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.: 104540 (FLUAS25-002)

Title: A phase I/II, open, controlled study in order to evaluate the reactogenicity and the immunogenicity of GlaxoSmithKline (GSK) Biologicals influenza candidate vaccine containing the adjuvant AS25 (FluAS25) in an elderly population aged over 65 years (> 65 years-old) previously vaccinated in 2004 with the same candidate vaccine in FLUAS25-001 clinical trial. For immunogenicity and safety evaluations, Fluarix™ (known as α-Rix™ in Belgium) vaccine will be used as reference.
FluAS25 (Flu 1): GSK Biologicals' influenza vaccine adjuvanted with AS25
Fluarix™ (Flu 2): GSK Biologicals' trivalent inactivated split virion influenza vaccine

Rationale: The aim of the study was to evaluate the immunogenicity and safety of a re-vaccination with Flu 1 vaccine about 1 year after administration of the first dose of vaccine in the study Flu-AS25-001 (103304).
Please refer to the 103304 CTRS for results of the Flu-AS25-001 study.

Phase: I/II

Study Period: 03 October 2005 to 04 November 2005

Study Design: Open, controlled, single centre study with 2 parallel groups.

Centres: 1 centre in Belgium.

Indication: Immunisation against influenza disease in an elderly population aged over 65 years (>65 years old).

Treatment: The 2 treatment groups were as follows:

- Flu 1 Group: Subjects in this group received 1 dose of the investigational Flu 1 vaccine at Day 0.
- Flu 2 Group: Subjects in this group received 1 dose of commercially available Flu 2 vaccine at Day 0.

The vaccines were administered intramuscularly (IM) in the deltoid region of the non-dominant arm.

Objective:

- To evaluate the safety of a re-vaccination with Flu 1 vaccine during the 21-day following the IM administration of the vaccine. Flu 2 vaccine was used as reference.

Primary Outcome/Efficacy Variable:

- 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 and overall.
- 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 and overall.
- Occurrence of serious adverse events (SAEs) during the entire study.

Secondary Outcome/Efficacy Variable(s):
For the humoral immune response

Observed variables:

- At Days 0 and 21: serum haemagglutination-inhibition (HI) antibody titres, tested separately against each of the three influenza virus strains represented in the vaccine.

Derived variables (with 95% confidence intervals (CIs)):

- Geometric mean titres (GMTs) of serum HI antibodies with 95% confidence intervals (95% CI) pre and post-vaccination
- Seroconversion rates* with 95% CI at Day 21
- Conversion factors** with 95% CI at Day 21
- Seroprotection rates*** with 95% CI at Day 21

* Seroconversion rate defined as the percentage of vaccinees 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, for each vaccine strain.
**Conversion factor defined as the fold increase in serum HI GMTs on Day 21 compared to Day 0, for each vaccine strain.
***Protection rate defined as the percentage of vaccinees with a serum HI titre ≥ 1:40 after vaccination (for each vaccine strain) that usually is accepted as indicating protection.

Observed variables:

- At Days 0 and 21: Anti-3-deacylated Monophosphoryl Lipid A (anti-MPL) antibody titres

Derived variables (with 95% CIs):

- Geometric mean titres (GMTs) of serum anti-MPL antibodies with 95% CI pre and post-vaccination

For the 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 CD4/CD8 cells per 10^6 in tests producing at least two different cytokines (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).

- Difference between post (Day 21) and pre (Day 0) vaccination expressed as frequency of Influenza-specific antibody forming cells per million of antibody forming cells

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

Statistical Methods:

The 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 vaccinated subjects (i.e., those meeting all eligibility criteria, who complied with the procedures defined in the protocol, with no elimination criteria during the study) for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination.

Analysis of immunogenicity:

The analysis of immunogenicity was performed on the ATP cohort for Immunogenicity.

For Humoral immune response and for each group, the following parameters were tabulated with 95% CIs

- Seropositivity rate and GMTs for HI antibody titres at Days 0 and 21.
- Seroconversion rates for HI antibody titres at Day 21
- Seroconversion factors for HI antibody titres at Day 21
- Seroprotection rates for HI antibody titres at Days 0 and 21
- Geometric mean concentrations (GMCs) for anti-MPL antibody titres at Days 0 and 21

For the CMI response, the frequency of CD4/CD8 T-cells was summarised for each group, each antigen and for each test at Days 0 and 21; descriptive statistics in individual difference between Day 21 and Day 0 (Post-Pre) responses were tabulated for each group and each antigen at each test.

Analysis of safety:

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

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

The percentage of subjects with at least one report of unsolicited adverse event (AE) classified by Medical Dictionary for Regulatory Activities (MedDRA) preferred term and reported within 21 days (Days 0–20) following vaccination was tabulated. The same tabulation was done for grade 3 AEs and for AEs with relationship to vaccination.

The percentage of subjects with at least one report of SAE occurring during the study and classified by MedDRA preferred term was also tabulated.

Study Population: Healthy male or female aged over 65 years (> 65 years old) at the time of the re-vaccination, who received either the Flu 1 vaccine formulation or Flu 2 vaccine during the previous study 103304 were included . Subjects with history of confirmed influenza infection since a year from the date of previous vaccination were excluded. Written informed consent was obtained from the subjects prior to study entry.

Number of subjects	**Flu 1 Group**	**Flu 2 Group**
Planned, N	50	50
Randomized, N (Total Vaccinated cohort)	38	45

Completed, n (%)	38 (100)	45 (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)	38	45
Females: Males	22:16	27:18
Mean Age, years (SD)	71.4 (4.86)	71.7 (5.57)
White/Caucasian – European heritage, n (%)	38 (100.0)	44 (97.8)

Primary Outcome Variable(s): 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**
Haematoma	Any	38	3	7.9	1.7	21.4	45	1	2.2	0.1	11.8
	> 50 mm	38	0	0.0	0.0	9.3	45	0	0.0	0.0	7.9
Pain	Any	38	19	50.0	33.4	66.6	45	9	20.0	9.6	34.6
	Grade 3	38	0	0.0	0.0	9.3	45	0	0.0	0.0	7.9
Redness	Any	38	6	15.8	6.0	31.3	45	5	11.1	3.7	24.1
	> 50 mm	38	2	5.3	0.6	17.7	45	0	0.0	0.0	7.9
Swelling	Any	38	5	13.2	4.4	28.1	45	1	2.2	0.1	11.8
	> 50 mm	38	3	7.9	1.7	21.4	45	0	0.0	0.0	7.9

N: number of subjects with the administered dose
n (%): number (percentage) of subjects reporting the symptom at least once
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 Outcome Variable(s): 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**
Fatigue	Any	38	11	28.9	15.4	45.9	45	2	4.4	0.5	15.1
	Grade 3	38	0	0.0	0.0	9.3	45	0	0.0	0.0	7.9
	Related	38	10	26.3	13.4	43.1	45	2	4.4	0.5	15.1
Fever (Axillary)	≥37.5°C	38	3	7.9	1.7	21.4	45	0	0.0	0.0	7.9
	> 39.0°C	38	0	0.0	0.0	9.3	45	0	0.0	0.0	7.9
	Related	38	3	7.9	1.7	21.4	45	0	0.0	0.0	7.9
Headache	Any	38	9	23.7	11.4	40.2	45	6	13.3	5.1	26.8
	Grade 3	38	0	0.0	0.0	9.3	45	0	0.0	0.0	7.9
	Related	38	9	23.7	11.4	40.2	45	6	13.3	5.1	26.8
Joint pain in the arm of the injection	Any	38	7	18.4	7.7	34.3	45	3	6.7	1.4	18.3
	Grade 3	38	1	2.6	0.1	13.8	45	0	0.0	0.0	7.9
	Related	38	7	18.4	7.7	34.3	45	2	4.4	0.5	15.1
Joint pain at other locations	Any	38	5	13.2	4.4	28.1	45	1	2.2	0.1	11.8
	Grade 3	38	2	5.3	0.6	17.7	45	0	0.0	0.0	7.9
	Related	38	4	10.5	2.9	24.8	45	0	0.0	0.0	7.9
Muscle aches	Any	38	14	36.8	21.8	54.0	45	5	11.1	3.7	24.1
	Grade 3	38	2	5.3	0.6	17.7	45	0	0.0	0.0	7.9
	Related	38	14	36.8	21.8	54.0	45	5	11.1	3.7	24.1
Shivering	Any	38	6	15.8	6.0	31.3	45	2	4.4	0.5	15.1
	Grade 3	38	1	2.6	0.1	13.8	45	0	0.0	0.0	7.9
	Related	38	6	15.8	6.0	31.3	45	2	4.4	0.5	15.1

N: number of subjects with the administered dose

n (%): number (percentage) of subjects reporting the symptom at least once
95% CI: exact 95% confidence interval; LL: lower limit, UL: upper limit
Any: incidence of a particular symptom regardless of intensity grade and relationship to vaccination
Grade 3: symptom which prevented normal everyday activities
Related: symptom considered by the investigator to have a causal relationship to study vaccination

Primary Outcome Variable(s): For results about unsolicited adverse events and serious adverse events, please refer to safety section

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies at pre and post-vaccination for each vaccine strain (ATP cohort for Immunogenicity)

				≥ 1:10				GMT		
						95% CI			95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
A/New Caledonia	Flu 1	PRE	38	32	84.2	68.7	94.0	45.8	29.5	71.3
		PI(D21)	38	38	100	90.7	100	142.1	99.0	204.0
	Flu 2	PRE	45	39	86.7	73.2	94.9	35.6	23.4	54.1
		PI(D21)	45	44	97.8	88.2	99.9	90.5	61.0	134.3
A/New York	Flu 1	PRE	38	34	89.5	75.2	97.1	36.2	25.4	51.6
		PI(D21)	38	37	97.4	86.2	99.9	316.9	204.8	490.5
	Flu 2	PRE	45	43	95.6	84.9	99.5	41.2	31.4	54.1
		PI(D21)	45	45	100	92.1	100	248.2	178.2	345.9
B/Jiangsu	Flu 1	PRE	38	36	94.7	82.3	99.4	51.1	35.7	73.0
		PI(D21)	38	38	100	90.7	100	259.4	200.2	336.1
	Flu 2	PRE	45	44	97.8	88.2	99.9	56.1	43.8	71.9
		PI(D21)	45	45	100	92.1	100	174.1	130.1	233.0

GMT: geometric mean titre calculated on all subjects
N: number of subjects with available results
n (%):number/percentage of subjects with titres within the specified range
95% CI: 95% confidence interval; LL: lower limit; UL: upper limit
PRE: pre-vaccination blood sample at Day 0
PI(D21): post-vaccination blood sample at Day 21

Secondary Outcome Variable(s): Seroconversion rates (SCR) for HI antibody titres at Day 21 (ATP cohort for Immunogenicity)

Vaccine strain	**Group**	**N**	**Seroconversion rates**			
			n	**%**	**95%CI**	
					LL	**UL**
A/New Caledonia	Flu 1	38	12	31.6	17.5	48.7
	Flu 2	45	14	31.1	18.2	46.6
A/New York	Flu 1	38	30	78.9	62.7	90.4
	Flu 2	45	31	68.9	53.4	81.8
B/Jiangsu	Flu 1	38	22	57.9	40.8	73.7
	Flu 2	45	17	37.8	23.8	53.5

Seroconversion rate defined as the percentage of vaccinees 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, for each vaccine strain.
N: number of subjects with available results
n (%): number (percentage) of seroconverted subjects
95% CI: 95% confidence interval; LL: lower limit; UL: upper limit

Secondary Outcome Variable(s): Seroconversion factors (SCF) for HI antibody titres at Day 21(ATP cohort for Immunogenicity)

Vaccine strain	**Group**	**N**	**SCF**	**95%CI**	
				LL	**UL**
A/New Caledonia	Flu 1	38	3.1	2.2	4.4
	Flu 2	45	2.5	1.8	3.5
A/New York	Flu 1	38	8.8	6.1	12.5
	Flu 2	45	6.0	4.4	8.3
B/Jiangsu	Flu 1	38	5.1	3.7	7.0

	Flu 2	45	3.1	2.4	4.0

N: number of subjects with available results
95% CI: 95% confidence interval; LL: lower limit; UL: upper limit
SCF: defined as the fold increase in serum HI GMTs on Day 21 compared to Day 0, for each vaccine strain

Secondary Outcome Variable(s): Seroprotection rates for HI antibodies at pre and post-vaccination (ATP cohort for Immunogenicity)

Vaccine strain	Group	Timing	N	≥ 1:40			
				n	%	95%CI	
						LL	UL
A/New Caledonia	Flu 1	PRE	38	26	68.4	51.35	82.50
		PI(D21)	38	34	89.5	75.20	97.06
	Flu 2	PRE	45	22	48.9	33.70	64.23
		PI(D21)	45	37	82.2	67.95	92.00
A/New York	Flu 1	PRE	38	23	60.5	43.39	75.96
		PI(D21)	38	35	92.1	78.62	98.34
	Flu 2	PRE	45	30	66.7	51.05	80.00
		PI(D21)	45	43	95.6	84.85	99.46
B/Jiangsu	Flu 1	PRE	38	23	60.5	43.39	75.96
		PI(D21)	38	38	100.0	90.75	100.00
	Flu 2	PRE	45	33	73.3	58.06	85.40
		PI(D21)	45	45	100.0	92.13	100.00

N: number of subjects with available results
n (%): number (percentage) of seroprotected subjects (antibody titre ≥ 1:40)
95% CI: 95% confidence interval; LL: Lower limit; UL: Upper limit
PRE: pre-vaccination blood sample at Day 0
PI(D21): post-vaccination blood sample at Day 21.

Secondary Outcome Variable(s): Seropositivity rates and GMCs for anti-MPL antibodies (ATP cohort for Immunogenicity)

				≥ 59 EL.U/mL				GMC(EL.U/mL)		
						95% CI			95% CI	
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL
New Anti-MPL	Flu 1	PRE	37	33	89.2	74.6	97.0	199.2	144.3	275.1
		PI(D21)	38	37	97.4	86.2	99.9	661.5	461.7	947.7
	Flu 2	PRE	43	24	55.8	39.9	70.9	74.7	56.5	98.9
		PI(D21)	43	30	69.8	53.9	82.8	111.4	81.6	152.0

GMC = geometric mean concentration calculated on all subjects
N = number of subjects with available results
n(%) = number(percentage) of subjects with concentration within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE= pre-vaccination blood sample at Day 0
PI(D21) = post-vaccination blood sample at Day 21

Secondary Outcome Variable(s): Descriptive Statistics for the frequency of positive CD4 T-cells (per million CD4 T-cells) at each time point (ATP cohort for Immunogenicity)

Vaccine Strain	Test Description	Vaccine Group	Timing	N	GM	Mean	SD	Median
pool flu	CD4- ALL DOUBLES	Flu 1	Day 0	37	1771.08	1923.54	809.90	1646.00
			Day 21	37	2207.97	3070.92	1575.21	3022.00
		Flu 2	Day 0	44	1273.05	1507.36	810.18	1332.50
			Day 21	42	1475.63	1967.74	1093.59	1844.00
	CD4- CD40L	Flu 1	Day 0	37	1754.44	1901.38	784.12	1618.00
			Day 21	37	2150.00	3009.51	1560.01	3007.00
		Flu 2	Day 0	44	1253.00	1486.05	790.06	1305.00
			Day 21	42	1441.60	1921.74	1062.71	1849.00
	CD4- IFNγ	Flu 1	Day 0	37	1172.14	1323.86	641.69	1221.00
			Day 21	37	1386.41	2087.46	1194.93	2228.00
		Flu 2	Day 0	44	795.59	962.27	570.17	803.50
			Day 21	42	1087.62	1328.40	816.55	1146.00

	CD4- IL2	Flu 1	Day 0	37	1577.35	1728.22	761.31	1510.00
			Day 21	37	1803.09	2552.43	1410.93	2643.00
		Flu 2	Day 0	44	1159.71	1377.27	760.73	1256.50
			Day 21	42	1277.79	1695.05	953.98	1597.50
	CD4- TFNα	Flu 1	Day 0	37	1141.47	1282.11	624.48	1138.00
			Day 21	37	1291.84	1810.59	1044.32	1737.00
		Flu 2	Day 0	44	811.74	986.59	574.22	793.50
			Day 21	42	888.21	1188.31	705.56	1072.00
A/New Caledonia	CD4- ALL DOUBLES	Flu 1	Day 0	36	1251.36	1412.06	730.43	1275.00
			Day 21	37	1754.16	2552.76	1688.74	2330.00
		Flu 2	Day 0	44	947.62	1169.77	824.29	922.00
			Day 21	43	918.64	1325.35	858.83	1227.00
	CD4- CD40L	Flu 1	Day 0	36	1238.98	1391.53	704.67	1274.00
			Day 21	37	1682.32	2517.05	1695.20	2295.00
		Flu 2	Day 0	44	931.40	1156.41	825.25	891.00
			Day 21	43	908.77	1307.14	849.30	1183.00
	CD4- IFNγ	Flu 1	Day 0	36	774.32	923.44	563.10	795.00
			Day 21	37	1223.31	1689.95	1198.58	1540.00
		Flu 2	Day 0	44	549.97	747.70	640.27	524.00
			Day 21	43	639.80	883.16	596.86	754.00
	CD4- IL2	Flu 1	Day 0	36	1087.79	1232.33	665.35	1112.00
			Day 21	37	1385.04	2072.43	1443.23	1737.00
		Flu 2	Day 0	44	817.51	1037.45	772.70	821.00
			Day 21	43	855.23	1090.86	697.00	989.00
	CD4- TFNα	Flu 1	Day 0	36	741.39	861.14	519.55	649.50
			Day 21	37	1043.61	1490.95	1183.01	1344.00
		Flu 2	Day 0	44	541.11	715.23	558.55	559.00
			Day 21	43	529.11	766.05	517.73	699.00
A/New York	CD4- ALL DOUBLES	Flu 1	Day 0	37	594.48	743.14	533.24	596.00
			Day 21	37	714.88	1075.86	734.33	927.00
		Flu 2	Day 0	44	353.78	526.57	365.95	469.00
			Day 21	43	458.48	669.51	499.31	528.00
	CD4- CD40L	Flu 1	Day 0	37	591.77	740.78	516.05	597.00
			Day 21	37	738.20	1044.54	719.36	912.00
		Flu 2	Day 0	44	349.03	520.64	363.30	469.00
			Day 21	43	459.87	660.77	488.62	528.00
	CD4- IFNγ	Flu 1	Day 0	37	406.98	510.24	350.90	408.00
			Day 21	37	413.27	770.32	554.66	663.00
		Flu 2	Day 0	44	242.15	352.09	282.21	268.50
			Day 21	43	362.75	470.14	358.35	343.00
	CD4- IL2	Flu 1	Day 0	37	491.45	633.95	475.46	511.00
			Day 21	37	565.37	788.70	592.32	660.00
		Flu 2	Day 0	44	311.08	449.48	310.57	391.00
			Day 21	43	367.76	533.44	422.74	416.00
	CD4- TFNα	Flu 1	Day 0	37	296.14	473.73	356.49	377.00
			Day 21	37	393.11	653.24	512.09	504.00
		Flu 2	Day 0	44	197.91	312.34	242.49	282.50
			Day 21	43	202.95	425.14	385.15	320.00
B/Jiangsu	CD4- ALL DOUBLES	Flu 1	Day 0	37	827.20	927.59	445.33	830.00
			Day 21	37	1141.30	1523.84	794.89	1304.00
		Flu 2	Day 0	44	557.62	746.45	436.40	657.00
			Day 21	43	845.97	1073.49	732.76	799.00
	CD4- CD40L	Flu 1	Day 0	37	815.93	913.08	431.74	813.00
			Day 21	37	1109.34	1484.84	783.16	1304.00
		Flu 2	Day 0	44	551.72	737.48	431.73	632.00

			Day 21	43	832.05	1060.79	731.47	809.00
	CD4- IFNγ	Flu 1	Day 0	37	544.29	639.54	344.12	549.00
			Day 21	37	720.73	1052.00	629.01	989.00
		Flu 2	Day 0	44	348.43	479.86	364.02	389.50
			Day 21	43	569.75	760.09	571.64	534.00
	CD4- IL2	Flu 1	Day 0	37	758.06	846.24	395.44	743.00
			Day 21	37	1044.18	1279.32	708.39	1071.00
		Flu 2	Day 0	44	508.47	682.25	415.45	600.00
			Day 21	43	756.62	933.98	626.94	705.00
	CD4- TFNα	Flu 1	Day 0	37	493.57	569.70	293.97	566.00
			Day 21	37	652.87	887.03	486.71	841.00
		Flu 2	Day 0	44	348.32	481.66	302.37	386.00
			Day 21	43	437.93	651.60	487.24	547.00

N: Number of subjects with available results
All doubles: cells producing at least two different cytokines (CD40L, IFNγ, IL-2, TFNα)
GM: Geometric Mean
SD: Standard Deviation

Secondary Outcome Variable (s): Descriptive Statistics on the individual difference between Day 21 and Day 0 in frequency of cytokine-positive CD4 T-cells (per million CD4 T-cells) (ATP cohort for Immunogenicity)

Vaccine strain	Test Description	Vaccine Group	N	Mean	SD	Median
pool flu	CD4- ALL DOUBLES	Flu 1	37	1147.38	1482.87	1216.00
		Flu 2	41	391.10	859.60	401.00
	CD4- CD40L	Flu 1	37	1108.14	1475.49	1181.00
		Flu 2	41	368.29	856.18	359.00
	CD4- IFNγ	Flu 1	37	763.59	1118.32	759.00
		Flu 2	41	310.73	623.66	259.00
	CD4- IL2	Flu 1	37	824.22	1321.11	766.00
		Flu 2	41	257.32	782.19	276.00
	CD4- TFNα	Flu 1	37	528.49	920.35	577.00
		Flu 2	41	149.51	546.34	154.00
A/New Caledonia	CD4- ALL DOUBLES	Flu 1	36	960.00	1263.66	1028.50
		Flu 2	42	129.40	759.94	129.00
	CD4- CD40L	Flu 1	36	943.25	1277.17	1030.00
		Flu 2	42	123.74	756.94	141.00
	CD4- IFNγ	Flu 1	36	653.53	908.74	600.00
		Flu 2	42	106.67	556.97	116.50
	CD4- IL2	Flu 1	36	680.14	1060.19	612.00
		Flu 2	42	39.26	652.35	11.50
	CD4- TFNα	Flu 1	36	482.42	767.62	532.50
		Flu 2	42	24.26	463.93	39.00
A/New York	CD4- ALL DOUBLES	Flu 1	37	332.73	574.29	320.00
		Flu 2	42	117.50	429.29	96.00
	CD4- CD40L	Flu 1	37	303.76	580.32	275.00
		Flu 2	42	115.50	417.00	100.00
	CD4- IFNγ	Flu 1	37	260.08	472.53	276.00
		Flu 2	42	97.52	310.29	81.50
	CD4- IL2	Flu 1	37	154.76	466.25	175.00
		Flu 2	42	66.40	354.53	25.00
	CD4- TFNα	Flu 1	37	179.51	376.67	147.00
		Flu 2	42	97.62	280.82	59.00
B/Jiangsu	CD4- ALL DOUBLES	Flu 1	37	596.24	600.66	579.00
		Flu 2	42	271.31	580.04	196.50
	CD4- CD40L	Flu 1	37	571.76	611.74	593.00
		Flu 2	42	266.24	581.63	204.50
	CD4- IFNγ	Flu 1	37	412.46	500.52	420.00

		Flu 2	42	238.19	389.13	190.00
	CD4- IL2	Flu 1	37	433.08	555.91	416.00
		Flu 2	42	208.62	531.35	135.50
	CD4- TFNα	Flu 1	37	317.32	375.42	289.00
		Flu 2	42	144.50	416.82	100.50

N: Number of subjects with available results
All doubles: cells producing at least two different cytokines (CD40L, IFNγ, IL-2, TFNα)
SD: Standard Deviation

Secondary Outcome Variable (s): Descriptive Statistics for the frequency of cytokine-positive CD8 T-cells (per million CD8 T-cells) at each time point (ATP cohort for Immunogenicity)

Vaccine Strain	Test Description	Vaccine Group	Timing	N	GM	Mean	SD	Median
pool flu	CD8- ALL DOUBLES	Flu 1	Day 0	36	11.17	75.94	104.13	29.50
			Day 21	36	20.92	131.06	198.54	67.00
		Flu 2	Day 0	44	6.90	69.45	111.36	1.00
			Day 21	42	7.60	78.00	142.68	1.00
	CD8- CD40L	Flu 1	Day 0	36	2.26	24.64	57.18	1.00
			Day 21	36	3.16	28.50	55.75	1.00
		Flu 2	Day 0	44	1.56	9.07	26.82	1.00
			Day 21	42	1.55	10.93	33.75	1.00
	CD8- IFNγ	Flu 1	Day 0	36	6.81	69.39	120.25	1.00
			Day 21	36	11.98	107.78	179.97	9.50
		Flu 2	Day 0	44	4.59	60.55	111.14	1.00
			Day 21	42	8.51	77.52	130.93	1.00
	CD8- IL2	Flu 1	Day 0	36	4.03	31.97	52.76	1.00
			Day 21	36	11.20	86.81	134.47	14.50
		Flu 2	Day 0	44	3.21	31.89	67.06	1.00
			Day 21	42	3.38	34.00	69.62	1.00
	CD8- TFNα	Flu 1	Day 0	36	6.46	53.50	78.22	1.00
			Day 21	36	9.21	94.44	180.74	1.00
		Flu 2	Day 0	44	6.27	60.70	102.06	1.00
			Day 21	42	5.32	67.62	141.34	1.00
A/New Caledonia	CD8- ALL DOUBLES	Flu 1	Day 0	35	5.32	68.46	128.71	1.00
			Day 21	36	5.69	90.92	266.98	1.00
		Flu 2	Day 0	44	8.50	85.98	155.17	1.00
			Day 21	43	5.61	87.65	203.20	1.00
	CD8- CD40L	Flu 1	Day 0	35	1.54	19.14	77.59	1.00
			Day 21	36	2.34	19.19	44.28	1.00
		Flu 2	Day 0	44	1.32	4.93	15.41	1.00
			Day 21	43	1.71	13.05	34.51	1.00
	CD8- IFNγ	Flu 1	Day 0	35	4.10	59.77	127.55	1.00
			Day 21	36	4.46	79.81	271.25	1.00
		Flu 2	Day 0	44	6.99	81.43	154.10	1.00
			Day 21	43	5.77	84.12	196.48	1.00
	CD8- IL2	Flu 1	Day 0	35	3.48	45.00	98.87	1.00
			Day 21	36	3.61	64.92	174.42	1.00
		Flu 2	Day 0	44	3.28	36.52	78.55	1.00
			Day 21	43	2.93	45.42	111.75	1.00
	CD8- TFNα	Flu 1	Day 0	35	4.44	42.29	71.46	1.00
			Day 21	36	4.51	73.19	216.14	1.00
		Flu 2	Day 0	44	6.34	76.07	145.56	1.00
			Day 21	43	5.15	80.37	195.20	1.00
A/New York	CD8- ALL DOUBLES	Flu 1	Day 0	37	4.55	27.51	37.62	1.00
			Day 21	36	4.72	41.17	74.26	1.00
		Flu 2	Day 0	44	3.53	32.05	61.62	1.00

			Day 21	43	2.26	16.16	33.47	1.00
	CD8- CD40L	Flu 1	Day 0	37	1.59	8.84	22.94	1.00
			Day 21	36	2.00	18.67	53.70	1.00
		Flu 2	Day 0	44	1.70	16.59	58.91	1.00
			Day 21	43	1.11	2.91	12.50	1.00
	CD8- IFNγ	Flu 1	Day 0	37	2.57	17.92	33.04	1.00
			Day 21	36	2.83	29.00	68.37	1.00
		Flu 2	Day 0	44	2.38	26.07	67.65	1.00
			Day 21	43	1.54	10.88	33.25	1.00
	CD8- IL2	Flu 1	Day 0	37	2.50	16.14	30.03	1.00
			Day 21	36	2.81	26.61	55.60	1.00
		Flu 2	Day 0	44	2.32	19.82	41.96	1.00
			Day 21	43	1.82	11.19	25.66	1.00
	CD8- TFNα	Flu 1	Day 0	37	3.62	23.86	36.77	1.00
			Day 21	36	2.67	22.69	45.72	1.00
		Flu 2	Day 0	44	2.49	19.16	37.98	1.00
			Day 21	43	1.88	14.26	35.72	1.00
B/Jiangsu	CD8- ALL DOUBLES	Flu 1	Day 0	36	4.55	35.14	56.05	1.00
			Day 21	36	7.90	53.03	78.51	2.00
		Flu 2	Day 0	44	3.44	41.52	84.72	1.00
			Day 21	43	4.57	47.60	108.88	1.00
	CD8- CD40L	Flu 1	Day 0	36	1.91	17.11	45.63	1.00
			Day 21	36	3.25	22.17	42.06	1.00
		Flu 2	Day 0	44	1.50	9.32	28.29	1.00
			Day 21	43	1.98	15.12	42.71	1.00
	CD8- IFNγ	Flu 1	Day 0	36	3.88	27.11	41.33	1.00
			Day 21	36	4.52	36.11	62.51	1.00
		Flu 2	Day 0	44	2.98	33.30	72.02	1.00
			Day 21	43	3.05	39.53	114.23	1.00
	CD8- IL2	Flu 1	Day 0	36	3.09	26.47	52.26	1.00
			Day 21	36	4.26	35.36	67.57	1.00
		Flu 2	Day 0	44	2.35	23.75	58.42	1.00
			Day 21	43	3.35	27.00	53.52	1.00
	CD8- TFNα	Flu 1	Day 0	36	3.03	22.64	40.24	1.00
			Day 21	36	4.82	36.67	59.99	1.00
		Flu 2	Day 0	44	2.98	32.30	68.41	1.00
			Day 21	43	2.70	34.33	101.32	1.00

N: Number of subjects with available results
GM: Geometric Mean
All doubles: cells producing at least two different cytokines (CD40L, IFNγ, IL-2, TFNα)
SD: Standard Deviation

Secondary Outcome Variable(s): Descriptive statistics on the individual difference between Day 21 and Day 0 in frequency of cytokine-positive CD8 T-cells (per million CD8 T-cells) (ATP cohort for Immunogenicity)

Vaccine strain	Test Description	Vaccine Group	N	Mean	SD	Median
pool flu	CD8- ALL DOUBLES	Flu 1	35	33.11	148.96	0.00
		Flu 2	41	8.83	83.89	0.00
	CD8- CD40L	Flu 1	35	3.97	74.32	0.00
		Flu 2	41	1.51	45.75	0.00
	CD8- IFNγ	Flu 1	35	20.03	177.88	0.00
		Flu 2	41	19.63	74.94	0.00
	CD8- IL2	Flu 1	35	41.51	100.89	0.00
		Flu 2	41	4.07	69.27	0.00
	CD8- TFNα	Flu 1	35	18.54	126.37	0.00
		Flu 2	41	4.22	104.40	0.00

A/New Caledonia	CD8- ALL DOUBLES	Flu 1	34	-19.41	145.00	0.00
		Flu 2	42	-0.31	149.99	0.00
	CD8- CD40L	Flu 1	34	-2.29	87.48	0.00
		Flu 2	42	8.21	39.61	0.00
	CD8- IFNγ	Flu 1	34	-24.71	112.48	0.00
		Flu 2	42	0.83	129.33	0.00
	CD8- IL2	Flu 1	34	-8.76	132.98	0.00
		Flu 2	42	8.26	90.13	0.00
	CD8- TFNα	Flu 1	34	-1.74	107.79	0.00
		Flu 2	42	2.62	132.14	0.00
A/New York	CD8- ALL DOUBLES	Flu 1	36	15.28	78.32	0.00
		Flu 2	42	-14.14	74.76	0.00
	CD8- CD40L	Flu 1	36	9.61	60.95	0.00
		Flu 2	42	-14.38	62.07	0.00
	CD8- IFNγ	Flu 1	36	12.97	61.31	0.00
		Flu 2	42	-13.29	78.59	0.00
	CD8- IL2	Flu 1	36	10.06	66.35	0.00
		Flu 2	42	-9.29	54.05	0.00
	CD8- TFNα	Flu 1	36	0.56	56.86	0.00
		Flu 2	42	-2.60	52.35	0.00
B/Jiangsu	CD8- ALL DOUBLES	Flu 1	35	16.49	106.34	0.00
		Flu 2	42	1.95	100.81	0.00
	CD8- CD40L	Flu 1	35	3.09	61.76	0.00
		Flu 2	42	5.74	45.02	0.00
	CD8- IFNγ	Flu 1	35	7.14	77.51	0.00
		Flu 2	42	2.36	97.12	0.00
	CD8- IL2	Flu 1	35	7.23	92.13	0.00
		Flu 2	42	2.79	83.09	0.00
	CD8- TFNα	Flu 1	35	12.51	77.58	0.00
		Flu 2	42	-1.93	86.69	0.00

N: Number of subjects with available results
All doubles: cells producing at least two different cytokines (CD40L, IFNγ, IL-2, TFNα)
SD: Standard Deviation

Safety results: Number (%) of subjects with unsolicited adverse events occurring within the 21-day post-vaccination period (Total Vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Days 0-20 following vaccination)	**Flu 1 Group N = 38**	**Flu 2 Group N = 45**
At least one symptom	6 (15.8)	5 (11.1)
Subjects with grade 3 AE(s), n (%)	1 (2.6)	0 (0.0)
Subjects with related AE(s), n (%)	1 (2.6)	1 (2.2)
Injection site inflammation	-	1 (2.2)
Injection site pruritus	1 (2.6)	-
Bronchitis	-	1 (2.2)
Herpes simplex	1 (2.6)	-
Nasopharyngitis	1 (2.6)	1 (2.2)
Rhinitis	-	1 (2.2)
Upper respiratory tract infection	1 (2.6)	-
Back pain	1 (2.6)	-
Exostosis	1 (2.6)	-
Dysuria	1 (2.6)	-
Pharyngolaryngeal pain	1 (2.6)	-
Acne	1 (2.6)	-
Hypertension	-	1 (2.2)

-= Adverse event absent.

Safety Results: Number (%) of subjects with SAEs during the entire study period (Total Vaccinated cohort)

SAEs, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	**Flu 1 Group N = 38**	**Flu 2 Group N = 45**
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 = 38**	**Flu 2 Group N = 45**
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 follow-up after vaccination, pain was the most frequently reported solicited local symptom in both the Flu 1 (50.0% of subjects) and the Flu 2 (20.0% of subjects) groups. Muscle aches and headache were the most frequently reported solicited general symptoms in the Flu 1 Group (36.8% of subjects) and the Flu 2 Group (11.1% of subjects), respectively. Within the 21-day post vaccination period, at least one unsolicited AE was reported for 6 (15.8%) subjects in the Flu 1 Group and 5 (11.1%) subjects in the Flu 2 Group. One subject in both groups reported one unsolicited AE that was considered as related to the vaccination by the investigators. No SAEs were reported during the entire study period.

Date updated: 21-July-2014