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.: 111737 (FLU NG-036 EXT: 025 Y1)

Title: Observer-blind safety and immunogenicity study of GlaxoSmithKline Biologicals' influenza vaccine GSK2186877A when administered to elderly subjects.

Rationale: The aim of the study was to evaluate the safety and immunogenicity of FLU NG vaccine after repeated vaccination. Subjects previously vaccinated in study 110847 (Flu-AS25-025 PRI) were revaccinated with FLU NG vaccine in this study and *Fluarix*™ was used as a reference.
FLU NG: GlaxoSmithKline (GSK) Biological's AS adjuvanted influenza vaccine.
Fluarix™ (Flu vaccine): GSK Biologicals' licensed influenza vaccine.
This CTRS presents the results of the study 111737. Please refer to the CTRS on Flu-AS25-025 PRI (110847) for data about the primary vaccination.

Phase: III

Study Period: 06 October 2008 to 15 May 2009

Study Design: Multi-country, multi-centre, observer-blind for subjects ≥ 65 years and open for subjects aged between 18 and 41 years, controlled study with 3 parallel groups.

Centres: 26 centres in 3 countries (21 centres in Germany, 2 centres in The Netherlands and 3 centres in Sweden)

Indication: Immunization against influenza in male and female subjects aged 18-41 years and ≥ 65 years.

Treatment: The subjects enrolled in this study were assigned to the same treatment group as in study Flu-AS25-025 PRI (110847). The study groups were as follows:

- FLU NG Group: subjects aged ≥65 years received 1 dose of FLU NG vaccine.
- Flu Eld Group: subjects aged ≥65 years received 1 dose of Flu vaccine.
- Flu Yng Group: subjects aged 18-41 years received 1 dose of Flu vaccine.

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

Objectives:
To assess the safety during the entire study period in subjects aged ≥65 years (previously enrolled in the 110847 study) vaccinated with the FLU NG vaccine or with Flu vaccine, and in subjects aged 18-41 years (previously enrolled in the 110847 study) vaccinated with Flu vaccine.

Primary Outcome/Efficacy Variable:

- Occurrence, intensity, duration and relationship to vaccination of solicited local and general adverse events (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 and relationship to vaccination of AEs with 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 adverse events of specific interest including autoimmune diseases (AID) during the entire study period.

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

- At Days 0, 21 and 180, 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, 21 and 180.
- Seropositivity rates at Days 0, 21 and 180.
- Seroconversion rates (SCR)* at Days 21 and 180.
- Seroconversion factors (SCF)** at Days 21 and 180.
- Seroprotection rates (SPR)*** at Days 0, 21 and 180.

* SCR is defined as the percentage of vaccinees who have either a prevaccination titre <1:10 and a post-vaccination titre ≥1:40 or a pre-vaccination titre ≥1:10 and at least a 4-fold increase in post-vaccination titre.
**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 titre ≥1:40 that usually is accepted as indicating protection.

Cell mediated Immunity (CMI) response (only for subjects in the CMI subset)

Observed variables

At Days 0 and 21:

- Frequency of immune response marker-positive cluster of differentiation (CD4) T-cells per 10^6 in tests producing at least 2 different markers (CD40L, Interleukin-2 [IL-2], tumor necrosis factor-α [TNF-α], Interferon-γ [IFN-γ]).
- Frequency of immune response marker-positive CD4 T-cells per 10^6 in tests producing at least one of the 4 markers and another one (CD40L, IL-2, TNF-α, IFN-γ).

Derived variables:

- For each test, geometric mean (GM) of specific influenza CD4 T-lymphocytes at Days 0 and 21.

Statistical Methods:

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

- The Total Vaccinated cohort included all subjects with one vaccine administration documented.
- The ATP immunogenicity cohort for HI included all evaluable subjects who met all eligibility criteria, who complied with the procedures and intervals defined in the protocol for HI data, with no elimination criteria during the study, for whom data concerning immunogenicity HI 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 at Day 21.
- The ATP immunogenicity cohort for CMI included all evaluable subjects who met all eligibility criteria, who complied with the procedures and intervals defined in the protocol for CMI data, with no elimination criteria during the study, for whom data concerning immunogenicity CMI outcome measures were available. This included subjects for whom at least one frequency of cytokine-positive CD4 results were available at Day 21.
- The ATP cohort for persistence included all evaluable subjects who met all eligibility criteria, who complied with the procedures and intervals (at Day 180) defined in the protocol, who did not meet the elimination criteria until Day 180, who had not received a vaccine not specified or forbidden in the protocol from Day 21 and 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 at Day 180.

Analysis of immunogenicity

The analyses were based on the ATP immunogenicity cohort for HI, the ATP immunogenicity cohort for CMI and the ATP cohort for persistence.

On the ATP immunogenicity cohort for HI for each vaccination group and for each strain, GMTs of HI antibody, SCF, SCR and SPR were calculated with exact 95% confidence intervals (95% CI). The same parameters were calculated on the ATP cohort for persistence at Day 180.

On the ATP immunogenicity cohort for CMI the frequency of influenza-specific cytokine-positive CD4 T-lymphocytes was summarized (descriptive statistics) for each vaccine group, for each different test and for pooled and per vaccine strains.

Analysis of safety

The analysis was based on the Total Vaccinated cohort.

For each vaccine group, the percentages of subjects with at least one solicited local or general symptom during the 7-day solicited follow-up period (Day 0 to Day 6) were tabulated with exact 95% CI. The same tabulation was performed for symptoms of any intensity, those with intensity of Grade 3, as well as for solicited general symptoms assessed by the investigator as related to vaccination. All solicited local reactions were assessed as causally related to vaccination. The duration of each solicited local and general symptoms during the 7-day (Day 0-6) solicited follow-up period was tabulated.

The percentages of subjects with at least one report of an unsolicited adverse event, 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), were tabulated. The same tabulation was performed for Grade 3 AEs and for AEs assessed as related to vaccination.

The percentages of subjects with at least one report of AE with medically attended visit or AE of specific interest including AID, classified by the MedDRA preferred terms and reported during the entire study period, were tabulated. The same tabulation was performed for Grade 3 AEs and for AEs assessed as related to vaccination.

SAEs were collected and summarized by MedDRA preferred terms during the entire study period.

Study Population: Healthy men or women aged 18-41 years or ≥ 65 years at the time of the vaccination, free of an acute aggravation of the health status and who participated in the 110847 study and completed the 6-month follow-up. Women of childbearing potential had to practice adequate contraception for 30 days prior to vaccination, to have a negative pregnancy test and were to continue such precautions for 2 months after vaccination. Written informed consent was obtained from the subject before study start.

Number of subjects	**FLU NG Group**	**Flu Eld Group**	**Flu Yng Group**
Planned, N	404	200	203
Randomised, N (Total Vaccinated Cohort)	266	144	116
Completed, n (%)	261 (98.1)	142 (98.6)	111 (95.7)
Total Number Subjects Withdrawn, n (%)	5 (1.9)	2 (1.4)	5 (4.3)
Withdrawn due to Adverse Events, n (%)	5 (1.9)	2 (1.4)	0
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0	0	5 (4.3)
Demographics	**FLU NG Group**	**Flu Eld Group**	**Flu Yng Group**
N (Total Vaccinated Cohort)	266	144	116
Females: Males	143:123	68:76	53:63
Mean Age, years (SD)	73.5 (5.27)	73.8 (5.54)	28.2 (6.34)
White - Caucasian / European heritage, n (%)	262 (98.5)	144 (100)	113 (97.4)

Primary Efficacy Results: Incidence of 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	265	2	0.8	0.1	2.7	144	2	1.4	0.2	4.9	115	1	0.9	0.0	4.7
	>100 mm	265	0	0.0	0.0	1.4	144	0	0.0	0.0	2.5	115	0	0.0	0.0	3.2
Pain	Any	265	108	40.8	34.8	46.9	144	18	12.5	7.6	19.0	115	61	53.0	43.5	62.4
	Grade 3	265	0	0.0	0.0	1.4	144	0	0.0	0.0	2.5	115	0	0.0	0.0	3.2
Redness	Any	265	43	16.2	12.0	21.2	144	5	3.5	1.1	7.9	115	3	2.6	0.5	7.4
	>100 mm	265	1	0.4	0.0	2.1	144	0	0.0	0.0	2.5	115	0	0.0	0.0	3.2
Swelling	Any	265	20	7.5	4.7	11.4	144	7	4.9	2.0	9.8	115	1	0.9	0.0	4.7
	>100 mm	265	0	0.0	0.0	1.4	144	0	0.0	0.0	2.5	115	0	0.0	0.0	3.2

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

Primary Efficacy results: Number of days with any grade local symptoms reported during the 7-day (Day 0-6) post-vaccination period (Total Vaccinated Cohort)

Solicited symptom	**Group**	**N**	**Mean**	**Median**
Ecchymosis	FLU NG	2	6.0	6.0
	Flu Eld	2	4.0	4.0
	Flu Yng	1	7.0	7.0
Pain	FLU NG	108	2.2	2.0
	Flu Eld	18	2.4	2.0
	Flu Yng	61	2.1	2.0
Redness	FLU NG	43	2.5	2.0
	Flu Eld	5	2.4	2.0
	Flu Yng	3	1.7	2.0
Swelling	FLU NG	20	2.5	2.0
	Flu Eld	7	2.6	3.0
	Flu Yng	1	2.0	2.0

N = number of subjects with the symptom
The grade for quantifiable symptoms: Ecchymosis, Redness, Swelling: > 20mm

Primary Efficacy Results: Incidence of 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	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Arthralgia	Any	265	30	11.3	7.8	15.8	144	6	4.2	1.5	8.8	115	10	8.7	4.2	15.4

	Grade 3	265	0	0.0	0.0	1.4	144	0	0.0	0.0	2.5	115	0	0.0	0.0	3.2
	Related	265	20	7.5	4.7	11.4	144	5	3.5	1.1	7.9	115	7	6.1	2.5	12.1
Fatigue	Any	265	51	19.2	14.7	24.5	144	11	7.6	3.9	13.3	115	27	23.5	16.1	32.3
	Grade 3	265	1	0.4	0.0	2.1	144	0	0.0	0.0	2.5	115	2	1.7	0.2	6.1
	Related	265	39	14.7	10.7	19.6	144	10	6.9	3.4	12.4	115	19	16.5	10.3	24.6
Gastrointestinal Symptoms	Any	265	24	9.1	5.9	13.2	144	5	3.5	1.1	7.9	115	9	7.8	3.6	14.3
	Grade 3	265	0	0.0	0.0	1.4	144	0	0.0	0.0	2.5	115	2	1.7	0.2	6.1
	Related	265	13	4.9	2.6	8.2	144	4	2.8	0.8	7.0	115	2	1.7	0.2	6.1
Headache	Any	265	39	14.7	10.7	19.6	144	7	4.9	2.0	9.8	115	30	26.1	18.3	35.1
	Grade 3	265	1	0.4	0.0	2.1	144	0	0.0	0.0	2.5	115	4	3.5	1.0	8.7
	Related	265	24	9.1	5.9	13.2	144	4	2.8	0.8	7.0	115	17	14.8	8.9	22.6
Myalgia	Any	265	42	15.8	11.7	20.8	144	8	5.6	2.4	10.7	115	16	13.9	8.2	21.6
	Grade 3	265	0	0.0	0.0	1.4	144	0	0.0	0.0	2.5	115	0	0.0	0.0	3.2
	Related	265	31	11.7	8.1	16.2	144	6	4.2	1.5	8.8	115	12	10.4	5.5	17.5
Shivering	Any	265	37	14.0	10.0	18.7	144	6	4.2	1.5	8.8	115	10	8.7	4.2	15.4
	Grade 3	265	0	0.0	0.0	1.4	144	0	0.0	0.0	2.5	115	1	0.9	0.0	4.7
	Related	265	29	10.9	7.5	15.3	144	4	2.8	0.8	7.0	115	7	6.1	2.5	12.1
Temperature/ (Orally) (°C)	≥38.0	265	5	1.9	0.6	4.3	144	1	0.7	0.0	3.8	115	5	4.3	1.4	9.9
	>40.0	265	0	0.0	0.0	1.4	144	0	0.0	0.0	2.5	115	0	0.0	0.0	3.2
	Related	265	4	1.5	0.4	3.8	144	1	0.7	0.0	3.8	115	3	2.6	0.5	7.4

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 their intensity grade or relationship to vaccination.
Grade 3 Symptoms: symptoms that prevented normal activity
Related = general symptom assessed by the investigator as causally related to the study vaccination

Primary Efficacy Results: Number of days with any general symptoms (any grade) during the 7-day (Day 0-6) post-vaccination period (Total Vaccinated cohort)

Solicited symptom	Group	N	Mean	Median
Arthralgia	FLU NG	30	2.1	2.0
	Flu Eld	6	1.7	1.5
	Flu Yng	10	2.8	3.0
Fatigue	FLU NG	51	1.9	2.0
	Flu Eld	11	2.5	2.0
	Flu Yng	27	2.2	2.0
Gastrointestinal symptoms	FLU NG	24	1.8	1.0
	Flu Eld	5	2.6	2.0
	Flu Yng	9	1.6	1.0
Headache	FLU NG	39	2.0	1.0
	Flu Eld	7	1.6	1.0
	Flu Yng	30	1.8	1.5
Myalgia	FLU NG	42	1.9	2.0
	Flu Eld	8	2.5	2.0
	Flu Yng	16	2.6	2.0
Shivering	FLU NG	37	1.5	1.0
	Flu Eld	6	1.7	2.0
	Flu Yng	10	1.2	1.0
Fever	FLU NG	5	2.4	1.0
	Flu Eld	1	1.0	1.0
	Flu Yng	5	1.0	1.0

N = number of subjects with the symptom
The grade for Fever: ≥38.0°C

Primary Efficacy Results: Number (%) of subjects with unsolicited AE that resulted in a medically attended visit during the vaccination phase of the study (Total vaccinated cohort)

Most frequent adverse events On-Therapy (occurring within Day 0-20 following vaccination)	FLU NG Group N =266	Flu Eld Group N = 144	Flu Yng Group N = 116
Subjects with any AE(s), n(%)	20 (7.5)	8 (5.6)	9 (7.8)
Subjects with grade 3* AE(s), n (%)	4 (1.5)	1 (0.7)	1 (0.9)
Subjects with related** AE(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Cough	1 (0.4)	-	2 (1.7)
Dyspnoea	2 (0.8)	-	-
Hypertension	2 (0.8)	-	-
Nasopharyngitis	-	-	2 (1.7)
Toothache	1 (0.4)	-	1 (0.9)
Arthralgia	1 (0.4)	-	-
Back pain	-	1 (0.7)	-
Breast haematoma	1 (0.4)	-	-
Bronchitis	1 (0.4)	-	-
Cardiac failure	1 (0.4)	-	-
Central nervous system lymphoma	1 (0.4)	-	-
Concussion	1 (0.4)	-	-
Conjunctivitis	1 (0.4)	-	-
Contusion	1 (0.4)	-	-
Dyspepsia	-	-	1 (0.9)
Eczema	1 (0.4)	-	-
Facial bones fracture	1 (0.4)	-	-
Gingivitis	1 (0.4)	-	-
Headache	-	-	1 (0.9)
Heart rate increased	-	1 (0.7)	-
Inflammation	1 (0.4)	-	-
Intestinal haemorrhage	-	1 (0.7)	-
Locked-in syndrome	1 (0.4)	-	-
Neck pain	1 (0.4)	-	-
Neuralgia	-	1 (0.7)	-
Oedema peripheral	-	1 (0.7)	-
Oral fungal infection	-	-	1 (0.9)
Osteoarthritis	-	1 (0.7)	-
Otitis media	-	-	1 (0.9)
Pharyngitis	-	-	1 (0.9)
Pneumonia	-	1 (0.7)	-
Postoperative wound infection	1 (0.4)	-	-
Pyrexia	-	-	1 (0.9)
Rash	-	1 (0.7)	-
Renal failure acute	1 (0.4)	-	-
Sciatica	-	-	1 (0.9)
Sinusitis	-	-	1 (0.9)
Skin cancer	-	1 (0.7)	-
Skin laceration	1 (0.4)	-	-
Testicular torsion	-	-	1 (0.9)
Tonsillitis	-	1 (0.7)	-
Tooth infection	1 (0.4)	-	-
Transient ischaemic attack	1 (0.4)	-	-
Upper respiratory tract infection	1 (0.4)	-	-

- : Adverse event absent
*Grade 3 AE: an AE which prevented normal everyday activities.
**Related AE: assessed by the investigator as possibly related to the study vaccination

Primary Efficacy Results: Number (%) of subjects with adverse events that resulted in a medically attended visit between Day 21 and Day 179 (Total vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 21-179 following vaccination)	FLU NG Group N = 266	Flu Eld Group N = 144	Flu Yng Group N = 116
Subjects with any AE(s), n (%)	103 (38.7)	48 (33.3)	33 (28.4)
Subjects with grade 3* AE(s), n (%)	26 (9.8)	8 (5.6)	9 (7.8)
Subjects with related** AE(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Bronchitis	10 (3.8)	2 (1.4)	3 (2.6)
Back pain	7 (2.6)	3 (2.1)	-
Nasopharyngitis	4 (1.5)	2 (1.4)	4 (3.4)
Osteoarthritis	7 (2.6)	3 (2.1)	-
Hypertension	4 (1.5)	4 (2.8)	-
Urinary tract infection	4 (1.5)	2 (1.4)	-
Angina pectoris	4 (1.5)	-	-
Upper respiratory tract infection	4 (1.5)	-	-
Arthralgia	-	3 (2.1)	-
Cerebrovascular accident	3 (1.1)	-	-
Cough	3 (1.1)	-	-
Epicondylitis	3 (1.1)	-	-
Gastritis	-	-	3 (2.6)
Gastroenteritis	-	-	3 (2.6)
Intercostal neuralgia	3 (1.1)	-	-
Musculoskeletal pain	3 (1.1)	-	-
Sinusitis	-	-	3 (2.6)
Abdominal pain	-	-	2 (1.7)
Cystitis	-	-	2 (1.7)
Fungal infection	-	2 (1.4)	-
Gastrointestinal disorder	-	2 (1.4)	-
Gastrointestinal infection	-	-	2 (1.7)
Glaucoma	-	2 (1.4)	-
Intestinal polyp	-	2 (1.4)	-
Rhinitis allergic	-	-	2 (1.7)
Tonsillitis	-	-	2 (1.7)
Viral infection	-	-	2 (1.7)

- : Adverse event absent or not meeting the selected rule(s).
Detail of rule: More than 30 subjects per treatment group and ≤ 3 groups: display the most frequent 10 events in each group.
*Grade 3 AE: an AE which prevented normal everyday activities.
**Related AE: assessed by the investigator as possibly related to the study vaccination.

Primary Efficacy Results: Number of subjects with AEs of specific interest including AID reported during the entire study period (Total vaccinated cohort)

Most frequent adverse events On-Therapy (occurring within Day 0-179 following vaccination)	FLU NG Group N =266	Flu Eld Group N = 144	Flu Yng Group N = 116
Subjects with any AE(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Subjects with grade 3* AE(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Subjects with related** AE(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)

*Grade 3 AE: an AE which prevented normal everyday activities.
**Related AE: assessed by the investigator as possibly related to the study vaccination.

Primary Efficacy Results: Occurrence of unsolicited AEs and SAEs: please refer to the safety section of the document.

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

				≥ 1:10				GMT		
						95% CI			95% CI	
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL
A/Brisbane	FLU NG	PRE	253	226	89.3	84.9	92.8	27.9	24.7	31.6
		PI(D21)	253	251	99.2	97.2	99.9	74.6	66.7	83.3

	Flu Eld	PRE	142	125	88.0	81.5	92.9	22.9	19.6	26.7
		PI(D21)	142	141	99.3	96.1	100	57.5	49.5	66.8
	Flu Yng	PRE	108	97	89.8	82.5	94.8	43.2	33.9	54.9
		PI(D21)	108	108	100	96.6	100	164.7	133.9	202.5
A/Uruguay	FLU NG	PRE	253	212	83.8	78.7	88.1	28.1	24.3	32.6
		PI(D21)	253	253	100	98.6	100	243.9	213.5	278.7
	Flu Eld	PRE	142	116	81.7	74.3	87.7	22.8	19.0	27.4
		PI(D21)	142	140	98.6	95.0	99.8	134.8	107.9	168.4
	Flu Yng	PRE	108	90	83.3	74.9	89.8	28.9	22.9	36.5
		PI(D21)	108	108	100	96.6	100	171.1	141.0	207.7
B/Brisbane	FLU NG	PRE	253	253	100	98.6	100	126.5	111.5	143.5
		PI(D21)	253	253	100	98.6	100	519.0	467.1	576.6
	Flu Eld	PRE	142	142	100	97.4	100	159.9	136.1	188.0
		PI(D21)	142	142	100	97.4	100	402.5	344.2	470.6
	Flu Yng	PRE	108	108	100	96.6	100	192.7	150.6	246.7
		PI(D21)	108	108	100	96.6	100	711.5	611.2	828.2

GMT = geometric mean antibody titre calculated on all subjects
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 (Day 0)
PI(D21) = Post-vaccination Dose 1 (Day 21)

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

			≥ 1:10				**GMT**		
					95% CI			**95% CI**	
Vaccine strain	**Group**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
A/Brisbane	FLU NG	240	226	94.2	90.4	96.8	34.9	30.9	39.4
	Flu Eld	130	123	94.6	89.2	97.8	27.7	23.9	32.0
	Flu Yng	103	102	99.0	94.7	100	99.5	79.8	124.0
A/Uruguay	FLU NG	240	235	97.9	95.2	99.3	90.1	77.0	105.4
	Flu Eld	130	125	96.2	91.3	98.7	69.9	55.8	87.6
	Flu Yng	103	99	96.1	90.4	98.9	86.1	68.2	108.7
B/Brisbane	FLU NG	241	241	100	98.5	100	278.7	248.4	312.6
	Flu Eld	130	130	100	97.2	100	255.7	218.9	298.7
	Flu Yng	103	103	100	96.5	100	463.3	384.0	558.9

GMT = geometric mean antibody titre calculated
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

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

			SCR			
					95% CI	
Vaccine strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/Brisbane	FLU NG	253	77	30.4	24.8	36.5
	Flu Eld	142	46	32.4	24.8	40.8
	Flu Yng	108	48	44.4	34.9	54.3
A/Uruguay	FLU NG	253	209	82.6	77.4	87.1
	Flu Eld	142	97	68.3	60.0	75.9
	Flu Yng	108	67	62.0	52.2	71.2
B/Brisbane	FLU NG	253	130	51.4	45.0	57.7
	Flu Eld	142	47	33.1	25.4	41.5
	Flu Yng	108	50	46.3	36.7	56.2

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 rate (SCR) for HI antibody titres at Day 180 (ATP cohort for persistence)

			SCR			
					95% CI	
Vaccine strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/Brisbane	FLU NG	240	15	6.3	3.5	10.1
	Flu Eld	130	11	8.5	4.3	14.6
	Flu Yng	103	31	30.1	21.5	39.9
A/Uruguay	FLU NG	240	99	41.3	35.0	47.8
	Flu Eld	130	47	36.2	27.9	45.0
	Flu Yng	103	37	35.9	26.7	46.0
B/Brisbane	FLU NG	241	64	26.6	21.1	32.6
	Flu Eld	130	19	14.6	9.0	21.9
	Flu Yng	103	36	35.0	25.8	45.0

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 titres at Day 21 (ATP immunogenicity cohort for HI)

			SCF		
				95% CI	
Vaccine strain	**Group**	**N**	**Value**	**LL**	**UL**
A/Brisbane	FLU NG	253	2.7	2.4	3.0
	Flu Eld	142	2.5	2.1	2.9
	Flu Yng	108	3.8	3.0	4.9
A/Uruguay	FLU NG	253	8.7	7.5	9.9
	Flu Eld	142	5.9	4.9	7.2
	Flu Yng	108	5.9	4.8	7.3
B/Brisbane	FLU NG	253	4.1	3.6	4.6
	Flu Eld	142	2.5	2.2	2.9
	Flu Yng	108	3.7	3.0	4.5

N = Number of subjects with pre- and post-vaccination results available
SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

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

			SCF		
				95% CI	
Vaccine strain	**Group**	**N**	**Value**	**LL**	**UL**
A/Brisbane	FLU NG	240	1.3	1.1	1.4
	Flu Eld	130	1.2	1.1	1.4
	Flu Yng	103	2.4	1.9	2.9
A/Uruguay	FLU NG	240	3.4	3.0	3.8
	Flu Eld	130	2.9	2.4	3.6
	Flu Yng	103	3.1	2.5	3.9
B/Brisbane	FLU NG	241	2.2	2.0	2.4
	Flu Eld	130	1.7	1.5	1.9

	Flu Yng	103	2.7	2.3	3.2

N = Number of subjects with pre- and post-vaccination results available
SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): Seroprotection rates (SPR) for HI antibody titres at Day 0 and 21 (ATP immunogenicity cohort for HI)

				SPR			
						95% CI	
Vaccine strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
A/Brisbane	FLU NG	PRE	253	124	49.0	42.7	55.3
		PI(D21)	253	222	87.7	83.1	91.5
	Flu Eld	PRE	142	55	38.7	30.7	47.3
		PI(D21)	142	108	76.1	68.2	82.8
	Flu Yng	PRE	108	68	63.0	53.1	72.1
		PI(D21)	108	101	93.5	87.1	97.4
A/Uruguay	FLU NG	PRE	253	121	47.8	41.5	54.2
		PI(D21)	253	248	98.0	95.4	99.4
	Flu Eld	PRE	142	58	40.8	32.7	49.4
		PI(D21)	142	123	86.6	79.9	91.7
	Flu Yng	PRE	108	53	49.1	39.3	58.9
		PI(D21)	108	104	96.3	90.8	99.0
B/Brisbane	FLU NG	PRE	253	236	93.3	89.5	96.0
		PI(D21)	253	253	100	98.6	100
	Flu Eld	PRE	142	136	95.8	91.0	98.4
		PI(D21)	142	141	99.3	96.1	100
	Flu Yng	PRE	108	101	93.5	87.1	97.4
		PI(D21)	108	108	100	96.6	100

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

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

			SPR			
					95% CI	
Vaccine strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/Brisbane	FLU NG	240	143	59.6	53.1	65.8
	Flu Eld	130	65	50.0	41.1	58.9
	Flu Yng	103	89	86.4	78.2	92.4
A/Uruguay	FLU NG	240	193	80.4	74.8	85.2
	Flu Eld	130	94	72.3	63.8	79.8
	Flu Yng	103	87	84.5	76.0	90.9
B/Brisbane	FLU NG	241	241	100	98.5	100
	Flu Eld	130	129	99.2	95.8	100
	Flu Yng	103	103	100	96.5	100

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

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

Test description	**Stimulating antigen**	**Group**	**Timing**	**N**	**GM**	**SD**
CD4-ALL DOUBLES	A/ Brisbane	FLU NG	PRE	66	751.28	492.55
			PI(D21)	66	1431.41	679.60

		Flu Eld	PRE	34	682.47	759.31
			PI(D21)	34	972.14	1204.18
		Flu Yng	PRE	22	1179.17	1031.92
			PI(D21)	19	1513.30	798.38
	A/ Uruguay	FLU NG	PRE	65	451.86	419.39
			PI(D21)	66	912.85	496.53
		Flu Eld	PRE	33	444.42	578.82
			PI(D21)	32	592.66	518.19
		Flu Yng	PRE	22	743.45	552.48
			PI(D21)	19	912.28	476.16
	B/ Brisbane	FLU NG	PRE	65	828.74	840.19
			PI(D21)	64	1361.30	799.10
		Flu Eld	PRE	34	679.28	702.37
			PI(D21)	34	935.28	1130.22
		Flu Yng	PRE	22	1045.61	510.95
			PI(D21)	19	1403.64	580.53
CD4-CD40L	A/ Brisbane	FLU NG	PRE	66	694.63	452.67
			PI(D21)	66	1305.74	622.93
		Flu Eld	PRE	34	616.27	682.26
			PI(D21)	34	855.81	974.19
		Flu Yng	PRE	22	1127.82	946.50
			PI(D21)	19	1379.47	735.06
	A/ Uruguay	FLU NG	PRE	65	392.35	368.33
			PI(D21)	66	803.34	459.33
		Flu Eld	PRE	33	361.18	498.91
			PI(D21)	32	543.41	463.96
		Flu Yng	PRE	22	646.92	542.81
			PI(D21)	19	816.08	447.79
	B/ Brisbane	FLU NG	PRE	65	775.18	754.90
			PI(D21)	64	1230.63	731.08
		Flu Eld	PRE	34	630.27	630.81
			PI(D21)	34	850.96	901.02
		Flu Yng	PRE	22	959.42	465.42
			PI(D21)	19	1275.70	508.40
CD4-IFNγ	A/ Brisbane	FLU NG	PRE	66	430.40	373.24
			PI(D21)	66	839.94	536.38
		Flu Eld	PRE	34	338.29	613.41
			PI(D21)	34	481.04	976.79
		Flu Yng	PRE	22	777.72	837.25
			PI(D21)	19	985.11	713.98
	A/ Uruguay	FLU NG	PRE	65	282.79	321.42
			PI(D21)	66	628.36	400.49
		Flu Eld	PRE	33	301.64	426.04
			PI(D21)	32	399.84	387.97
		Flu Yng	PRE	22	501.13	482.16
			PI(D21)	19	638.93	418.36
	B/ Brisbane	FLU NG	PRE	65	447.23	708.32
			PI(D21)	64	800.89	648.91
		Flu Eld	PRE	34	299.25	441.05
			PI(D21)	34	478.15	851.02
		Flu Yng	PRE	22	681.49	413.65
			PI(D21)	19	934.53	471.32
CD4-IL2	A/ Brisbane	FLU NG	PRE	66	645.57	445.17
			PI(D21)	66	1176.29	568.05

		Flu Eld	PRE	34	542.90	700.45
			PI(D21)	34	816.63	1114.87
		Flu Yng	PRE	22	1033.28	884.01
			PI(D21)	19	1259.69	691.36
	A/ Uruguay	FLU NG	PRE	65	385.93	375.33
			PI(D21)	66	745.33	428.75
		Flu Eld	PRE	33	392.63	488.21
			PI(D21)	32	505.78	459.04
		Flu Yng	PRE	22	599.02	523.72
			PI(D21)	19	745.61	444.27
	B/ Brisbane	FLU NG	PRE	65	711.32	760.06
			PI(D21)	64	1112.52	725.72
		Flu Eld	PRE	34	547.71	646.50
			PI(D21)	34	778.12	1034.69
		Flu Yng	PRE	22	852.51	479.69
			PI(D21)	19	1156.73	494.36
CD4-TNFα	A/ Brisbane	FLU NG	PRE	66	606.82	442.61
			PI(D21)	66	1057.44	568.35
		Flu Eld	PRE	34	610.09	669.96
			PI(D21)	34	749.70	1068.11
		Flu Yng	PRE	22	900.67	914.33
			PI(D21)	19	1096.74	689.90
	A/ Uruguay	FLU NG	PRE	65	405.12	403.06
			PI(D21)	66	740.68	448.67
		Flu Eld	PRE	33	414.27	508.57
			PI(D21)	32	449.51	463.77
		Flu Yng	PRE	22	575.28	509.48
			PI(D21)	19	685.63	429.55
	B/ Brisbane	FLU NG	PRE	65	646.27	718.92
			PI(D21)	64	1021.43	690.24
		Flu Eld	PRE	34	558.87	591.29
			PI(D21)	34	715.45	973.99
		Flu Yng	PRE	22	818.77	441.82
			PI(D21)	19	1023.28	475.97

N = number of subjects with available results for post and pre time points
SD = Standard Deviation
All doubles: cells producing at least two different cytokines (CD40L, IFNγ, IL-2, TFNα)
PRE = Pre-vaccination Dose 1 (Day 0)
PI(D21) = Post-vaccination Dose 1 (Day 21)

Safety results: Number (%) of subjects with unsolicited adverse events during the vaccination phase of the study (Total vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)	**FLU NG Group N = 266**	**Flu Eld Group N = 144**	**Flu Yng Group N = 116**
Subjects with any AE(s), n (%)	49 (18.4)	20 (13.9)	18 (15.5)
Subjects with grade 3* AE(s), n (%)	6 (2.3)	1 (0.7)	4 (3.4)
Subjects with related** AE(s), n (%)	1 (0.4)	2 (1.4)	0 (0.0)
Nasopharyngitis	11 (4.1)	4 (2.8)	8 (6.9)
Headache	5 (1.9)	1 (0.7)	5 (4.3)
Oropharyngeal pain	2 (0.8)	2 (1.4)	3 (2.6)
Musculoskeletal pain	3 (1.1)	1 (0.7)	-
Abdominal pain	-	-	1 (0.9)
Diarrhoea	-	-	1 (0.9)
Dyspepsia	-	-	1(0.9)
Ear pain	-	-	1(0.9)

Gastroenteritis	-	-	1 (0.9)
Oral fungal infection	-	-	1 (0.9)
Otitis media	-	-	1 (0.9)
Pharyngitis	-	-	1 (0.9)
Rhinitis	-	-	1 (0.9)
Sciatica	-	-	1 (0.9)
Sinusitis	-	-	1 (0.9)
Testicular torsion	-	-	1 (0.9)
Toothache	-	-	1 (0.9)
Cough	3 (1.1)	-	2 (1.7)
Pyrexia	2 (0.8)	-	1 (0.9)
Arthralgia	2 (0.8)	-	-
Back pain	-	2 (1.4)	-
Dyspnoea	2 (0.8)	-	-
Gastritis	2 (0.8)	-	-
Hypertension	2 (0.8)	-	-
Neck pain	2 (0.8)	-	-
Rhinorrhoea	2 (0.8)	-	-
Bronchitis	-	1 (0.7)	-
Dizziness	-	1 (0.7)	-
Heart rate increased	-	1 (0.7)	-
Injection site pruritus	-	1 (0.7)	-
Intestinal haemorrhage	-	1 (0.7)	-
Nausea	-	1 (0.7)	-
Neuralgia	-	1 (0.7)	-
Oedema peripheral	-	1 (0.7)	-
Osteoarthritis	-	1 (0.7)	-
Palpitations	-	1 (0.7)	-
Pneumonia	-	1 (0.7)	-
Rash	-	1 (0.7)	-
Skin cancer	-	1 (0.7)	-
Tonsillitis	-	1 (0.7)	-

*Grade 3 AE: an AE which prevented normal, everyday activities.
**Related AE: assessed by the investigator as possibly related to the study vaccination.
- : Adverse event absent or not meeting the selected rule(s).
Detail of rule: More than 30 subjects per treatment group and $\leq$ 3 groups: the most frequent 10 events in each group.

Safety results: Number (%) of subjects with serious adverse events from Day 0 to Day 20 (Total vaccinated cohort)

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

All SAEs	**FLU NG Group N = 266**	**Flu Eld Group N =144**	**Flu Yng Group N = 116**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	4 (1.5) [0]	2 (1.4) [0]	1 (0.9) [0]
Cardiac failure	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Central nervous system lymphoma	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Concussion	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Facial bones fracture	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Locked-in syndrome	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Osteoarthritis	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Pneumonia	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Postoperative wound infection	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Renal failure acute	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Skin laceration	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Testicular torsion	0 (0.0) [0]	0 (0.0) [0]	1 (0.9) [0]
Transient ischaemic attack	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]

Fatal SAEs	**FLU NG Group N = 266**	**Flu Eld Group N =144**	**Flu Yng Group N = 116**
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	2 (0.8) [0]	0 (0.0) [0]	0 (0.0) [0]
Cardiac failure	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Central nervous system lymphoma	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Locked-in syndrome	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Renal failure acute	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Safety results: Number (%) of subjects with serious adverse events between Day 21 and Day 179 (Total vaccinated cohort)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	**FLU NG Group N = 266**	**Flu Eld Group N = 144**	**Flu Yng Group N = 116**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	19 (7.1) [0]	7 (4.9) [0]	2 (1.7) [0]
Cerebrovascular accident	3 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]
Osteoarthritis	3 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]
Angina pectoris	2 (0.8) [0]	0 (0.0) [0]	0 (0.0) [0]
Myocardial infarction	1 (0.4) [0]	1 (0.7) [0]	0 (0.0) [0]
Pneumonia	2 (0.8) [0]	0 (0.0) [0]	0 (0.0) [0]
Abortion spontaneous	0 (0.0) [0]	0 (0.0) [0]	1 (0.9) [0]
Anoxic encephalopathy	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Arrhythmia	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Atrial fibrillation	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Atrioventricular block	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Back pain	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Cardiac failure	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cartilage injury	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cholecystitis chronic	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Contusion	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Convulsion	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Coronary artery disease	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Epididymitis	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Gastroenteritis norovirus	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Glaucoma	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Hypertension	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Hypoglycaemia	0 (0.0) [0]	0 (0.0) [0]	1 (0.9) [0]
Incisional hernia	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Large intestine perforation	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Peripheral arterial occlusive disease	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Prostate cancer	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Sepsis	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Subarachnoid haemorrhage	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Subdural haematoma	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Urinary retention	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Urinary tract infection	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Wound	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Fatal SAEs	**FLU NG Group N = 266**	**Flu Eld Group N = 144**	**Flu Yng Group N = 116**
Subjects with fatal SAE (s), n (%) [n assessed by investigator as related]	2 (0.8) [0]	1 (0.7) [0]	0 (0.0) [0]
Anoxic encephalopathy	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Cardiac failure	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Myocardial infarction	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]

Pneumonia	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Sepsis	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Safety results: Number (%) of subjects with serious adverse events from Day 180 to the study end (Total vaccinated cohort)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	**FLU NG Group N = 266**	**Flu Eld Group N = 144**	**Flu Yng Group N = 116**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	3 (2.1) [0]	0 (0.0) [0]
Dysuria	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Embolic cerebral infarction	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Respiratory failure	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Transient ischaemic attack	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Fatal SAEs	**FLU NG Group N = 266**	**Flu Eld Group N = 144**	**Flu Yng Group N = 116**
Subjects with fatal SAE (s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:
Pain at the injection site was the most frequently reported solicited local symptom (108 [40.8%] subjects in FLU NG Group, 18 [12.5%] in Flu Eld Group and 61 [53.0%] in Flu Yng Group). Fatigue was the most frequently reported solicited general symptom in FLU NG and Flu Eld groups (51 [19.2%] and 11 [7.6%] subjects, respectively). Headache was the most frequently reported solicited general symptom in Flu Yng Group (30 [26.1%] subjects). Unsolicited AEs were reported by 49 (18.4%), 20 (13.9%) and 18 (15.5%) subjects in FLU NG, Flu Eld and Flu Yng groups, respectively. During the vaccination phase of the study, unsolicited AEs that resulted in a medically attended visit were reported by 20 (7.5%), 8 (5.6%) and 9 (7.8%) subjects in FLU NG, Flu Eld and Flu Yng groups, respectively. During the safety follow-up phase, unsolicited AEs that resulted in a medically attended visit were reported by 103 (38.7%), 48 (33.3%) and 33 (28.4%) subjects in FLU NG, Flu Eld and Flu Yng groups, respectively. No AE of specific interest was reported during the study. Until Day 21, SAEs were reported for 7 subjects (4 [1.5%] in FLU NG Group, 2 [1.4%] in Flu Eld Group and 1 [0.9%] in Flu Yng Group); 2 SAEs were fatal. Between Day 21 and Day 179, SAEs were reported for 19 (7.1%) subjects in FLU NG Group, 7 (4.9%) subjects in Flu Eld Group and 2 (1.7%) subjects in Flu Yng Group; 5 of these SAEs (reported for 2 subjects in Flu NG Group and 1 subject in Flu Eld Group) were fatal. From Day 180 until the study end, SAEs were reported by 3 (2.1%) subjects of Flu Eld Group; none of them were fatal. All the SAEs reported during this study were assessed by the investigators as not related to the study vaccination.

Date updated: 09-July-2014