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.: 112147 (FLU NG-038 PRI)

Title: Observer-blind immunogenicity study of GSK Biologicals' influenza vaccine GSK2186877A in elderly subjects GSK2186877A (Flu NG): GlaxoSmithKline (GSK) Biologicals' new generation influenza vaccine

Rationale: The aim of this study was to evaluate the cell-mediated immune (CMI) response, the immunogenicity and the safety of Flu NG vaccine administered in elderly adults (aged 65 years or older) compared to *Fluarix*™ administered in elderly (aged 65 years or older) and young adults (18-40 years).
Fluarix™ (Flu): GSK Biologicals' licensed influenza vaccine

Phase: III

Study Period: 16 October 2008 to 17 December 2009

Study Design: Observer-blind (for subjects ≥65 years) or open (for subjects aged 18-40 year), randomized, multi-centre study with 3 parallel groups.

Centers: 4 centers (3 in Spain and 1 in the United States)

Indication: Seasonal vaccination against influenza virus in subjects 18 to 40 years and 65 years or older.

Treatment: The study groups were as follows:

- Flu NG Group: subjects aged ≥ 65 years receiving 1 dose of Flu NG vaccine at Day 0
- Flu Eld Group: subjects aged ≥ 65 years receiving 1 dose of Flu vaccine at Day 0
- Flu Yng Group: subjects aged 18-40 years receiving 1 dose of Flu vaccine at Day 0.

All vaccines were given intramuscularly in the deltoid of the non dominant arm.

Objectives:

- To demonstrate, in subjects aged ≥65 years, that the frequency of influenza-specific Cluster of Differentiation 4 (CD4) T-cells per 10^6 CD4+ T-cells identified after in vitro stimulation with pooled vaccine strains as producing at least 2 different markers (Cluster of Differentiation 40 Ligand [CD40L], Interleukin-2 [IL-2], Tumor Necrosis Factor α [TNF-α], Interferon-γ [IFN-γ]) induced by the Flu NG vaccine was superior to the one induced by Flu vaccine at Day 21 after vaccination.

Primary Outcome/Efficacy Variable:

- The frequency of influenza-specific CD4 T-cells per 10^6 CD4+ T-cells identified after in vitro stimulation with pooled vaccine strains as producing at least 2 different markers (CD40L, IL-2, TNF-α, IFN-γ) in the Flu NG and Flu Eld groups at Day 21 after vaccination.

Secondary Outcome/Efficacy Variable(s):

CMI response

At Day 0, 21, 42 and 180 in each vaccine group

- Frequency of influenza-specific CD4 T-cells per 10^6 CD4+ T-cells identified after in vitro stimulation with pooled vaccine strains and with each vaccine strain separately as producing at least 2 different markers (CD40L, IL-2, TNF-α, IFN-γ).
- For pooled vaccine strains and for each vaccine strain separately, frequency of influenza-specific CD4 T-cells per 10^6 CD4+ T-cells defined on the expression profile of each of the immune markers CD40L, IL-2, IFN-γ, TNF-α plus another immune marker (CD40L, IL-2, TNF-α, IFN-γ).

  Derived variables:

  For each test, geometric mean (GM) of specific influenza CD4 T-lymphocytes.

Humoral immune response

- At Day 0, 21, 42 and 180 serum hemagglutination-inhibition (HI) antibody titers against each of the 3 vaccine strains.

  Derived variables:
  - Geometric mean titers (GMTs) of HI antibody titers at Day 0, 21, 42 and 180
  - Seropositivity rates at Day 0, 21, 42 and 180
  - Seroconversion rates (SCR)* at Day 21, 42 and 180.
  - Seroconversion factors (SCF)** at Day 21, 42 and 180.
  - Seroprotection rates (SPR)*** at Day 0, 21, 42 and 180.

* SCR is defined as the percentage of vaccinees who have either a prevaccination titer < 1:10 and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least a 4-fold increase in post-vaccination titer.
**SCF is defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.

***SPR is defined as the percentage of vaccinees with a serum HI titer ≥1:40 that usually is accepted as indicating protection.

Safety

- Occurrence, intensity, duration of solicited local adverse events (AEs) during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after vaccination.
- Occurrence, intensity, duration and relationship to vaccination of solicited general AEs during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after vaccination.
- Occurrence, intensity and relationship to vaccination of unsolicited AEs during a 21-day follow-up period (i.e. day of vaccination and 20 subsequent days) after vaccination.
- Occurrence, intensity and relationship to vaccination of AEs with a medically attended visit during a 180 day follow-up period (i.e. day of vaccination and 179 subsequent days) after vaccination.
- Occurrence and relationship to vaccination of serious adverse events (SAEs) and AEs of specific interest[£] (AESI) including autoimmune diseases (AID) during the entire study period.

[£] AESI Adverse events of specific interest for safety monitoring also called potential Immune-Mediated Diseases (pIMDs), are a subset of AEs that include both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which may or may not have an autoimmune etiology.

Statistical Methods:

The analyses were performed on the Total Vaccinated cohort and the According-to-Protocol (ATP) Immunogenicity cohort.

- The Total Vaccinated cohort included all subjects with the vaccine administration documented.
- The ATP Immunogenicity cohort included all evaluable subjects (who met all eligibility criteria, complied with the procedures and intervals defined in the protocol up to Day 180 and with no elimination criteria during the study up to Day 180) for whom data concerning immunogenicity data were available.

Analysis of immunogenicity:

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

Inferential analysis

Adjusted geometric means of post-vaccination CD4 T-cell frequency following induction were computed together with their 90% confidence intervals (CIs) for Flu NG and Flu Eld groups. The ratio of Flu NG over Flu Eld was calculated with its 90% CI. Superiority of Flu NG over Flu Eld at Day 21 after vaccination was demonstrated if the lower limit of the 90% confidence interval of their ratio was > 1.

Descriptive analysis

The frequency of influenza-specific cytokine-positive CD4 T-lymphocytes was summarized with descriptive statistics at Days 0, 21, 42 and 180, for each different cytokine test and for pooled and separate vaccine strains.

GMTs of HI antibody titers, seropositivity rates and SPRs at Days 0, 21, 42 and 180 and SCRs and SCFs at Days 21, 42 and 180 were calculated with their 95% CIs for each vaccine strain.

Analysis of safety:

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

For each vaccine group, the following parameters were tabulated:

- The percentage of subjects reporting each individual solicited local and general symptom during the 7-day solicited follow-up period (Day 0 to Day 6) with exact 95% CI. The same tabulation was performed for grade 3 symptoms and for general symptoms assessed by the investigators as related to vaccination.
- The number of days experiencing each solicited local and general symptom during the 7-day solicited follow-up period.
- The percentage of subjects with at least one report of an unsolicited AE classified by the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms and reported within the 21-day follow-up period after vaccination (Day 0 to Day 20). The same tabulations was performed for Grade 3 AEs and for AEs assessed by the investigator as causally related to the study vaccination.
- The percentage of subjects with at least one report of AE with medically attended visit classified by the MedDRA and reported within the 180-day follow-up period after vaccination (Day 0 to Day 179). The same tabulations were performed for Grade 3 AEs and for AEs assessed by the investigator as causally related to the study vaccination.
- The percentage of subjects with at least one report of an AESI including AID during the entire study period
- The percentage of subjects with at least one report of SAE classified by the MedDRA preferred terms and reported from Day 0 to Day 364.

Study Population: Man or woman 65 years of age or older or man or woman between the ages of 18 and 40 years inclusive, free of an acute aggravation of the health status as established by medical history and clinical examination before entering into the study. Women were to be of non-childbearing potential or, if of childbearing potential, had to practice

adequate contraception for 30 days prior to vaccination, have a negative pregnancy test and continue such precautions for 2 months after vaccination. Written informed consent was obtained from the subject prior to any study procedure.

Number of subjects	**Flu NG Group**	**Flu Eld Group**	**Flu Yng Group**
Planned, N	75	75	50
Randomized, N (Total Vaccinated cohort)	69	73	50
Completed, n (%)	68 (98.6)	73 (100)	49 (98.0)
Total Number Subjects Withdrawn, n (%)	1 (1.4)	0 (0.0)	1 (2.0)
Withdrawn due to Adverse Events, n (%)	1 (1.4)	0 (0.0)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	0 (0.0)	1 (2.0)
Demographics	**Flu NG Group**	**Flu Eld Group**	**Flu Yng Group**
N (Total Vaccinated cohort)	69	73	50
Females:Males	36:33	29:44	27:23
Mean Age, years (SD)	71.5 (5.44)	71.5 (5.32)	26.0 (4.91)
White - Caucasian / European heritage, n (%)	68 (98.6)	71 (97.3)	40 (80.0)

Primary Efficacy Results: Adjusted ratios of CD4 ALL-DOUBLES T-cells frequency GM of Flu NG Group over Flu Eld Group for pooled vaccine strains at Day 21 (ATP Immunogenicity cohort)

Flu NG Group				**Flu Eld Group**				**Adjusted GM ratio (Flu NG Group / Flu Eld Group)**		
	Adjusted GM				**Adjusted GM**					
N	**Value**	**90% CI**		**N**	**Value**	**90% CI**			**90% CI***	
		LL	**UL**			**LL**	**UL**	**Value**	**LL****	**UL**
62	3633.9	3133.6	4214.1	58	2222.2	1954.3	2526.7	1.64	1.35	1.99

CD4 ALL-DOUBLES = CD4 T-cells producing at least 2 different markers
Adjusted GM = geometric mean adjusted for baseline
N = Number of subjects with available results
90% CI = 90% confidence interval for the adjusted GM
90% CI* = 90% confidence interval for the adjusted GM ratio (ANCOVA model for repeated measurement: adjustment for baseline including vaccine group, visit and the vaccine group by visit interaction as fixed effects); LL = lower limit, UL = upper limit
**Superiority criterion: lower limit of the 90% confidence interval of the ratio (Flu NG Group / Flu Eld Group) > 1.

Primary Efficacy Results: Descriptive Statistics on the frequency of influenza-specific CD4 T-cells (per million CD4 T-cells) for pooled vaccine strains at Day 0, 21, 42 and 180 (ATP Immunogenicity cohort)

Immune marker	**Group**	**Timing**	**N**	**Nmiss**	**GM**	**Median**
CD4-ALL DOUBLES	Flu NG	PRE	62	0	1269.34	1335.50
		PI(D21)*	62	0	3371.11	3500.50
		PI(D42)	61	1	2657.07	2981.00
		PI(D180)	60	2	2105.66	2298.50
	Flu Eld	PRE	61	5	1309.30	1218.00
		PI(D21)*	61	5	2108.10	2313.00
		PI(D42)	64	2	1540.08	1654.50
		PI(D180)	63	3	1484.11	1526.00
	Flu Yng	PRE	44	0	2026.14	1986.00
		PI(D21)	43	1	3228.91	3019.00
		PI(D42)	44	0	2669.41	2635.50
		PI(D180)	42	2	2746.76	2573.50
CD4-CD40L	Flu NG	PRE	62	0	1104.24	1220.00
		PI(D21)	62	0	2817.50	3154.00
		PI(D42)	61	1	2447.37	2739.00
		PI(D180)	60	2	2036.70	2246.00
	Flu Eld	PRE	61	5	1211.72	1141.00
		PI(D21)	61	5	1935.66	2126.00
		PI(D42)	64	2	1425.02	1472.50
		PI(D180)	63	3	1416.78	1486.00
	Flu Yng	PRE	44	0	1879.85	1801.00

		PI(D21)	43	1	2929.86	2747.00
		PI(D42)	44	0	2436.43	2447.00
		PI(D180)	42	2	2619.74	2374.50
CD4- IFN-γ	Flu NG	PRE	62	0	832.47	921.00
		PI(D21)	62	0	2305.58	2527.00
		PI(D42)	61	1	1775.61	2059.00
		PI(D180)	60	2	1495.36	1687.50
	Flu Eld	PRE	61	5	835.22	800.00
		PI(D21)	61	5	1341.17	1394.00
		PI(D42)	64	2	997.25	1114.00
		PI(D180)	63	3	1019.64	1101.00
	Flu Yng	PRE	44	0	1403.57	1300.50
		PI(D21)	43	1	2258.27	2250.00
		PI(D42)	44	0	1849.44	1937.00
		PI(D180)	42	2	2102.93	2103.00
CD4- IL-2	Flu NG	PRE	62	0	1085.32	1161.00
		PI(D21)	62	0	2534.86	2830.50
		PI(D42)	61	1	2205.91	2524.00
		PI(D180)	60	2	1837.60	2020.00
	Flu Eld	PRE	61	5	1119.34	1042.00
		PI(D21)	61	5	1779.41	1847.00
		PI(D42)	64	2	1310.05	1415.50
		PI(D180)	63	3	1285.14	1267.00
	Flu Yng	PRE	44	0	1717.41	1719.50
		PI(D21)	43	1	2690.36	2628.00
		PI(D42)	44	0	2199.18	2259.50
		PI(D180)	42	2	2302.51	2088.00
CD4-TNF-α	Flu NG	PRE	62	0	874.43	890.00
		PI(D21)	62	0	2114.47	2076.50
		PI(D42)	61	1	1741.65	1979.00
		PI(D180)	60	2	1413.29	1569.50
	Flu Eld	PRE	61	5	928.86	890.00
		PI(D21)	61	5	1284.20	1457.00
		PI(D42)	64	2	1012.42	1149.00
		PI(D180)	63	3	1015.29	1051.00
	Flu Yng	PRE	44	0	1425.50	1394.50
		PI(D21)	43	1	1999.07	1999.00
		PI(D42)	44	0	1752.99	1806.00
		PI(D180)	42	2	1821.04	1695.50

CD4 ALL-DOUBLES = CD4 T-cells producing at least 2 different markers
CD4-CD40L = CD4 T-cells producing at least CD40L and another marker
CD4- IFN-γ = CD4 T-cells producing at least I IFN-γ and another marker
CD4- IL-2 = CD4 T-cells producing at least IL-2 and another marker
CD4- TNF-α = CD4 T-cells producing at least TNF-α and another marker
N = number of subjects with available results
Nmiss = number of subjects with missing results
GM= Geometric Mean
PRE = Pre-vaccination Dose 1 (Day 0)
PI(D21) = Post-vaccination Dose 1 (Day 21)
PI(D42) = Post-vaccination Dose 1 (Day 42)
PI(D180) = Post-vaccination Dose 1 (Day 180)
*Primary outcome variables

Secondary Outcome Variable(s): Descriptive Statistics on the frequency of influenza-specific CD4 T-cells (per million CD4 T-cells) for each vaccine strain at Day 0, 21, 42 and 180 (ATP Immunogenicity cohort)

Immune marker	Stimulating	Group	Timing	N	Nm	GM	Median

	antigen				iss		
CD4-ALL DOUBLES	A/Brisbane	Flu NG	PRE	62	0	402.28	437.50
			PI(D21)	62	0	1062.79	1006.50
			PI(D42)	60	2	822.07	879.00
			PI(D180)	60	2	669.67	878.00
		Flu Eld	PRE	61	5	340.57	397.00
			PI(D21)	61	5	462.34	629.00
			PI(D42)	64	2	392.04	485.00
			PI(D180)	63	3	463.94	501.00
		Flu Yng	PRE	44	0	793.58	858.00
			PI(D21)	42	2	982.18	926.50
			PI(D42)	43	1	874.34	868.00
			PI(D180)	42	2	973.29	960.50
	A/Uruguay	Flu NG	PRE	62	0	342.58	362.50
			PI(D21)	62	0	930.98	1014.00
			PI(D42)	59	3	678.88	750.00
			PI(D180)	59	3	640.97	732.00
		Flu Eld	PRE	61	5	274.47	361.00
			PI(D21)	61	5	497.49	594.00
			PI(D42)	64	2	331.62	423.00
			PI(D180)	62	4	331.02	426.50
		Flu Yng	PRE	44	0	437.07	483.50
			PI(D21)	43	1	667.38	697.00
			PI(D42)	44	0	473.17	628.50
			PI(D180)	41	3	654.30	628.00
	B/Brisbane	Flu NG	PRE	61	1	672.58	645.00
			PI(D21)	62	0	1755.55	1778.00
			PI(D42)	58	4	1325.35	1467.50
			PI(D180)	57	5	1034.78	1094.00
		Flu Eld	PRE	61	5	504.36	604.00
			PI(D21)	60	6	1149.98	1331.00
			PI(D42)	62	4	807.46	846.00
			PI(D180)	60	6	778.13	772.50
		Flu Yng	PRE	44	0	1183.48	1293.50
			PI(D21)	43	1	1861.66	1887.00
			PI(D42)	44	0	1572.47	1520.00
			PI(D180)	42	2	1640.71	1535.50
CD4-CD40L	A/Brisbane	Flu NG	PRE	62	0	387.76	430.50
			PI(D21)	62	0	980.10	946.00
			PI(D42)	60	2	771.49	819.50
			PI(D180)	60	2	653.13	835.00
		Flu Eld	PRE	61	5	320.29	376.00
			PI(D21)	61	5	462.64	629.00
			PI(D42)	64	2	365.94	472.00
			PI(D180)	63	3	466.55	450.00
		Flu Yng	PRE	44	0	750.57	815.50
			PI(D21)	42	2	919.30	882.00
			PI(D42)	43	1	818.54	807.00
			PI(D180)	42	2	922.06	938.00
	A/Uruguay	Flu NG	PRE	62	0	308.73	362.00
			PI(D21)	62	0	805.56	885.00
			PI(D42)	59	3	592.88	696.00
			PI(D180)	59	3	609.34	638.00
		Flu Eld	PRE	61	5	227.76	321.00

			PI(D21)	61	5	451.52	561.00
			PI(D42)	64	2	286.06	369.50
			PI(D180)	62	4	298.70	384.00
		Flu Yng	PRE	44	0	384.02	422.50
			PI(D21)	43	1	602.51	630.00
			PI(D42)	44	0	417.15	490.00
			PI(D180)	41	3	584.68	572.00
	B/Brisbane	Flu NG	PRE	61	1	647.94	622.00
			PI(D21)	62	0	1607.98	1728.00
			PI(D42)	58	4	1246.10	1398.50
			PI(D180)	57	5	1011.39	1045.00
		Flu Eld	PRE	61	5	515.89	602.00
			PI(D21)	60	6	1077.12	1267.50
			PI(D42)	62	4	763.04	812.00
			PI(D180)	60	6	757.17	760.00
		Flu Yng	PRE	44	0	1129.44	1223.50
			PI(D21)	43	1	1737.45	1813.00
			PI(D42)	44	0	1472.48	1473.00
			PI(D180)	42	2	1570.98	1459.50
CD4- IFN-γ	A/Brisbane	Flu NG	PRE	62	0	279.24	344.50
			PI(D21)	62	0	725.55	755.00
			PI(D42)	60	2	572.87	586.00
			PI(D180)	60	2	586.26	676.50
		Flu Eld	PRE	61	5	258.94	307.00
			PI(D21)	61	5	344.39	415.00
			PI(D42)	64	2	326.66	340.00
			PI(D180)	63	3	363.03	366.00
		Flu Yng	PRE	44	0	563.26	534.00
			PI(D21)	42	2	680.40	660.00
			PI(D42)	43	1	623.21	610.00
			PI(D180)	42	2	773.40	769.50
	A/Uruguay	Flu NG	PRE	62	0	214.92	262.00
			PI(D21)	62	0	641.94	698.00
			PI(D42)	59	3	458.72	558.00
			PI(D180)	59	3	426.59	493.00
		Flu Eld	PRE	61	5	164.78	226.00
			PI(D21)	61	5	314.63	399.00
			PI(D42)	64	2	246.18	299.00
			PI(D180)	62	4	228.06	301.50
		Flu Yng	PRE	44	0	283.81	327.00
			PI(D21)	43	1	403.00	482.00
			PI(D42)	44	0	331.47	370.00
			PI(D180)	41	3	451.90	492.00
	B/Brisbane	Flu NG	PRE	61	1	342.59	449.00
			PI(D21)	62	0	1219.72	1228.00
			PI(D42)	58	4	903.71	989.00
			PI(D180)	57	5	697.03	839.00
		Flu Eld	PRE	61	5	319.38	361.00
			PI(D21)	60	6	721.43	776.00
			PI(D42)	62	4	517.83	555.00
			PI(D180)	60	6	510.37	481.00
		Flu Yng	PRE	44	0	824.76	825.50
			PI(D21)	43	1	1361.31	1416.00
			PI(D42)	44	0	1095.12	1092.00

			PI(D180)	42	2	1253.33	1186.00
CD4- IL-2	A/Brisbane	Flu NG	PRE	62	0	346.00	408.00
			PI(D21)	62	0	872.32	886.50
			PI(D42)	60	2	696.36	805.50
			PI(D180)	60	2	570.30	732.50
		Flu Eld	PRE	61	5	319.16	343.00
			PI(D21)	61	5	427.26	556.00
			PI(D42)	64	2	393.67	442.50
			PI(D180)	63	3	387.63	437.00
		Flu Yng	PRE	44	0	677.11	707.50
			PI(D21)	42	2	816.95	776.00
			PI(D42)	43	1	720.28	703.00
			PI(D180)	42	2	817.80	771.50
	A/Uruguay	Flu NG	PRE	62	0	278.66	305.00
			PI(D21)	62	0	680.16	805.00
			PI(D42)	59	3	534.07	650.00
			PI(D180)	59	3	526.12	624.00
		Flu Eld	PRE	61	5	240.26	302.00
			PI(D21)	61	5	391.84	533.00
			PI(D42)	64	2	295.90	361.00
			PI(D180)	62	4	299.67	325.50
		Flu Yng	PRE	44	0	369.77	387.50
			PI(D21)	43	1	510.88	538.00
			PI(D42)	44	0	438.09	467.50
			PI(D180)	41	3	514.55	464.00
	B/Brisbane	Flu NG	PRE	61	1	587.16	641.00
			PI(D21)	62	0	1496.41	1590.50
			PI(D42)	58	4	1144.72	1269.50
			PI(D180)	57	5	933.06	998.00
		Flu Eld	PRE	61	5	451.89	528.00
			PI(D21)	60	6	1004.17	1134.50
			PI(D42)	62	4	724.10	766.00
			PI(D180)	60	6	704.18	708.00
		Flu Yng	PRE	44	0	1019.08	1032.00
			PI(D21)	43	1	1592.61	1514.00
			PI(D42)	44	0	1322.64	1289.50
			PI(D180)	42	2	1439.92	1360.00
CD4- TNF-α	A/Brisbane	Flu NG	PRE	62	0	262.44	324.00
			PI(D21)	62	0	621.35	586.50
			PI(D42)	60	2	500.13	656.50
			PI(D180)	60	2	462.60	545.00
		Flu Eld	PRE	61	5	247.22	304.00
			PI(D21)	61	5	289.38	401.00
			PI(D42)	64	2	238.28	302.50
			PI(D180)	63	3	308.96	353.00
		Flu Yng	PRE	44	0	536.34	669.00
			PI(D21)	42	2	497.77	618.50
			PI(D42)	43	1	564.91	599.00
			PI(D180)	42	2	616.75	713.50
	A/Uruguay	Flu NG	PRE	62	0	223.83	285.50
			PI(D21)	62	0	600.99	644.00
			PI(D42)	59	3	452.35	501.00
			PI(D180)	59	3	370.86	496.00
		Flu Eld	PRE	61	5	191.52	265.00

			PI(D21)	61	5	320.59	405.00
			PI(D42)	64	2	211.12	269.50
			PI(D180)	62	4	230.70	293.00
		Flu Yng	PRE	44	0	284.69	376.00
			PI(D21)	43	1	411.24	447.00
			PI(D42)	44	0	333.52	370.00
			PI(D180)	41	3	477.18	474.00
	B/Brisbane	Flu NG	PRE	61	1	414.10	477.00
			PI(D21)	62	0	967.79	1028.50
			PI(D42)	58	4	775.92	1060.00
			PI(D180)	57	5	642.05	705.00
		Flu Eld	PRE	61	5	305.51	369.00
			PI(D21)	60	6	639.74	708.50
			PI(D42)	62	4	413.38	521.00
			PI(D180)	60	6	475.44	488.00
		Flu Yng	PRE	44	0	773.44	869.50
			PI(D21)	43	1	1057.83	1106.00
			PI(D42)	44	0	953.30	930.50
			PI(D180)	42	2	1051.51	1009.00

CD4 ALL-DOUBLES = CD4 T-cells producing at least two different markers
CD4-CD40L = CD4 T-cells producing at least CD40L and another marker
CD4- IFN-γ = CD4 T-cells producing at least I IFN-γ and another marker
CD4- IL-2 = CD4 T-cells producing at least IL-2 and another marker
CD4- TNF-α = CD4 T-cells producing at least TNF-α and another marker
N = number of subjects with available results
Nmiss = number of subjects with missing results
GM= Geometric Mean
PRE = Pre-vaccination Dose 1 (Day 0)
PI(D21) = Post-vaccination Dose 1 (Day 21)
PI(D42) = Post-vaccination Dose 1 (Day 42)
PI(D180) = Post-vaccination Dose 1 (Day 180)

Secondary Outcome Variable(s):

Seropositivity rates and GMTs for HI antibodies against A/Brisbane, A/Uruguay and B/Brisbane at Day 0, 21, 42 and 180 (ATP Immunogenicity cohort)

				≥ 1:10				**GMT**		
						95% CI			**95% CI**	
Strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
A/Brisbane	Flu NG	PRE	62	43	69.4	56.3	80.4	16.5	12.7	21.5
		PI(D21)	62	61	98.4	91.3	100	105.1	80.3	137.6
		PI(D42)	61	60	98.4	91.2	100	82.3	64.5	105.0
		PI(D180)	62	57	91.9	82.2	97.3	38.4	30.3	48.7
	Flu Eld	PRE	66	40	60.6	47.8	72.4	14.3	10.9	18.7
		PI(D21)	66	62	93.9	85.2	98.3	67.2	49.6	91.2
		PI(D42)	65	62	95.4	87.1	99.0	56.8	42.0	77.0
		PI(D180)	66	57	86.4	75.7	93.6	32.1	24.0	42.8
	Flu Yng	PRE	44	25	56.8	41.0	71.7	20.5	13.0	32.3
		PI(D21)	43	43	100	91.8	100	220.8	163.3	298.7
		PI(D42)	44	44	100	92.0	100	181.4	133.5	246.6
		PI(D180)	43	40	93.0	80.9	98.5	90.3	60.7	134.2
A/Uruguay	Flu NG	PRE	62	41	66.1	53.0	77.7	21.4	15.0	30.4
		PI(D21)	62	62	100	94.2	100	330.9	239.8	456.7
		PI(D42)	61	60	98.4	91.2	100	254.8	182.1	356.5
		PI(D180)	62	61	98.4	91.3	100	117.0	83.0	164.9
	Flu Eld	PRE	66	45	68.2	55.6	79.1	17.5	13.2	23.3
		PI(D21)	66	63	95.5	87.3	99.1	164.2	113.3	238.0

		PI(D42)	65	62	95.4	87.1	99.0	110.1	77.4	156.6
		PI(D180)	66	59	89.4	79.4	95.6	59.9	41.8	85.9
	Flu Yng	PRE	44	24	54.5	38.8	69.6	16.4	11.0	24.5
		PI(D21)	43	41	95.3	84.2	99.4	179.0	115.1	278.4
		PI(D42)	44	42	95.5	84.5	99.4	130.3	86.6	196.1
		PI(D180)	43	39	90.7	77.9	97.4	74.4	47.6	116.2
B/Brisbane	Flu NG	PRE	62	59	95.2	86.5	99.0	92.0	66.2	127.8
		PI(D21)	62	62	100	94.2	100	699.9	538.4	909.8
		PI(D42)	61	61	100	94.1	100	487.2	372.2	637.8
		PI(D180)	62	62	100	94.2	100	254.5	195.3	331.6
	Flu Eld	PRE	66	65	98.5	91.8	100	97.0	72.9	129.2
		PI(D21)	66	66	100	94.6	100	502.6	388.6	650.0
		PI(D42)	65	65	100	94.5	100	393.9	310.3	500.0
		PI(D180)	66	66	100	94.6	100	238.4	188.4	301.6
	Flu Yng	PRE	44	42	95.5	84.5	99.4	169.0	108.2	263.9
		PI(D21)	43	43	100	91.8	100	1229.4	972.8	1553.8
		PI(D42)	44	44	100	92.0	100	971.6	778.0	1213.3
		PI(D180)	43	43	100	91.8	100	677.2	513.7	892.7

GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination Dose 1 (Day 0)
PI(D21) = Post-vaccination Dose 1 (Day 21)
PI(D42) = Post-vaccination Dose 1 (Day 42)
PI(D180) = Post-vaccination Dose 1 (Day 180)

Secondary Outcome Variable(s): SCR for HI antibodies against A/Brisbane, A/Uruguay and B/Brisbane at Day 21, 42 and 180 (ATP Immunogenicity cohort)

				SCR			
						95% CI	
Strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
A/Brisbane	Flu NG	PI(D21)	62	36	58.1	44.8	70.5
		PI(D42)	61	33	54.1	40.8	66.9
		PI(D180)	62	16	25.8	15.5	38.5
	Flu Eld	PI(D21)	66	32	48.5	36.0	61.1
		PI(D42)	65	25	38.5	26.7	51.4
		PI(D180)	66	16	24.2	14.5	36.4
	Flu Yng	PI(D21)	43	29	67.4	51.5	80.9
		PI(D42)	44	29	65.9	50.1	79.5
		PI(D180)	43	23	53.5	37.7	68.8
A/Uruguay	Flu NG	PI(D21)	62	52	83.9	72.3	92.0
		PI(D42)	61	48	78.7	66.3	88.1
		PI(D180)	62	36	58.1	44.8	70.5
	Flu Eld	PI(D21)	66	50	75.8	63.6	85.5
		PI(D42)	65	44	67.7	54.9	78.8
		PI(D180)	66	28	42.4	30.3	55.2
	Flu Yng	PI(D21)	43	33	76.7	61.4	88.2
		PI(D42)	44	30	68.2	52.4	81.4
		PI(D180)	43	20	46.5	31.2	62.3
B/Brisbane	Flu NG	PI(D21)	62	44	71.0	58.1	81.8
		PI(D42)	61	38	62.3	49.0	74.4
		PI(D180)	62	22	35.5	23.7	48.7
	Flu Eld	PI(D21)	66	38	57.6	44.8	69.7
		PI(D42)	65	35	53.8	41.0	66.3

		PI(D180)	66	22	33.3	22.2	46.0
	Flu Yng	PI(D21)	43	29	67.4	51.5	80.9
		PI(D42)	44	25	56.8	41.0	71.7
		PI(D180)	43	20	46.5	31.2	62.3

Seroconversion defined as:
- For initially seronegative subjects, antibody titer ≥1: 40 after vaccination
- For initially seropositive subjects, antibody titer after vaccination ≥ 4-fold the pre-vaccination antibody titer

N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D21) = Post-vaccination Dose 1 (Day 21)
PI(D42) = Post-vaccination Dose 1 (Day 42)
PI(D180) = Post-vaccination Dose 1 (Day 180)

Secondary Outcome Variable(s): SCF for HI antibodies against A/Brisbane, A/Uruguay and B/Brisbane at Day 21, 42 and 180 (ATP Immunogenicity cohort)

				SCF		
					95% CI	
Strain	**Group**	**Timing**	**N**	**Value**	**LL**	**UL**
A/Brisbane	Flu NG	PI(D21)	62	6.4	4.5	9.0
		PI(D42)	61	5.1	3.7	7.0
		PI(D180)	62	2.3	1.8	3.0
	Flu Eld	PI(D21)	66	4.7	3.4	6.6
		PI(D42)	65	3.9	2.8	5.4
		PI(D180)	66	2.2	1.7	3.0
	Flu Yng	PI(D21)	43	10.6	6.3	17.9
		PI(D42)	44	8.9	5.3	14.7
		PI(D180)	43	4.6	2.9	7.2
A/Uruguay	Flu NG	PI(D21)	62	15.5	10.8	22.2
		PI(D42)	61	12.2	8.5	17.4
		PI(D180)	62	5.5	4.1	7.3
	Flu Eld	PI(D21)	66	9.4	6.6	13.2
		PI(D42)	65	6.4	4.7	8.6
		PI(D180)	66	3.4	2.5	4.6
	Flu Yng	PI(D21)	43	11.3	7.2	17.8
		PI(D42)	44	7.9	5.3	11.9
		PI(D180)	43	4.5	3.0	6.9
B/Brisbane	Flu NG	PI(D21)	62	7.6	5.6	10.3
		PI(D42)	61	5.4	4.0	7.2
		PI(D180)	62	2.8	2.2	3.4
	Flu Eld	PI(D21)	66	5.2	3.8	7.1
		PI(D42)	65	4.1	3.1	5.4
		PI(D180)	66	2.5	1.9	3.1
	Flu Yng	PI(D21)	43	7.4	4.7	11.6
		PI(D42)	44	5.8	3.7	8.9
		PI(D180)	43	4.0	2.8	5.8

N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D21) = Post-vaccination Dose 1 (Day 21)
PI(D42) = Post-vaccination Dose 1 (Day 42)
PI(D180) = Post-vaccination Dose 1 (Day 180)

Secondary Outcome Variable(s): SPR for HI antibodies against A/Brisbane, A/Uruguay and B/Brisbane at Day 0, 21, 42 and 180 (ATP Immunogenicity cohort)

	SPR	
		95% CI

Strain	Group	Timing	N	n	%	LL	UL
A/Brisbane	Flu NG	PRE	62	20	32.3	20.9	45.3
		PI(D21)	62	57	91.9	82.2	97.3
		PI(D42)	61	56	91.8	81.9	97.3
		PI(D180)	62	39	62.9	49.7	74.8
	Flu Eld	PRE	66	16	24.2	14.5	36.4
		PI(D21)	66	53	80.3	68.7	89.1
		PI(D42)	65	47	72.3	59.8	82.7
		PI(D180)	66	34	51.5	38.9	64.0
	Flu Yng	PRE	44	18	40.9	26.3	56.8
		PI(D21)	43	42	97.7	87.7	99.9
		PI(D42)	44	42	95.5	84.5	99.4
		PI(D180)	43	36	83.7	69.3	93.2
A/Uruguay	Flu NG	PRE	62	26	41.9	29.5	55.2
		PI(D21)	62	61	98.4	91.3	100
		PI(D42)	61	59	96.7	88.7	99.6
		PI(D180)	62	53	85.5	74.2	93.1
	Flu Eld	PRE	66	24	36.4	24.9	49.1
		PI(D21)	66	57	86.4	75.7	93.6
		PI(D42)	65	53	81.5	70.0	90.1
		PI(D180)	66	48	72.7	60.4	83.0
	Flu Yng	PRE	44	16	36.4	22.4	52.2
		PI(D21)	43	39	90.7	77.9	97.4
		PI(D42)	44	39	88.6	75.4	96.2
		PI(D180)	43	33	76.7	61.4	88.2
B/Brisbane	Flu NG	PRE	62	51	82.3	70.5	90.8
		PI(D21)	62	62	100	94.2	100
		PI(D42)	61	61	100	94.1	100
		PI(D180)	62	60	96.8	88.8	99.6
	Flu Eld	PRE	66	57	86.4	75.7	93.6
		PI(D21)	66	65	98.5	91.8	100
		PI(D42)	65	64	98.5	91.7	100
		PI(D180)	66	65	98.5	91.8	100
	Flu Yng	PRE	44	39	88.6	75.4	96.2
		PI(D21)	43	43	100	91.8	100
		PI(D42)	44	44	100	92.0	100
		PI(D180)	43	42	97.7	87.7	99.9

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination dose 1 (Day 0)
PI(D21) = Post-vaccination Dose 1 (Day 21)
PI(D42) = Post-vaccination Dose 1 (Day 42)
PI(D180) = Post-vaccination Dose 1 (Day 180)

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

		Flu NG Group					Flu Eld Group					Flu Yng Group				
					95 % CI					95 % CI					95 % CI	
Symptom	Intensity	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Ecchymosis	Any	69	2	2.9	0.4	10.1	73	1	1.4	0.0	7.4	50	0	0.0	0.0	7.1
	>100mm	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
Pain	Any	69	43	62.3	49.8	73.7	73	15	20.5	12.0	31.6	50	35	70.0	55.4	82.1
	Grade 3	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
Redness	Any	69	5	7.2	2.4	16.1	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1

	>100mm	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
Swelling	Any	69	8	11.6	5.1	21.6	73	1	1.4	0.0	7.4	50	0	0.0	0.0	7.1
	>100mm	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1

N= number of subjects with the documented dose
n/%= number/percentage of subjects reporting at least once the symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = occurrence of any local symptom, regardless of intensity grade
Grade 3 pain = considerable pain at rest, that prevented normal everyday activity

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

Symptom	Group	N	Mean	Median
Ecchymosis	Flu NG	2	3.5	3.5
	Flu Eld	1	5.0	5.0
Pain	Flu NG	43	2.3	2.0
	Flu Eld	15	1.6	1.0
	Flu Yng	35	2.0	2.0
Redness	Flu NG	5	2.6	2.0
Swelling	Flu NG	8	3.3	4.0
	Flu Eld	1	5.0	5.0

N = Number of subjects with the symptom

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

		Flu NG Group					Flu Eld Group					Flu Yng Group				
					95 % CI					95 % CI					95 % CI	
Symptom	**Intensity/ Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Arthralgia	Any	69	14	20.3	11.6	31.7	73	3	4.1	0.9	11.5	50	4	8.0	2.2	19.2
	Grade 3	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
	Related	69	12	17.4	9.3	28.4	73	1	1.4	0.0	7.4	50	3	6.0	1.3	16.5
Fatigue	Any	69	22	31.9	21.2	44.2	73	12	16.4	8.8	27.0	50	21	42.0	28.2	56.8
	Grade 3	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
	Related	69	21	30.4	19.9	42.7	73	8	11.0	4.9	20.5	50	11	22.0	11.5	36.0
Gastrointestinal symptoms	Any	69	6	8.7	3.3	18.0	73	4	5.5	1.5	13.4	50	6	12.0	4.5	24.3
	Grade 3	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
	Related	69	5	7.2	2.4	16.1	73	1	1.4	0.0	7.4	50	4	8.0	2.2	19.2
Headache	Any	69	22	31.9	21.2	44.2	73	7	9.6	3.9	18.8	50	14	28.0	16.2	42.5
	Grade 3	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
	Related	69	17	24.6	15.1	36.5	73	2	2.7	0.3	9.5	50	7	14.0	5.8	26.7
Myalgia	Any	69	17	24.6	15.1	36.5	73	8	11.0	4.9	20.5	50	11	22.0	11.5	36.0
	Grade 3	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
	Related	69	16	23.2	13.9	34.9	73	7	9.6	3.9	18.8	50	9	18.0	8.6	31.4
Shivering	Any	69	11	15.9	8.2	26.7	73	0	0.0	0.0	4.9	50	2	4.0	0.5	13.7
	Grade 3	69	0	0.0	0.0	5.2	73	0	0.0	0.0	4.9	50	1	2.0	0.1	10.6
	Related	69	8	11.6	5.1	21.6	73	0	0.0	0.0	4.9	50	1	2.0	0.1	10.6
Temperature/ (Orally)	≥ 38.0°C	69	2	2.9	0.4	10.1	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
	≥ 39.0	69	1	1.4	0.0	7.8	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1
	Related	69	2	2.9	0.4	10.1	73	0	0.0	0.0	4.9	50	0	0.0	0.0	7.1

N= number of subjects with the documented dose
n/%= number/percentage of subjects reporting at least once the symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = occurrence of any general symptom, regardless of intensity or relation to vaccination
Grade 3 = general symptom that prevented normal activity
Related = general symptom assessed by the investigator as causally related to the study vaccination

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

Symptom	Group	N	Mean	Median
Arthralgia	Flu NG	14	2.8	2.0
	Flu Eld	3	2.0	2.0
	Flu Yng	4	2.5	1.5
Fatigue	Flu NG	22	2.6	2.0
	Flu Eld	12	2.7	2.5
	Flu Yng	21	2.4	2.0
Gastrointestinal	Flu NG	6	1.3	1.0
	Flu Eld	4	2.0	2.0
	Flu Yng	6	1.3	1.0
Headache	Flu NG	22	1.8	1.0
	Flu Eld	7	2.0	2.0
	Flu Yng	14	1.6	1.5
Myalgia	Flu NG	17	2.5	2.0
	Flu Eld	8	1.6	1.5
	Flu Yng	11	1.2	1.0
Shivering	Flu NG	11	1.9	1.0
	Flu Yng	2	2.5	2.5
Temperature	Flu NG	2	2.0	2.0

N = Number of subjects with the symptom and without the missing confirmed grade

Secondary Outcome Variable(s): Number (%) of subjects reporting the occurrence of any adverse events with medically attended visit (MAEs) within the 180-day (Days 0-179) post-vaccination period (Total Vaccinated cohort)

Most frequent MAEs (occurring within Day 0-179 following vaccination)	Flu NG Group N = 69	Flu Eld Group N = 73	Flu Yng Group N = 50
Subjects with any MAE(s), n (%)	24 (34.8)	21 (28.8)	13 (26.0)
Subjects with grade 3 MAE(s), n (%)	4 (5.8)	9 (12.3)	3 (6.0)
Subjects with related MAE(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Bronchitis	3 (4.3)	4 (5.5)	-
Upper respiratory tract infection	1 (1.4)	3 (4.1)	2 (4.0)
Toothache	1 (1.4)	1 (1.4)	1 (2.0)
Gastrooesophageal reflux disease	2 (2.9)	-	-
Haematuria	-	2 (2.7)	-
Hypercholesterolaemia	-	2 (2.7)	-
Joint sprain	1 (1.4)	-	1 (2.0)
Lymphadenitis	1 (1.4)	-	1 (2.0)
Myalgia	1 (1.4)	1 (1.4)	-
Rib fracture	1 (1.4)	1 (1.4)	-
Viral infection	-	1 (1.4)	1 (2.0)
Anaemia	1 (1.4)	-	-
Anxiety	-	1 (1.4)	-
Aphonia	1 (1.4)	-	-
Arthralgia	-	-	1 (2.0)
Atrial flutter	1 (1.4)	-	-
Back pain	-	1 (1.4)	-
Brain neoplasm	-	1 (1.4)	-
Cardiac failure congestive	1 (1.4)	-	-
Cholecystitis acute	-	1 (1.4)	-
Contusion	-	-	1 (2.0)
Depressed mood	-	1 (1.4)	-
Depression	-	1 (1.4)	-
Dizziness	-	1 (1.4)	-
Face oedema	-	1 (1.4)	-
Folate deficiency	1 (1.4)	-	-
Foot deformity	-	1 (1.4)	-

Fungal infection	-	1 (1.4)	-
Gastroenteritis	-	-	1 (2.0)
Genital infection fungal	1 (1.4)	-	-
Groin abscess	-	-	1 (2.0)
Headache	-	1 (1.4)	-
Humerus fracture	-	1 (1.4)	-
Hypertension	-	1 (1.4)	-
Influenza like illness	-	-	1 (2.0)
Insomnia	1 (1.4)	-	-
Iron deficiency anaemia	-	-	1 (2.0)
Ligament rupture	-	1 (1.4)	-
Limb injury	1 (1.4)	-	-
Lower respiratory tract infection	-	1 (1.4)	-
Lumbar hernia	1 (1.4)	-	-
Lymphoma	-	1 (1.4)	-
Meningioma	1 (1.4)	-	-
Metastases to lung	-	1 (1.4)	-
Nasopharyngitis	1 (1.4)	-	-
Nephritis	-	1 (1.4)	-
Neuroma	1 (1.4)	-	-
Non-cardiac chest pain	-	1 (1.4)	-
Osteonecrosis	1 (1.4)	-	-
Pain in extremity	-	1 (1.4)	-
Paraproteinaemia	1 (1.4)	-	-
Paronychia	-	-	1 (2.0)
Pharyngitis	-	1 (1.4)	-
Pyrexia	-	-	1 (2.0)
Rectal haemorrhage	1 (1.4)	-	-
Respiratory tract infection	1 (1.4)	-	-
Rhinorrhoea	1 (1.4)	-	-
Rotator cuff syndrome	1 (1.4)	-	-
Sinusitis	-	1 (1.4)	-
Skin infection	-	-	1 (2.0)
Syncope	-	1 (1.4)	-
Synovial cyst	1 (1.4)	-	-
Tooth extraction	1 (1.4)	-	-
Tracheitis	-	-	1 (2.0)
Urinary incontinence	1 (1.4)	-	-
Urinary tract infection	-	1 (1.4)	-
Urinary tract neoplasm	-	1 (1.4)	-
Varicose vein	-	-	1 (2.0)
Vertigo	1 (1.4)	-	-
- : MAE absent Grade 3 = event that prevented normal, everyday activities Related = event assessed by the investigator as causally related to the study vaccination			
Secondary Outcome Variable(s): Number (%) of subjects reporting the occurrence of any AESI including AID within the 365-day (Days 0-364) post-vaccination period (Total Vaccinated cohort)			
Most frequent AESI - (occurring within Day 0-364 following vaccination)	**Flu NG Group N = 69**	**Flu Eld Group N = 73**	**Flu Yng Group N = 50**
Subjects with any AESI(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)

Safety results: Number (%) of subjects reporting the occurrence of any adverse events within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort)			
Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)	**Flu NG Group N = 69**	**Flu Eld Group N = 73**	**Flu Yng Group N = 50**
Subjects with any AE(s), n (%)	13 (18.8)	21 (28.8)	15 (30.0)
Subjects with grade 3 AE(s), n (%)	2 (2.9)	2 (2.7)	1 (2.0)
Subjects with related AE(s), n (%)	3 (4.3)	2 (2.7)	1 (2.0)
Nasopharyngitis	2 (2.9)	2 (2.7)	4 (8.0)
Upper respiratory tract infection	1 (1.4)	3 (4.1)	1 (2.0)
Back pain	1 (1.4)	1 (1.4)	1 (2.0)
Bronchitis	-	2 (2.7)	-
Constipation	-	1 (1.4)	1 (2.0)
Headache	-	-	2 (4.0)
Lymphadenopathy	-	1 (1.4)	1 (2.0)
Malaise	1 (1.4)	-	1 (2.0)
Myalgia	2 (2.9)	-	-
Oropharyngeal pain	-	-	2 (4.0)
Postnasal drip	-	-	2 (4.0)
Toothache	2 (2.9)	-	-
Abnormal dreams	-	1 (1.4)	-
Anxiety	-	1 (1.4)	-
Arthralgia	-	-	1 (2.0)
Atrial flutter	1 (1.4)	-	-
Cardiac failure congestive	1 (1.4)	-	-
Chest pain	1 (1.4)	-	-
Dizziness	-	1 (1.4)	-
Dysgeusia	-	1 (1.4)	-
Ear disorder	1 (1.4)	-	-
Fatigue	-	1 (1.4)	-
Gastrooesophageal reflux disease	-	1 (1.4)	-
Gouty arthritis	-	1 (1.4)	-
Hypercholesterolaemia	-	1 (1.4)	-
Injection site pruritus	1 (1.4)	-	-
Laryngitis	-	1 (1.4)	-
Medical device complication	-	-	1 (2.0)
Muscle injury	-	1 (1.4)	-
Muscle rigidity	-	-	1 (2.0)
Musculoskeletal pain	1 (1.4)	-	-
Musculoskeletal stiffness	1 (1.4)	-	-
Oral herpes	-	-	1 (2.0)
Pain in extremity	-	1 (1.4)	-
Rash	1 (1.4)	-	-
Rhinitis	-	-	1 (2.0)
Rotator cuff syndrome	-	1 (1.4)	-
Sinus headache	-	1 (1.4)	-
Sinusitis	1 (1.4)	-	-
Throat irritation	-	1 (1.4)	-
- : Adverse event absent Grade 3 = event that prevented normal, everyday activities Related = event assessed by the investigator as causally related to the study vaccination			
Safety results: Number (%) of subjects with serious adverse events within the 365-day (Days 0-364) post-vaccination period (Total Vaccinated cohort)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	**Flu NG Group N = 69**	**Flu Eld Group N = 73**	**Flu Yng Group N = 50**

Subjects with any SAE(s), n (%) [n assessed by investigator as related]	5 (7.2) [0]	11 (15.1) [0]	1 (2.0) [0]
Abdominal hernia	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Amnesia	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Anaemia	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Arrhythmia	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Atrial flutter	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Brain neoplasm	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Cholecystitis acute	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Hypersensitivity	0 (0.0) [0]	0 (0.0) [0]	1 (2.0) [0]
Ligament rupture	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Lymphoma	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Meningioma	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Metastases to lung	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Myocardial infarction	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Nephritis	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Non-cardiac chest pain	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Rectal haemorrhage	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Rib fracture	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Syncope	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Urinary tract neoplasm	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Uterine cancer	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]
Vertigo	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**Flu NG Group N = 69**	**Flu Eld Group N = 73**	**Flu Yng Group N = 50**
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Myocardial infarction	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:
The geometric mean of influenza-specific CD4 T-cells per 10^6 CD4+ T-cells producing at least 2 different markers at Day 21 after vaccination was 3371.11 and 2108.10 in the Flu NG Group and the Flu Eld Group, respectively.
During the 21-day follow-up period after vaccination, at least one unsolicited adverse event was reported by 13 (18.8%) subject in the Flu NG Group, 21 (28.8%) subjects in the Flu Eld Group and 15 (30.0%) subjects in the Flu Yng Group.
Throughout the study, SAEs were reported by 5 (7.2%) subjects in the Flu NG Group, 11 (15.1%) subjects in the Flu Eld Group and 1 (2.0%) subject in the Flu Yng Group; 1 fatal SAE (myocardial infarction) was reported in the Flu NG Group. All the SAEs were assessed by the investigators as not causally related to the study vaccination.

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