1 Group and the Flu-2 Group, respectively. During the same period, 3 (8.3%) subjects in the Flu-1 Group reported grade 3 unsolicited AEs and 2 (5.6%) subjects and 1 (2.6%) subject in the Flu-1 and the Flu-2 groups, respectively, reported unsolicited AEs assessed by the investigator as causally related to the vaccination. No SAEs were reported throughout this study.

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