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.: 113094 (FLU NG-039 EXT: FLU-AS25-025 Y2)

Title: Observer-blind safety and immunogenicity study of GlaxoSmithKline (GSK) Biologicals' influenza vaccine GSK2186877A when administered to elderly subjects.
GSK2186877A (Flu NG): GSK Biologicals' trivalent inactivated new generation influenza split vaccine.

Rationale: The aim of this study was to evaluate the safety and immunogenicity of Flu NG vaccine after repeated vaccination. Subjects who were previously vaccinated in the 110847 (FLU-AS25-025 PRI) study and re-vaccinated for the first time in the 111737 (FLU NG-036 EXT 025 Y1) study, were re-vaccinated again in the current study. *Fluarix*™ was used as a reference.
Fluarix™ (Flu): GSK Biologicals' licensed influenza vaccine

Note: For results on the first and second vaccinations in this repeated vaccination series please refer to CTRSs 110847 and 111737.

Phase: III

Study Period: 15 October 2009 to 27 May 2010

Study Design: Multicountry, multicentre, observer-blind for subjects ≥ 66 years and open for subjects aged 18-43 years, controlled study with 3 parallel groups.

Centres: 25 centres in 3 countries (3 in Sweden, 20 in Germany and 2 in the Netherlands)

Indication: Immunization against influenza in male and female subjects aged 19-43 years and ≥66 years.

Treatment: The study groups were as follows:

- Flu NG Group: subjects aged ≥66 years receiving one dose of Flu NG vaccine.
- Flu Eld Group: subjects aged ≥66 years receiving one dose of Flu vaccine.
- Flu Yng Group: subjects aged 19-43 years receiving one dose of Flu vaccine.

Both vaccines were administered intramuscularly in the deltoid of the non-dominant arm.

Objectives:

- To assess the safety during the entire study period in subjects aged ≥66 years (previously enrolled in the 111737 study) vaccinated with the Flu NG vaccine or with Flu vaccine, and in subjects aged 19-43 years (previously enrolled in the 111737 study) vaccinated with Flu vaccine.

Primary Outcome/Efficacy Variable:
Safety

- Solicited local and general symptoms
  - Occurrence, intensity and 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.
- Unsolicited AEs
  - 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.
- Predefined AEs
  - Occurrence, intensity 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, intensity and relationship to vaccination of AEs of specific interest during the entire study period.
- Serious adverse events (SAEs)
  - Occurrence and relationship to vaccination of SAEs during the entire study period.

Secondary Outcome/Efficacy Variable(s):
Immunogenicity

- Humoral immune response in terms of Haemagglutination Inhibition (HI) antibodies.
  - At Days 0, 21 and 180, serum HI antibody titre against each of the three 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 was defined as the percentage of vaccinees who had either a pre-vaccination titre <1:10 and a post-vaccination titre ≥1:40 or a pre-vaccination titre ≥1:10 and at least a four-fold increase in post-vaccination titre.
**SCF was defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.
***SPR was defined as the percentage of vaccinees with a serum HI titre ≥1:40 that usually is accepted as indicating protection.

- Cell-mediated immune (CMI) response.
  - CMI response (only for subjects in the CMI sub-cohort) at Days 0, 21 and 180: Frequency of immune response marker-positive CD4 T-cells per 10^6 expressing at least two different markers (cluster of differentiation (CD40L), interleukin 2 (IL-2), tumour necrosis factor alpha (TNF-α), interferon gamma (IF-γ)) and frequency of immune response marker-positive CD4 T-cells per 10^6 expressing the different combinations of the four markers (CD40L, IL-2, TNF-α, IFN-γ).

Derived variables:

- For each test, geometric mean (GM) of the frequency of specific influenza CD4 T lymphocytes at Days 0, 21 and 180.

Statistical Methods:

The analyses were performed on the Total Vaccinated cohort, the According-To-Protocol (ATP) cohort of humoral immunogenicity Day 21, the ATP cohort of humoral immunogenicity Day 180, the ATP cohort for cell-mediated immunogenicity (CMI) Day 21 and the ATP cohort for CMI Day 180:

- The Total Vaccinated cohort included all subjects with the vaccine administration documented.
- The ATP cohort for humoral immunogenicity Day 21 included all evaluable subjects (e.g. who met all eligibility criteria, who complied with the procedures and intervals defined in the protocol, who did not meet any of the criteria for elimination from an ATP analysis up to Day 21, who did not present with a medical condition leading to exclusion from an ATP analysis up to Day 21), who have received one dose of study vaccine/comparator according to their random assignment from the 111737 study, for whom data concerning immunogenicity outcome measures were available. This cohort included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination.
- The ATP cohort for humoral immunogenicity Day 180 included all evaluable subjects (e.g. who met all eligibility criteria, who complied with the procedures and intervals defined in the protocol, who did not meet any of the criteria for elimination from an ATP analysis up to Day 180, who did not present with a medical condition leading to exclusion from an ATP analysis up to Day 180), who have received one dose of study vaccine/comparator according to their random assignment from the 111737 study, for whom data concerning immunogenicity outcome measures were available. This cohort included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination.
- The ATP cohort for CMI Day 21 included all evaluable subjects in the CMI sub-cohort (e.g. who met all eligibility criteria, who complied with the procedures and intervals defined in the protocol, who did not meet any of the criteria for elimination from an ATP analysis up to Day 21, who did not present with a medical condition leading to exclusion from an ATP analysis up to Day 21), who have received one dose of study vaccine/comparator according to their random assignment from the 111737 study, for whom data concerning CMI outcome measures were available. This cohort included subjects for whom assay results were available for at least one test, 21 days after vaccination.
- The ATP cohort for CMI Day 180 included all evaluable subjects in the CMI sub-cohort (e.g. who met all eligibility criteria, who complied with the procedures and intervals defined in the protocol, who did not meet any of the criteria for elimination from an ATP analysis up to Day 180, who did not present with a medical condition leading to exclusion from an ATP analysis up to Day 180), who have received one dose of study vaccine/comparator according to their random assignment from the 111737 study, for whom data concerning CMI outcome measures were available. This cohort included subjects for whom assay results were available for at least one test, 180 days after vaccination.

Analysis of safety:

The analysis of safety was based on the Total Vaccinated cohort.
For each vaccine group, the percentages of subjects with at least one solicited local symptom and with at least one solicited 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 grade 3 solicited symptoms and for general solicited symptoms assessed by the investigators as causally related to the vaccination. The duration of each solicited local and general symptom during the 7-day (Day 0-6) solicited follow-up period was also tabulated.

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), was tabulated. The same tabulation was performed for Grade 3 AEs and for AEs assessed by the investigators as related vaccination.
The percentage of subjects with at least one report of AE with medically attended visit, classified by MedDRA preferred terms, was tabulated during the entire study period, as well as those of Grade 3 and those assessed by the investigators as related to vaccination.
The percentage of subjects with at least one report of AE of specific interest, including autoimmune diseases, classified by MedDRA preferred terms, was tabulated during the same period, as well as those of Grade 3 and those assessed by the investigators as related to vaccination.
SAEs classified by MedDRA preferred terms and reported during the entire study period, were summarized.

Analysis of immunogenicity:

- The analysis of the HI response was performed on the ATP cohorts for humoral immunogenicity Day 21 and Day 180.
  For each vaccination group and for each strain, the following parameters were calculated:
  - GMTs of HI antibody titres at Days 0, 21 and 180, with 95% CI
  - Seropositivity rates at Days 0, 21 and 180, with exact 95% CI
  - SCF at Days 21 and 180, with 95% CI
  - SCR at Days 21 and 180, with exact 95% CI
  - SPR at Days 0, 21 and 180, with exact 95% CI
- The analysis of the CMI response was based on the ATP cohorts for CMI Day 21 and Day 180.
  The frequency of influenza-specific cytokine-positive CD4 T-lymphocytes was summarized (descriptive statistics) for each vaccine group at Days 0, 21 and 180 and for each vaccine strain.

Study Population: Healthy male or female subjects aged 19-43 years or ≥66 years at the time of the vaccination, who participated in the 111737 study and completed the 6-month follow-up and who were not vaccinated against influenza since January 2009. Female subjects were to be of non-childbearing potential or if of childbearing potential, had to practice adequate contraception for 30 days prior to vaccination, had to have a negative pregnancy test and had to continue such precautions for 2 months after the vaccination. Written informed consent was obtained from the subjects prior to study entry.

Number of subjects	**Flu NG Group**	**Flu Eld Group**	**Flu Yng Group**
Planned, N	266	144	116
Randomised, N (Total Vaccinated cohort)	180	104	86
Completed, n (%)	177 (98.3)	102 (98.1)	85 (98.8)
Total Number Subjects Withdrawn, n (%)	3 (1.7)	2 (1.9)	1 (1.2)
Withdrawn due to AEs, n (%)	2 (1.1)	1 (1.0)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	1 (0.6)	1 (1.0)	1 (1.2)
Demographics	**Flu NG Group**	**Flu Eld Group**	**Flu Yng Group**
N (Total Vaccinated cohort)	180	104	86
Females:Males	98:82	46:58	35:51
Mean Age, years (SD)	74.5 (5.18)	74.8 (5.26)	29.9 (6.55)
White - Caucasian / European heritage, n (%)	179 (99.4)	104 (100)	85 (98.8)

Primary Efficacy Results: Number/percentage of subjects reporting solicited local symptoms 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	180	1	0.6	0.0	3.1	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
	>100mm	180	0	0.0	0.0	2.0	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
Pain	Any	180	78	43.3	36.0	50.9	103	12	11.7	6.2	19.5	85	49	57.6	46.4	68.3
	Grade 3	180	0	0.0	0.0	2.0	103	0	0.0	0.0	3.5	85	1	1.2	0.0	6.4
Redness	Any	180	22	12.2	7.8	17.9	103	3	2.9	0.6	8.3	85	5	5.9	1.9	13.2
	>100mm	180	1	0.6	0.0	3.1	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
Swelling	Any	180	22	12.2	7.8	17.9	103	3	2.9	0.6	8.3	85	2	2.4	0.3	8.2
	>100mm	180	0	0.0	0.0	2.0	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2

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 intensity grade.
Grade 3 pain= considerable pain at rest, that prevented normal everyday activities.

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

Solicited symptom	Group	N	Mean	Median
Ecchymosis	Flu NG	1	3.0	3.0
Pain	Flu NG	78	2.1	2.0
	Flu Eld	12	2.0	2.0
	Flu Yng	49	2.0	2.0
Redness	Flu NG	21	2.4	2.0
	Flu Eld	3	2.0	2.0
	Flu Yng	5	2.4	3.0
Swelling	Flu NG	22	2.1	2.0
	Flu Eld	3	2.7	1.0
	Flu Yng	2	2.0	2.0

N= number of subjects with the symptom and without entry 'missing confirmed' in the database instead of an actual grade'

Primary Efficacy Results: Number/percentage of subjects reporting solicited general symptoms 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	180	23	12.8	8.3	18.6	103	3	2.9	0.6	8.3	85	3	3.5	0.7	10.0
	Grade 3	180	0	0.0	0.0	2.0	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
	Related	180	18	10.0	6.0	15.3	103	2	1.9	0.2	6.8	85	2	2.4	0.3	8.2
Fatigue	Any	180	53	29.4	22.9	36.7	103	12	11.7	6.2	19.5	85	21	24.7	16.0	35.3
	Grade 3	180	0	0.0	0.0	2.0	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
	Related	180	41	22.8	16.9	29.6	103	9	8.7	4.1	15.9	85	17	20.0	12.1	30.1
Gastro intestinal	Any	180	11	6.1	3.1	10.7	103	5	4.9	1.6	11.0	85	4	4.7	1.3	11.6
	Grade 3	180	0	0.0	0.0	2.0	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
	Related	180	6	3.3	1.2	7.1	103	2	1.9	0.2	6.8	85	4	4.7	1.3	11.6
Headache	Any	180	31	17.2	12.0	23.5	103	6	5.8	2.2	12.2	85	12	14.1	7.5	23.4
	Grade 3	180	1	0.6	0.0	3.1	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
	Related	180	25	13.9	9.2	19.8	103	6	5.8	2.2	12.2	85	8	9.4	4.2	17.7
Myalgia	Any	180	37	20.6	14.9	27.2	103	7	6.8	2.8	13.5	85	15	17.6	10.2	27.4
	Grade 3	180	1	0.6	0.0	3.1	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
	Related	180	29	16.1	11.1	22.3	103	5	4.9	1.6	11.0	85	15	17.6	10.2	27.4
Shivering	Any	180	20	11.1	6.9	16.6	103	5	4.9	1.6	11.0	85	5	5.9	1.9	13.2
	Grade 3	180	1	0.6	0.0	3.1	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
	Related	180	16	8.9	5.2	14.0	103	4	3.9	1.1	9.6	85	3	3.5	0.7	10.0
Temperature/ (Orally)	≥38.0°C	180	8	4.4	1.9	8.6	103	1	1.0	0.0	5.3	85	1	1.2	0.0	6.4
	≥ 39.0°C-≤ 40.0°C	180	0	0.0	0.0	2.0	103	0	0.0	0.0	3.5	85	0	0.0	0.0	4.2
	Related	180	8	4.4	1.9	8.6	103	1	1.0	0.0	5.3	85	1	1.2	0.0	6.4

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 intensity grade.
Grade 3 symptom= symptom that prevented normal everyday activities.
Related= general symptom assessed by the investigator as causally related to the study vaccination.

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

Solicited symptom	Group	N	Mean	Median
Arthralgia	Flu NG	23	2.3	1.0
	Flu Eld	3	4.0	4.0
	Flu Yng	3	2.0	1.0

Fatigue	Flu NG	53	2.3	2.0
	Flu Eld	12	3.3	3.0
	Flu Yng	21	2.5	2.0
Gastrointestinal	Flu NG	11	1.9	1.0
	Flu Eld	5	2.6	3.0
	Flu Yng	4	1.0	1.0
Headache	Flu NG	31	1.7	2.0
	Flu Eld	6	3.0	2.5
	Flu Yng	12	1.7	2.0
Myalgia	Flu NG	37	2.3	2.0
	Flu Eld	7	4.1	3.0
	Flu Yng	15	2.1	2.0
Shivering	Flu NG	20	1.8	1.0
	Flu Eld	5	1.8	1.0
	Flu Yng	5	2.2	2.0
Temperature	Flu NG	7	1.1	1.0
	Flu Eld	1	1.0	1.0
	Flu Yng	1	1.0	1.0
N= number of subjects with the symptom and without entry 'missing confirmed' in the database instead of an actual grade'				
Primary Efficacy Results: Number and percentage of subjects reporting the occurrence of any AEs with medically attended visit within the 180-day (Days 0-179) post-vaccination period (Total Vaccinated cohort)				
Most frequent AEs (occurring within Day 0-179 following vaccination)		**Flu NG Group N = 180**	**Flu Eld Group N = 104**	**Flu Yng Group N = 86**
Subjects with any AE(s), n (%)		81 (45.0)	34 (32.7)	21 (24.4)
Subject with at least one grade 3 AE(s), n (%)		21 (11.7)	5 (4.8)	6 (7.0)
Subjects with at least one related AE, n (%)		1 (0.6)	1 (1.0)	0 (0.0)
Hypertension		11 (6.1)	2 (1.9)	-
Bronchitis		6 (3.3)	3 (2.9)	2 (2.3)
Nasopharyngitis		4 (2.2)	1 (1.0)	3 (3.5)
Urinary tract infection		5 (2.8)	3 (2.9)	-
Back pain		3 (1.7)	2 (1.9)	1 (1.2)
Arthralgia		3 (1.7)	1 (1.0)	1 (1.2)
Atrial fibrillation		4 (2.2)	1 (1.0)	-
Cough		5 (2.8)	-	-
Cystitis		3 (1.7)	1 (1.0)	-
Osteoarthritis		-	4 (3.8)	-
Gastritis		-	1 (1.0)	2 (2.3)
Hyperlipidaemia		3 (1.7)	-	-
Pain in extremity		3 (1.7)	-	-
Anaemia		-	1 (1.0)	1 (1.2)
Contusion		-	-	2 (2.3)
Diarrhoea		-	2 (1.9)	-
Gastroenteritis		-	-	2 (2.3)
Influenza		-	-	2 (2.3)
Pyrexia		-	-	2 (2.3)
Rhinitis		-	1 (1.0)	1 (1.2)
Toothache		-	-	2 (2.3)
Wound		-	2 (1.9)	-
Abdominal pain		-	-	1 (1.2)
Adenovirus infection		-	1 (1.0)	-
Alcohol poisoning		-	-	1 (1.2)
Alopecia		-	-	1 (1.2)
Aphthous stomatitis		-	1 (1.0)	-
Arteriosclerosis		-	1 (1.0)	-
Asthma		-	1 (1.0)	-

Blood pressure increased	-	1 (1.0)	-
Cardiovascular disorder	-	1 (1.0)	-
Cerumen impaction	-	1 (1.0)	-
Cervical root pain	-	1 (1.0)	-
Cervical vertebral fracture	-	1 (1.0)	-
Cervicobrachial syndrome	-	1 (1.0)	-
Chest pain	-	1 (1.0)	-
Cholecystitis infective	-	1 (1.0)	-
Cholelithiasis	-	1 (1.0)	-
Confusional state	-	1 (1.0)	-
Conjunctivitis	-	-	1 (1.2)
Corneal disorder	-	1 (1.0)	-
Dehydration	-	-	1 (1.2)
Dermatitis allergic	-	1 (1.0)	-
Dyspnoea exertional	-	1 (1.0)	-
Fatigue	-	1 (1.0)	-
Fungal infection	-	-	1 (1.2)
Goitre	-	-	1 (1.2)
Gout	-	-	1 (1.2)
Headache	-	1 (1.0)	-
Hordeolum	-	1 (1.0)	-
Humerus fracture	-	1 (1.0)	-
Hyperglycaemia	-	-	1 (1.2)
Hypoglycaemia	-	1 (1.0)	-
Hypotension	-	1 (1.0)	-
Infection	-	1 (1.0)	-
Influenza like illness	-	1 (1.0)	-
Ingrowing nail	-	-	1 (1.2)
Insomnia	-	1 (1.0)	-
Intermittent claudication	-	1 (1.0)	-
Laryngitis	-	1 (1.0)	-
Lip haematoma	-	1 (1.0)	-
Lung neoplasm malignant	-	1 (1.0)	-
Mucous membrane disorder	-	1 (1.0)	-
Muscle strain	-	1 (1.0)	-
Musculoskeletal discomfort	-	1 (1.0)	-
Musculoskeletal pain	-	1 (1.0)	-
Myalgia	-	-	1 (1.2)
Myocarditis	-	-	1 (1.2)
Onychomycosis	-	-	1 (1.2)
Open wound	-	1 (1.0)	-
Oral fungal infection	-	-	1 (1.2)
Osteoporosis	-	1 (1.0)	-
Parkinsonism	-	1 (1.0)	-
Peripheral arterial occlusive disease	-	1 (1.0)	-
Pharyngitis	-	-	1 (1.2)
Prostate cancer	-	1 (1.0)	-
Restlessness	-	-	1 (1.2)
Rib fracture	-	1 (1.0)	-
Sciatica	-	-	1 (1.2)
Skin disorder	-	1 (1.0)	-
Sneezing	-	1 (1.0)	-
Syncope	-	1 (1.0)	-
Tendon rupture	-	1 (1.0)	-
Tenosynovitis	-	1 (1.0)	-

Tonsillitis	-	-	1 (1.2)
Tooth extraction	-	-	1 (1.2)
Upper respiratory tract infection	-	-	1 (1.2)
Venous insufficiency	-	1 (1.0)	-
Vertigo	-	1 (1.0)	-
Viral infection	-	1 (1.0)	-
Vitamin b12 deficiency	-	1 (1.0)	-
Vocal cord disorder	-	1 (1.0)	-

- : Adverse event absent or not meeting the selected rule: more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed.
Grade 3= event that prevented normal, everyday activities
Related= event assessed by the investigator as causally related to the study vaccination

Primary Efficacy Results: Number and percentage of subjects reporting AEs of specific interest including autoimmune diseases reported within the Day 180 (Days 0-179) post-vaccination period (Total Vaccinated cohort)

Most frequent AEs (occurring within Day 0-179 following vaccination)	**Flu NG Group N = 180**	**Flu Eld Group N = 104**	**Flu Yng Group N = 86**
Subjects with any AE(s), n (%)	2 (1.1)	0 (0.0)	0 (0.0)
Subject with at least one grade 3 AE(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Subjects with at least one related AE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Autoimmune thyroiditis	1 (0.6)	-	-
Polymyalgia rheumatica	1 (0.6)	-	-

- : AE absent
Grade 3= event that prevented normal, everyday activities
Related= event assessed by the investigator as causally related to the study vaccination

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

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against A/Brisbane, A/Uruguay and B/Brisbane at Days 0 and 21 (ATP cohort for humoral immunogenicity Day 21)

				≥ 1:10				**GMT**		
						95% CI			**95% CI**	
Strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
A/Brisbane	Flu NG	PRE	154	139	90.3	84.4	94.4	27.8	24.0	32.3
		PI(D21)	154	150	97.4	93.5	99.3	57.3	49.8	66.0
	Flu Eld	PRE	86	79	91.9	83.9	96.7	25.7	21.3	30.9
		PI(D21)	86	86	100	95.8	100	49.9	41.8	59.7
	Flu Yng	PRE	78	73	93.6	85.7	97.9	66.1	50.5	86.5
		PI(D21)	78	78	100	95.4	100	112.1	92.1	136.4
A/Uruguay	Flu NG	PRE	154	143	92.9	87.6	96.4	46.8	38.9	56.4
		PI(D21)	154	154	100	97.6	100	153.7	132.8	177.8
	Flu Eld	PRE	86	78	90.7	82.5	95.9	35.3	27.0	46.1
		PI(D21)	86	85	98.8	93.7	100	107.8	85.8	135.3
	Flu Yng	PRE	78	71	91.0	82.4	96.3	48.8	37.3	63.9
		PI(D21)	78	78	100	95.4	100	114.1	92.8	140.4
B/Brisbane	Flu NG	PRE	154	151	98.1	94.4	99.6	80.6	67.8	95.7
		PI(D21)	154	154	100	97.6	100	171.6	148.2	198.6
	Flu Eld	PRE	86	86	100	95.8	100	89.5	71.2	112.6
		PI(D21)	86	86	100	95.8	100	163.9	137.2	195.9
	Flu Yng	PRE	78	75	96.2	89.2	99.2	81.4	64.2	103.3
		PI(D21)	78	78	100	95.4	100	157.2	131.6	187.7

GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n(%) = number(percentage) of subjects with titre 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)

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against A/Brisbane, A/Uruguay and B/Brisbane at Day 180 (ATP cohort for humoral immunogenicity Day 180)

			≥ 1:10				GMT		
					95% CI			95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
A/Brisbane	Flu NG	134	127	94.8	89.5	97.9	33.2	28.6	38.5
	Flu Eld	75	70	93.3	85.1	97.8	28.7	23.5	34.9
	Flu Yng	72	71	98.6	92.5	100	73.0	56.2	94.8
A/Uruguay	Flu NG	134	131	97.8	93.6	99.5	66.9	56.2	79.6
	Flu Eld	75	72	96.0	88.8	99.2	52.0	40.1	67.5
	Flu Yng	72	68	94.4	86.4	98.5	64.4	49.5	83.8
B/Brisbane	Flu NG	134	132	98.5	94.7	99.8	97.9	82.2	116.6
	Flu Eld	75	75	100	95.2	100	115.3	91.9	144.6
	Flu Yng	72	70	97.2	90.3	99.7	99.9	79.6	125.2

GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n(%) = number (percentage) of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

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

			SCR			
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/Brisbane	Flu NG	154	29	18.8	13.0	25.9
	Flu Eld	86	16	18.6	11.0	28.4
	Flu Yng	78	9	11.5	5.4	20.8
A/Uruguay	Flu NG	154	73	47.4	39.3	55.6
	Flu Eld	86	34	39.5	29.2	50.7
	Flu Yng	78	21	26.9	17.5	38.2
B/Brisbane	Flu NG	154	39	25.3	18.7	33.0
	Flu Eld	86	13	15.1	8.3	24.5
	Flu Yng	78	15	19.2	11.2	29.7

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): SCR for HI antibodies against A/Brisbane, A/Uruguay and B/Brisbane at Day 180 (ATP cohort for humoral immunogenicity Day 180)

			SCR			
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/Brisbane	Flu NG	134	4	3.0	0.8	7.5
	Flu Eld	75	2	2.7	0.3	9.3
	Flu Yng	72	1	1.4	0.0	7.5
A/Uruguay	Flu NG	134	12	9.0	4.7	15.1
	Flu Eld	75	7	9.3	3.8	18.3
	Flu Yng	72	2	2.8	0.3	9.7
B/Brisbane	Flu NG	134	2	1.5	0.2	5.3
	Flu Eld	75	4	5.3	1.5	13.1
	Flu Yng	72	4	5.6	1.5	13.6

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): SCF for HI antibodies against A/Brisbane, A/Uruguay and B/Brisbane at Day 21 (ATP cohort for humoral immunogenicity Day 21)

			SCF		
				95% CI	
Strain	**Group**	**N**	**Value**	**LL**	**UL**
A/Brisbane	Flu NG	154	2.1	1.9	2.3
	Flu Eld	86	1.9	1.6	2.3
	Flu Yng	78	1.7	1.5	2.0
A/Uruguay	Flu NG	154	3.3	2.9	3.7
	Flu Eld	86	3.1	2.5	3.8
	Flu Yng	78	2.3	1.9	2.9
B/Brisbane	Flu NG	154	2.1	1.9	2.4
	Flu Eld	86	1.8	1.6	2.1
	Flu Yng	78	1.9	1.7	2.2

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

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

			SCF		
				95% CI	
Strain	**Group**	**N**	**Value**	**LL**	**UL**
A/Brisbane	Flu NG	134	1.2	1.1	1.3
	Flu Eld	75	1.1	1.0	1.2
	Flu Yng	72	1.2	1.1	1.4
A/Uruguay	Flu NG	134	1.4	1.3	1.6
	Flu Eld	75	1.5	1.3	1.7
	Flu Yng	72	1.3	1.2	1.5
B/Brisbane	Flu NG	134	1.2	1.1	1.4
	Flu Eld	75	1.2	1.1	1.4
	Flu Yng	72	1.2	1.1	1.4

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

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

				SPR			
						95% CI	
Strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
A/Brisbane	Flu NG	PRE	154	76	49.4	41.2	57.5
		PI(D21)	154	124	80.5	73.4	86.5
	Flu Eld	PRE	86	34	39.5	29.2	50.7
		PI(D21)	86	64	74.4	63.9	83.2
	Flu Yng	PRE	78	62	79.5	68.8	87.8
		PI(D21)	78	72	92.3	84.0	97.1
A/Uruguay	Flu NG	PRE	154	103	66.9	58.9	74.2
		PI(D21)	154	151	98.1	94.4	99.6
	Flu Eld	PRE	86	49	57.0	45.8	67.6
		PI(D21)	86	76	88.4	79.7	94.3
	Flu Yng	PRE	78	52	66.7	55.1	76.9
		PI(D21)	78	73	93.6	85.7	97.9
B/Brisbane	Flu NG	PRE	154	131	85.1	78.4	90.3
		PI(D21)	154	151	98.1	94.4	99.6
	Flu Eld	PRE	86	75	87.2	78.3	93.4
		PI(D21)	86	86	100	95.8	100

	Flu Yng	PRE	78	67	85.9	76.2	92.7
		PI(D21)	78	76	97.4	91.0	99.7

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): SPR for HI antibodies against A/Brisbane, A/Uruguay and B/Brisbane at Day 180 (ATP cohort for humoral immunogenicity Day 180)

				SPR		
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/Brisbane	Flu NG	134	77	57.5	48.6	66.0
	Flu Eld	75	35	46.7	35.1	58.6
	Flu Yng	72	56	77.8	66.4	86.7
A/Uruguay	Flu NG	134	111	82.8	75.4	88.8
	Flu Eld	75	52	69.3	57.6	79.5
	Flu Yng	72	56	77.8	66.4	86.7
B/Brisbane	Flu NG	134	119	88.8	82.2	93.6
	Flu Eld	75	69	92.0	83.4	97.0
	Flu Yng	72	67	93.1	84.5	97.7

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 influenza-specific cytokine-positive CD4 T-cells (per million CD4 T-cells) for each vaccine strain at Days 0 and 21 (ATP cohort for CMI Day 21)

Immune marker	**Stimulating antigen**	**Group**	**Timing**	**N**	**GM**	**SD**	**Median**
CD4-ALL DOUBLES	A/Brisbane	Flu NG	PRE	34	505.28	772.80	652.0
			PI(D21)	39	706.88	505.25	831.0
		Flu Eld	PRE	24	389.00	856.40	538.0
			PI(D21)	25	264.58	781.85	530.0
		Flu Yng	PRE	14	770.48	697.03	1340.5
			PI(D21)	14	1314.16	747.54	1484.5
	A/Uruguay	Flu NG	PRE	34	305.14	457.10	487.5
			PI(D21)	39	312.78	391.17	582.0
		Flu Eld	PRE	24	220.40	539.54	378.0
			PI(D21)	24	181.29	435.61	329.5
		Flu Yng	PRE	14	423.12	553.25	579.5
			PI(D21)	14	646.39	529.95	657.0
	B/Brisbane	Flu NG	PRE	34	579.12	929.73	597.0
			PI(D21)	38	833.66	873.42	851.5
		Flu Eld	PRE	24	395.07	401.74	580.0
			PI(D21)	24	381.76	708.30	492.0
		Flu Yng	PRE	14	1211.75	589.02	1431.0
			PI(D21)	14	1406.33	663.12	1233.5
CD4-CD40L	A/Brisbane	Flu NG	PRE	34	496.13	684.47	560.5
			PI(D21)	39	594.61	444.86	709.0
		Flu Eld	PRE	24	404.66	688.08	460.5
			PI(D21)	25	222.79	709.97	497.0
		Flu Yng	PRE	14	641.91	595.30	1197.5
			PI(D21)	14	1156.09	637.81	1359.0
	A/Uruguay	Flu NG	PRE	34	288.19	394.53	442.5
			PI(D21)	39	236.03	331.31	457.0
		Flu Eld	PRE	24	201.28	331.40	310.0
			PI(D21)	24	156.82	359.54	307.0
		Flu Yng	PRE	14	349.47	435.78	522.0

			PI(D21)	14	508.67	453.14	571.0
	B/Brisbane	Flu NG	PRE	34	532.51	808.78	546.5
			PI(D21)	38	632.53	819.98	713.5
		Flu Eld	PRE	24	351.89	341.86	536.5
			PI(D21)	24	337.96	600.56	455.5
		Flu Yng	PRE	14	1036.33	578.74	1234.0
			PI(D21)	14	1173.43	534.19	1025.0
CD4-IFNy	A/Brisbane	Flu NG	PRE	34	381.48	519.00	445.5
			PI(D21)	39	389.72	397.50	501.0
		Flu Eld	PRE	24	155.01	472.80	329.0
			PI(D21)	25	148.60	575.79	301.0
		Flu Yng	PRE	14	507.94	575.13	1073.5
			PI(D21)	14	912.64	564.57	1204.5
	A/Uruguay	Flu NG	PRE	34	165.87	395.96	336.0
			PI(D21)	39	188.82	293.17	316.0
		Flu Eld	PRE	24	91.55	351.37	253.0
			PI(D21)	24	85.83	260.52	168.5
		Flu Yng	PRE	14	245.90	490.89	413.0
			PI(D21)	14	449.17	407.25	493.5
	B/Brisbane	Flu NG	PRE	34	252.91	815.43	272.5
			PI(D21)	38	407.19	746.60	432.0
		Flu Eld	PRE	24	144.14	286.54	243.5
			PI(D21)	24	185.93	447.80	320.0
		Flu Yng	PRE	14	850.80	454.84	1060.0
			PI(D21)	14	1059.08	513.03	1019.5
CD4-IL2	A/Brisbane	Flu NG	PRE	34	501.25	632.36	647.0
			PI(D21)	39	603.99	401.78	736.0
		Flu Eld	PRE	24	336.49	703.76	521.5
			PI(D21)	25	231.87	687.91	447.0
		Flu Yng	PRE	14	641.34	620.52	1034.5
			PI(D21)	14	1119.71	663.02	1207.5
	A/Uruguay	Flu NG	PRE	34	246.44	364.77	403.5
			PI(D21)	39	223.89	301.93	435.0
		Flu Eld	PRE	24	159.48	449.91	266.5
			PI(D21)	24	151.95	362.38	214.0
		Flu Yng	PRE	14	307.21	428.94	434.0
			PI(D21)	14	507.44	466.62	408.0
	B/Brisbane	Flu NG	PRE	34	511.34	843.52	529.0
			PI(D21)	38	686.04	789.19	731.0
		Flu Eld	PRE	24	285.96	363.09	446.0
			PI(D21)	24	318.55	631.64	387.0
		Flu Yng	PRE	14	980.90	525.94	1127.5
			PI(D21)	14	1119.56	621.33	1016.5
CD4-TFN-α	A/Brisbane	Flu NG	PRE	34	354.67	688.18	521.5
			PI(D21)	39	579.83	447.33	623.0
		Flu Eld	PRE	24	277.02	793.58	436.5
			PI(D21)	25	279.39	719.36	408.0
		Flu Yng	PRE	14	689.52	585.40	1232.0
			PI(D21)	14	1083.09	642.04	1107.0
	A/Uruguay	Flu NG	PRE	34	268.96	407.82	417.5
			PI(D21)	39	350.86	329.74	496.0
		Flu Eld	PRE	24	176.04	464.08	357.5
			PI(D21)	24	208.35	392.20	276.5
		Flu Yng	PRE	14	250.20	480.89	491.5
			PI(D21)	14	575.88	473.30	548.5
	B/Brisbane	Flu NG	PRE	34	390.08	843.99	498.5

			PI(D21)	38	632.14	767.97	610.0
		Flu Eld	PRE	24	324.83	342.66	470.0
			PI(D21)	24	367.95	586.79	416.5
		Flu Yng	PRE	14	976.64	580.31	1163.0
			PI(D21)	14	1126.10	629.66	982.5

N = number of subjects with available results
GM= Geometric Mean
SD = Standard Deviation
PRE = Pre-vaccination dose 1 (Day 0)
PI(D21)= Post-vaccination dose 1 (Day 21)
CD4-ALL DOUBLES = CD4 T-cells expressing two cytokines
CD4-CD40L = CD4 T-cells expressing CD40L and another cytokine
CD4-IFNγ = CD4 T-cells expressing IFNγ and another cytokine
CD4-IL2 = CD4 T-cells expressing IL2 and another cytokine
CD4-TFN-α = CD4 T-cells expressing TFN-α and another cytokine

Secondary Outcome Variable(s): Descriptive Statistics on the frequency of influenza-specific cytokine-positive CD4 T-cells (per million CD4 T-cells) for each vaccine strain at Day 180 (ATP cohort for CMI Day 180)

Immune marker	Stimulating antigen	Group	N	GM	SD	Median
CD4-ALL DOUBLES	A/Brisbane	Flu NG	25	410.98	507.43	593.0
		Flu Eld	20	395.98	526.39	460.0
		Flu Yng	12	945.71	669.70	1037.0
	A/Uruguay	Flu NG	25	160.28	367.49	377.0
		Flu Eld	20	170.26	295.26	362.0
		Flu Yng	12	532.37	578.23	506.5
	B/Brisbane	Flu NG	25	411.94	885.94	598.0
		Flu Eld	20	514.93	530.05	503.5
		Flu Yng	12	1156.78	246.61	1096.5
CD4-CD40L	A/Brisbane	Flu NG	25	330.87	384.52	475.0
		Flu Eld	20	383.44	485.65	436.0
		Flu Yng	12	838.17	592.74	955.5
	A/Uruguay	Flu NG	25	117.10	334.47	305.0
		Flu Eld	20	188.07	251.35	332.5
		Flu Yng	12	444.32	493.66	465.0
	B/Brisbane	Flu NG	25	367.67	842.20	501.0
		Flu Eld	20	454.81	488.31	516.5
		Flu Yng	12	1024.05	242.01	989.5
CD4-IFNy	A/Brisbane	Flu NG	25	311.48	457.12	427.0
		Flu Eld	20	195.30	449.01	287.5
		Flu Yng	12	718.48	530.31	856.5
	A/Uruguay	Flu NG	25	90.26	326.33	148.0
		Flu Eld	20	93.12	214.88	159.5
		Flu Yng	12	344.50	475.04	367.0
	B/Brisbane	Flu NG	25	274.24	775.13	311.0
		Flu Eld	20	191.20	480.62	276.5
		Flu Yng	12	846.21	187.26	876.5
CD4-IL2	A/Brisbane	Flu NG	25	257.81	343.17	491.0
		Flu Eld	20	337.02	491.89	426.0
		Flu Yng	12	777.60	606.71	853.5
	A/Uruguay	Flu NG	25	136.94	259.79	307.0
		Flu Eld	20	156.64	247.58	265.0
		Flu Yng	12	364.47	472.06	397.0
	B/Brisbane	Flu NG	25	378.41	829.36	518.0
		Flu Eld	20	357.47	487.00	466.0
		Flu Yng	12	940.07	268.02	949.0
CD4-TFN-α	A/Brisbane	Flu NG	25	352.89	489.42	483.0
		Flu Eld	20	360.15	499.75	374.5

		Flu Yng	12	833.70	587.76	853.0
	A/Uruguay	Flu NG	25	162.57	332.69	285.0
		Flu Eld	20	211.11	261.05	314.5
		Flu Yng	12	487.90	502.24	455.0
	B/Brisbane	Flu NG	25	246.41	845.16	427.0
		Flu Eld	20	414.80	454.02	401.5
		Flu Yng	12	953.49	224.88	945.0

N = number of subjects with available results
GM= Geometric Mean
SD = Standard Deviation
CD4-ALL DOUBLES = CD4 T-cells expressing two cytokines
CD4-CD40L = CD4 T-cells expressing CD40L and another cytokine
CD4-IFNγ = CD4 T-cells expressing IFNγ and another cytokine
CD4-IL2 = CD4 T-cells expressing IL2 and another cytokine
CD4-TFN-α = CD4 T-cells expressing TFN-α and another cytokine

Safety Results: Number and percentage of subjects reporting the occurrence of AEs within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort)

Most frequent AEs - On-Therapy (occurring within Day 0-20 following vaccination)	**Flu NG Group N = 180**	**Flu Eld Group N = 104**	**Flu Yng Group N = 86**
Subjects with any AE(s), n (%)	24 (13.3)	17 (16.3)	16 (18.6)
Subject with at least one grade 3 AE(s), n (%)	2 (1.1)	0 (0.0)	3 (3.5)
Subjects with at least one related AE, n (%)	5 (2.8)	1 (1.0)	0 (0.0)
Back pain	4 (2.2)	3 (2.9)	-
Nasopharyngitis	1 (0.6)	3 (2.9)	3 (3.5)
Cough	6 (3.3)	-	-
Rhinitis	3 (1.7)	1 (1.0)	2 (2.3)
Arthralgia	-	-	2 (2.3)
Bronchitis	-	1 (1.0)	1 (1.2)
Headache	-	-	2 (2.3)
Hypertension	1 (0.6)	1 (1.0)	-
Musculoskeletal discomfort	1 (0.6)	1 (1.0)	-
Osteoarthritis	1 (0.6)	1 (1.0)	-
Pain in extremity	2 (1.1)	-	-
Pyrexia	-	-	2 (2.3)
Angiopathy	1 (0.6)	-	-
Atrial fibrillation	1 (0.6)	-	-
Blood pressure increased	-	1 (1.0)	-
Bone pain	1 (0.6)	-	-
Cervicobrachial syndrome	-	1 (1.0)	-
Deep vein thrombosis	1 (0.6)	-	-
Diarrhoea	-	-	1 (1.2)
Discomfort	1 (0.6)	-	-
Dysphonia	1 (0.6)	-	-
Dyspnoea exertional	-	1 (1.0)	-
Gastritis	-	-	1 (1.2)
Gastroenteritis	1 (0.6)	-	-
Gingivitis	-	-	1 (1.2)
Hyperglycaemia	-	-	1 (1.2)
Injection site reaction	1 (0.6)	-	-
Insomnia	1 (0.6)	-	-
Muscle spasms	-	1 (1.0)	-
Muscle tightness	-	-	1 (1.2)
Oral pain	-	-	1 (1.2)
Oropharyngeal pain	-	1 (1.0)	-
Paraesthesia	1 (0.6)	-	-
Pulmonary embolism	1 (0.6)	-	-

Rash	1 (0.6)	-	-
Respiratory tract infection	1 (0.6)	-	-
Restlessness	-	-	1 (1.2)
Rhinorrhoea	-	1 (1.0)	-
Sciatica	1 (0.6)	-	-
Sensation of blood flow	1 (0.6)	-	-
Sinusitis	1 (0.6)	-	-
Sneezing	-	1 (1.0)	-
Spinal column stenosis	1 (0.6)	-	-
Tenosynovitis	-	1 (1.0)	-
Tonsillitis	-	-	1 (1.2)
Toothache	1 (0.6)	-	-
Vocal cord disorder	-	1 (1.0)	-
- : AE 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 during the whole study 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 = 180**	**Flu Eld Group N = 104**	**Flu Yng Group N = 86**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	19 (10.6) [0]	6 (5.8) [0]	3 (3.5) [0]
Atrial fibrillation	3 (1.7) [0]	1 (1.0) [0]	0 (0.0) [0]
Cardiovascular disorder	1 (0.6) [0]	1 (1.0) [0]	0 (0.0) [0]
Alcohol poisoning	0 (0.0) [0]	0 (0.0) [0]	1 (1.2) [0]
Anaemia	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Aortic aneurysm	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Arachnoid cyst	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Arthralgia	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Autoimmune thyroiditis	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Bronchial carcinoma	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Calculus ureteric	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Cardiac failure	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Cholecystitis infective	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Cholelithiasis	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Circulatory collapse	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Confusional state	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Cystitis	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Deep vein thrombosis	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Dehydration	0 (0.0) [0]	0 (0.0) [0]	1 (1.2) [0]
Diarrhoea	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Duodenitis	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Fibula fracture	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Gastric cancer	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Gastritis	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Hyperglycaemia	0 (0.0) [0]	0 (0.0) [0]	1 (1.2) [0]
Hypoglycaemia	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Infective exacerbation of chronic obstructive airways disease	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Lung neoplasm malignant	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Meningioma	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Myocarditis	0 (0.0) [0]	0 (0.0) [0]	1 (1.2) [0]
Patella fracture	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Peripheral arterial occlusive disease	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Pleural mesothelioma	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Pulmonary embolism	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Skin ulcer	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]

Syncope	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Thrombophlebitis	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Upper limb fracture	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Vocal cord disorder	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Fatal SAEs	**Flu NG Group N = 180**	**Flu Eld Group N = 104**	**Flu Yng Group N = 86**
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	2 (1.1) [0]	1 (1.0) [0]	0 (0.0) [0]
Atrial fibrillation	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Bronchial carcinoma	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Cardiac failure	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Cardiovascular disorder	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Lung neoplasm malignant	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Peripheral arterial occlusive disease	0 (0.0) [0]	1 (1.0) [0]	0 (0.0) [0]
Safety Results: Number (%) of subjects with serious adverse events after Day 180* (Total Vaccinated cohort)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	**Flu NG Group N = 180**	**Flu Eld Group N = 104**	**Flu Yng Group N = 86**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Pleural effusion	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**Flu NG Group N = 180**	**Flu Eld Group N = 104**	**Flu Yng Group N = 86**
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Pleural effusion	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
* One fatal SAE was reported after the study completion.			

Conclusion:

Pain was the most frequently reported solicited local symptom during the 7-day post vaccination period with 78 subjects (43.3%) in the Flu NG Group, 12 subjects (11.7%) in the Flu Eld Group and 49 subjects (57.6%) in the Flu Yng Group. The average number of days with pain was 2.1, 2.0 and 2.0 for the Flu NG, Flu Eld and Flu Yng groups, respectively. During the same period, the most frequent solicited general symptom was fatigue which was reported by 53 subjects (29.4%), 12 subjects (11.7%) and 21 subjects (24.7%) in the Flu NG, Flu Eld and Flu Yng groups, respectively. The average number of days with fatigue was 2.3, 3.3 and 2.5 days, respectively.

24 (13.3%), 17 (16.3%) and 16 (18.6%) subjects in the Flu NG, Flu Eld and Flu Yng groups reported at least one unsolicited AE within the 21-day post-vaccination period. 5 subjects [2 (1.1%) in the Flu NG Group and 3 (3.5%) in the Flu Yng Group] reported at least one grade 3 unsolicited AE. 6 subjects [5 (2.8%) in the Flu NG Group and 1 (1.0%) in the Flu Eld Group] reported at least one related unsolicited AE.

Within the 180-day post-vaccination period, the number of subjects with at least one unsolicited AE that resulted in a medically-attended visit was 81 (45.0%), 34 (32.7%) and 21 (24.4%) in the Flu NG, Flu Eld and Flu Yng groups respectively. 21 (11.7%), 5 (4.8%) and 6 (7.0%) subjects reported at least one grade 3 AE with medically-attended visit in the Flu NG, Flu Eld and Flu Yng groups. 2 subjects (one in the Flu NG Group and one in the Flu Eld Group) reported at least one related AE with medically-attended visit.

Two AEs of specific interest (autoimmune thyroiditis and polymyaglia rheumatic) were reported by subjects of the Flu NG Group. They were assessed by the investigators as not related to the vaccination.

During the entire study period, SAEs were reported by 19 (10.6%) subjects in the Flu NG Group, 6 (5.8%) subjects in the Flu Eld Group and 3 (3.5%) subjects in the Flu Yng Group. None of the SAEs were assessed by the investigators as related to the vaccination. Fatal SAEs were reported for 2 subjects in the Flu NG Group and for one subject in the Flu Eld Group. One fatal SAE, assessed by the investigator as unrelated to the study vaccine was reported in the Flu NG Group after the end of the study.

For safety results on the first and second vaccinations please refer to CTRSs 110847 and 111737.

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