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.: 104438 (Flu-US-004)

Title: A randomized, double-blind, placebo-controlled, post-marketing, phase III study to evaluate the efficacy of GSK Biologicals' influenza vaccine (Fluarix™) administered intramuscularly in adults.
Fluarix™: GSK Biologicals' influenza vaccine (Flu)

Rationale: The aim of this study was to evaluate the efficacy of a single intramuscular dose (45 µg) of Flu vaccine in preventing culture-confirmed influenza.

Phase: III

Study Period: 01 September 2005 to 28 May 2006.

Study Design: Randomized (2:1), double-blind, placebo-controlled study with 2 parallel groups.

Centers: 2 study centers in the Czech Republic

Indication: Immunization of adults against influenza disease.

Treatment: The study groups were as follows:

- Placebo Group: subjects received a saline solution.
- Flu Group: subjects received a Flu vaccine

Vaccines were administered intramuscularly in the deltoid region of the non-dominant arm.

Objectives: To demonstrate the efficacy of Flu vaccine compared with placebo (normal saline solution) in the prevention of culture-confirmed influenza A and /or B in adults.

Primary Outcome/Efficacy Variable:
Incidence of culture-confirmed influenza A and/or B.

Secondary Outcome/Efficacy Variable(s):

Efficacy

- Incidence of influenza like illness (ILI)
- Number of days of fever, days of school/work absenteeism, medically attended visits related to influenza illness and hospitalization related to influenza illness.
- Incidence of pneumonia related to laboratory confirmed influenza occurring within 6 weeks following the onset of ILI.
- Incidence of pneumonia occurring during the active surveillance for ILI.
- Incidence of polymerase chain reaction (PCR) confirmed influenza A and/or B

Immunogenicity (in a subset of subjects)

At each time point:

- For each vaccine strain, Geometric Mean Titer (GMT) of serum haemagglutination inhibition (HI) antibodies.
- For each vaccine strain, seroprotection defined as the proportion of subjects with a serum HI titer $\geq$ 1:40.

At Day 21:

- For each vaccine strain, seroconversion rate, defined as the proportion of subjects with either a pre-vaccination HI titer < 1:10 and a post-vaccination titer $\geq$ 1:40 or a pre-vaccination titer $\geq$ 1:10 and a minimum four-fold increase in post-vaccination titer.

Safety

- Occurrence of serious adverse events (SAEs) in all subjects during the entire study.

In a subset of subjects:

- Percentage, intensity and relationship to vaccination of solicited local and general symptoms during a 4-day (Day 0-3) follow-up period after vaccination.
- Percentage, intensity and relationship to vaccination of unsolicited adverse events (AEs) during a 21-day (Day 0-20) follow-up period after vaccination.

Statistical Methods:

The analyses were performed on the Total Vaccinated Cohort, the Total Vaccinated Cohort for Safety, and the According-To-Protocol (ATP) cohort for Immunogenicity.

- The Total Vaccinated Cohort included all vaccinated subjects.
- The Total Vaccinated Cohort for Safety included a randomly allocated subset of the Total Vaccinated Cohort (i.e. all

subjects with at least one vaccine administration documented and for whom solicited/unsolicited symptoms were collected).

- The ATP cohort for immunogenicity included a randomly allocated subset among all evaluable subjects (i.e. those meeting all eligibility criteria, complying with procedures defined in the protocol with no elimination criteria during the study).

Analysis of efficacy

The analysis was performed on the Total Vaccinated Cohort.

The attack rate* and the vaccine efficacy* (VE) against culture-confirmed Influenza A and/or B was calculated using the formula of Greenwood-Yule, with their exact 95% confidence interval.

*Vaccine efficacy (VE) was to calculated as follows:

VE = 1 – RR = 1 - (ARV/ARU)

Where:

- RR was the relative risk of developing the disease in the vaccinated group compared to the placebo group.
- ARU was the disease attack rate in the unvaccinated group (estimated from the placebo group) = number of subjects reporting at least one episode of the disease of interest within the observation period / total number of subjects at risk in the placebo group.
- ARV was the disease attack rate in the vaccinated group = number of subjects reporting at least one episode of the disease of interest within the observation period / total number of subjects at risk in the Flu group.

Analysis of immunogenicity

The analysis was performed on the ATP cohort for immunogenicity.

The GMT at Day 0 and Day 21, together with their 95%CI was tabulated. The incidence of seroprotected subjects was tabulated together with the 95% CI. The seroconversion rate at Day 21 was calculated together with 95% CI.

Analysis of safety

The analysis was performed on the Total Vaccinated Cohort for Safety.

The incidence, severity and causality of each local and general solicited symptom reported during a 4-day (Day 0-3) follow-up after vaccination were tabulated together with their 95% CI. The number of subjects reporting AEs within 21 days after vaccination was reported according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms. The incidence of subjects with serious adverse events (SAEs) was tabulated according to MedDRA preferred terms using the Total Vaccinated Cohort.

Study Population: A male or female between 18 and 64 years of age at the time of the vaccination. Written informed consent was obtained from the subject prior to study entry. If a female subject was of childbearing potential, she had been abstinent or had used adequate contraceptive precautions for 30 days prior to vaccination, had had a negative pregnancy test at study entry and had agreed to continue such precautions for 2 months after vaccination.

Number of subjects	**Placebo Group**	**Flu Group**
Planned, N	2071	4142
Randomized, N (Total Vaccinated Cohort)	2066	4137
Total Number Subjects Withdrawn, n (%)	64 (3.1)	137 (3.3)
Withdrawn due to Adverse Events, n (%)	1 (0.0)	3 (0.1)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	63 (3.0)	134 (3.2)
Demographics	**Placebo Group**	**Flu Group**
N (Total Vaccinated Cohort)	2066	4137
Females:Males	1119:947	2288:1849
Mean Age, years (SD)	35.3 (13.33)	35.3 (13.24)
White/Caucasian, n (%)	2062 (99.8)	4127 (99.8)

Primary Efficacy Results:

Summary of attack rates and vaccine efficacy against culture-confirmed Influenza A and/or B by treatment group during passive and active surveillance for ILI in the (Total Vaccinated Cohort)

Group	**N**	**n+**	**n**	**n/N**			**VE**			**P-value**
				%	**95% CI**		**%**	**95% CI**		
					LL	**UL**		**LL**	**UL**	
Placebo	2066	18	18	0.9	0.5	1.4	-	-	-	-
Flu	4137	28	28	0.7	0.5	1.0	22.3	-49.1	58.5	0.433*

N=Number of subjects included in each treatment group in the total vaccinated cohort for efficacy/safety (excluding the 10 subjects who were vaccinated several times).

n+ =Number of culture-confirmed Influenza A and/or B events during passive and active surveillance for ILI.

n=Number of subjects reporting at least one culture-confirmed Influenza A and/or B events during passive and active

surveillance for ILI.
n/N (%)=Percentage of subjects reporting at least one culture-confirmed Influenza A and/or B events during passive and active surveillance for ILI.
VE (%) = Vaccine Efficacy (Conditional Method).
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Two-sided Fisher Exact test. The between-group difference in attack rates was not statistically significant.

Secondary Outcome variable (s):
No secondary efficacy results were tabulated as efficacy for the primary outcome variable was not demonstrated.

Secondary Outcome variable (s):
GMTs for HI antibody titers (ATP cohort for immunogenicity)

Vaccine strain	Group	Timing	GMT			
			N	value	95% CI	
					LL	UL
H1N1	Placebo	PRE	315	11.9	10.4	13.6
		PI(D21)	315	11.6	10.2	13.3
	Flu	PRE	632	13.6	12.2	15.1
		PI(D21)	632	730.5	648.1	823.3
H3N2	Placebo	PRE	315	13.8	12.1	15.6
		PI(D21)	315	13.5	11.9	15.3
	Flu	PRE	632	12.5	11.5	13.6
		PI(D21)	632	131.7	119.9	144.6
B	Placebo	PRE	315	18.0	15.8	20.5
		PI(D21)	315	17.9	15.7	20.3
	Flu	PRE	632	15.6	14.2	17.1
		PI(D21)	632	191.1	175.7	207.9

N = number of subjects with available results
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination dose 1
PI(D21) = Post-vaccination dose 1 (Day 21)

Secondary Outcome variable (s):
Seroconversion rates at Day 21 after vaccination (ATP cohort for immunogenicity)

Vaccine strain	Group	N	Seroconversion rate			
			n	%	95% CI	
					LL	UL
H1N1	Placebo	315	0	0.0	0.0	1.2
	Flu	632	564	89.2	86.6	91.5
H3N2	Placebo	315	1	0.3	0.0	1.8
	Flu	632	488	77.2	73.7	80.4
B	Placebo	315	0	0.0	0.0	1.2
	Flu	632	524	82.9	79.7	85.8

N = number of subjects with available results
n (%) = number (percentage) of subjects who seroconverted
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome variable (s):
Seroprotection rates at Days 0 and 21 (ATP cohort for immunogenicity)

Vaccine strain	Group	Timing	N	≥ 1:40			
				n	%	95% CI	
						LL	UL
H1N1	Placebo	PRE	315	70	22.2	17.75	27.22
		PI(D21)	315	69	21.9	17.46	26.88
	Flu	PRE	632	142	22.5	19.27	25.93
		PI(D21)	632	618	97.8	96.31	98.78
H3N2	Placebo	PRE	315	69	21.9	17.46	26.88
		PI(D21)	315	71	22.5	18.04	27.56
	Flu	PRE	632	131	20.7	17.63	24.10
		PI(D21)	632	557	88.1	85.35	90.55

B	Placebo	PRE	315	99	31.4	26.34	36.87
		PI(D21)	315	95	30.2	25.14	35.56
	Flu	PRE	632	167	26.4	23.02	30.05
		PI(D21)	632	606	95.9	94.03	97.30

N = number of subjects with available results
n (%) = number (percentage) of subjects who seroconverted
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination dose 1
PI(D21) = Post-vaccination dose 1 (Day 21)

Secondary Outcome Variable (s):
Number of subjects reporting solicited local symptoms during the 4-day (Day 0-3) post-vaccination period (Total Vaccinated Cohort for Safety)

Symptom	**Intensity**	**Placebo Group**					**Flu Group**				
		N	**n**	**%**	**95% CI**		**N**	**n**	**%**	**95% CI**	
					LL	**UL**				**LL**	**UL**
Pain	Any	320	42	13.1	9.6	17.3	640	301	47.0	43.1	51.0
	Grade 3	320	0	0.0	0.0	1.1	640	0	0.0	0.0	0.6
Redness	Any	320	43	13.4	9.9	17.7	640	146	22.8	19.6	26.3
	> 50 mm	320	0	0.0	0.0	1.1	640	11	1.7	0.9	3.1
Swelling	Any	320	6	1.9	0.7	4.0	640	69	10.8	8.5	13.4
	> 50 mm	320	1	0.3	0.0	1.7	640	15	2.3	1.3	3.8

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Any = Incidence of a particular symptom regardless of intensity grade
Grade 3 pain: pain that prevented normal activities

Secondary Outcome Variable (s):
Number of subjects reporting solicited general symptoms during the 4-day (Day 0-3) post-vaccination period (Total Vaccinated Cohort for Safety)

Symptom	**Intensity/ relation-ship**	**Placebo Group**					**Flu Group**				
		N	**n**	**%**	**95% CI**		**N**	**n**	**%**	**95% CI**	
					LL	**UL**				**LL**	**UL**
Fatigue	Any	320	63	19.7	15.5	24.5	640	170	26.6	23.2	30.2
	Grade 3	320	0	0.0	0.0	1.1	640	6	0.9	0.3	2.0
	Related	320	51	15.9	12.1	20.4	640	150	23.4	20.2	26.9
Fever (Orally)	≥ 37.5°C	320	6	1.9	0.7	4.0	640	5	0.8	0.3	1.8
	> 39.0°C	320	0	0.0	0.0	1.1	640	0	0.0	0.0	0.6
	Related	320	4	1.3	0.3	3.2	640	3	0.5	0.1	1.4
Headache	Any	320	46	14.4	10.7	18.7	640	129	20.2	17.1	23.5
	Grade 3	320	1	0.3	0.0	1.7	640	5	0.8	0.3	1.8
	Related	320	32	10.0	6.9	13.8	640	101	15.8	13.0	18.8
Joint pain	Any	320	18	5.6	3.4	8.7	640	51	8.0	6.0	10.3
	Grade 3	320	0	0.0	0.0	1.1	640	2	0.3	0.0	1.1
	Related	320	14	4.4	2.4	7.2	640	36	5.6	4.0	7.7
Muscle aches	Any	320	25	7.8	5.1	11.3	640	79	12.3	9.9	15.1
	Grade 3	320	1	0.3	0.0	1.7	640	4	0.6	0.2	1.6
	Related	320	18	5.6	3.4	8.7	640	67	10.5	8.2	13.1
Shivering	Any	320	7	2.2	0.9	4.5	640	17	2.7	1.6	4.2
	Grade 3	320	0	0.0	0.0	1.1	640	2	0.3	0.0	1.1
	Related	320	5	1.6	0.5	3.6	640	13	2.0	1.1	3.4

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Any = Incidence of a particular symptom regardless of grade and relationship to vaccination

Related = Symptoms considered by the investigator to have a causal relationship to study vaccination Grade 3 = Symptom which prevented normal everyday activities		
Safety Results: Number (%) of subjects with unsolicited adverse events (Total Vaccinated Cohort for Safety)		
Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)	**Placebo Group N = 320**	**Flu Group N = 640**
Subjects with any AE(s), n (%)	32 (10.0)	71 (11.1)
Subjects with any related AE(s), n (%)	5 (1.6)	9 (1.4)
Subjects with any Severe AE(s), n (%)	2 (0.6)	7 (1.1)
Upper respiratory tract infection	13 (4.1)	23 (3.6)
Pharyngolaryngeal pain	5 (1.6)	7 (1.1)
Rhinitis	4 (1.3)	6 (0.9)
Cough	1 (0.3)	5 (0.8)
Injection site bruising	2 (0.6)	4 (0.6)
Influenza like illness	0 (0.0)	5 (0.8)
Back pain	0 (0.0)	4 (0.6)
Diarrhea	2 (0.6)	2 (0.3)
Vertigo	3 (0.9)	1 (0.2)
Neck pain	1 (0.3)	2 (0.3)
Pruritus	1 (0.3)	2 (0.3)
Angina pectoris	0 (0.0)	2 (0.3)
Dyspepsia	1 (0.3)	1 (0.2)
Headache	1 (0.3)	1 (0.2)
Herpes simplex	0 (0.0)	2 (0.3)
Malaise	1 (0.3)	1 (0.2)
Oophoritis	1 (0.3)	0 (0.0)
Surgery	1 (0.3)	0 (0.0)
Syncope vasovagal	1 (0.3)	0 (0.0)
Vomiting	1 (0.3)	0 (0.0)
Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) (Total Vaccinated Cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	**Placebo Group N = 2066**	**Flu Group N = 4137**
Subjects with any SAE(s), n (%) [n related]	47 (2.3) [0]	96 (2.3) [0]
Abortion spontaneous	3 (0.1) [0]	3 (0.1) [0]
Cholelithiasis	3 (0.1) [0]	2 (0.0) [0]
Joint injury	4 (0.2) [0]	1 (0.0) [0]
Appendicitis	0 (0.0) [0]	4 (0.1) [0]
Inguinal hernia	0 (0.0) [0]	4 (0.1) [0]
Cellulitis pharyngeal	0 (0.0) [0]	3 (0.1) [0]
Meniscus lesion	1 (0.0) [0]	2 (0.0) [0]
Myocardial infarction	2 (0.1) [0]	1 (0.0) [0]
Radius fracture	1 (0.0) [0]	2 (0.0) [0]
Abortion missed	1 (0.0) [0]	1 (0.0) [0]
Ankle fracture	1 (0.0) [0]	1 (0.0) [0]
Benign prostatic hyperplasia	0 (0.0) [0]	2 (0.0) [0]
Carpal tunnel syndrome	1 (0.0) [0]	1 (0.0) [0]
Cerebral hemorrhage	0 (0.0) [0]	2 (0.0) [0]
Cervicobrachial syndrome	1 (0.0) [0]	1 (0.0) [0]
Chronic tonsillitis	2 (0.1) [0]	0 (0.0) [0]
Contusion	0 (0.0) [0]	2 (0.0) [0]
Dyspareunia	0 (0.0) [0]	2 (0.0) [0]
Hemorrhoids	2 (0.1) [0]	0 (0.0) [0]
Hydrocele	0 (0.0) [0]	2 (0.0) [0]
Joint dislocation	2 (0.1) [0]	0 (0.0) [0]
Limb injury	1 (0.0) [0]	1 (0.0) [0]

Osteoarthritis	1 (0.0) [0]	1 (0.0) [0]
Pulmonary embolism	1 (0.0) [0]	1 (0.0) [0]
Rotator cuff syndrome	2 (0.1) [0]	0 (0.0) [0]
Suicide attempt	0 (0.0) [0]	2 (0.0) [0]
Umbilical hernia	0 (0.0) [0]	2 (0.0) [0]
Urosepsis	0 (0.0) [0]	2 (0.0) [0]
Vestibular disorder	0 (0.0) [0]	2 (0.0) [0]
Acute psychosis	0 (0.0) [0]	1 (0.0) [0]
Adenocarcinoma pancreas	0 (0.0) [0]	1 (0.0) [0]
Angina pectoris	1 (0.0) [0]	0 (0.0) [0]
Antepartum hemorrhage	0 (0.0) [0]	1 (0.0) [0]
Arteriosclerosis coronary artery	0 (0.0) [0]	1 (0.0) [0]
Arthralgia	1 (0.0) [0]	0 (0.0) [0]
Asthma	1 (0.0) [0]	0 (0.0) [0]
Atrial fibrillation	0 (0.0) [0]	1 (0.0) [0]
Bacterial pyelonephritis	0 (0.0) [0]	1 (0.0) [0]
Benign hydatidiform mole	1 (0.0) [0]	0 (0.0) [0]
Bladder cancer	0 (0.0) [0]	1 (0.0) [0]
Brain contusion	1 (0.0) [0]	0 (0.0) [0]
Bursitis	1 (0.0) [0]	0 (0.0) [0]
Calculus ureteric	0 (0.0) [0]	1 (0.0) [0]
Cataract	0 (0.0) [0]	1 (0.0) [0]
Cerebellar syndrome	0 (0.0) [0]	1 (0.0) [0]
Cervical dysplasia	0 (0.0) [0]	1 (0.0) [0]
Cervix carcinoma	0 (0.0) [0]	1 (0.0) [0]
Colonic polyp	1 (0.0) [0]	0 (0.0) [0]
Concussion	0 (0.0) [0]	1 (0.0) [0]
Crohn’s disease	0 (0.0) [0]	1 (0.0) [0]
Delirium tremens	0 (0.0) [0]	1 (0.0) [0]
Diabetes mellitus	1 (0.0) [0]	0 (0.0) [0]
Diaphragmatic hernia	0 (0.0) [0]	1 (0.0) [0]
Drug toxicity	0 (0.0) [0]	1 (0.0) [0]
Ectopic pregnancy	0 (0.0) [0]	1 (0.0) [0]
Encephalitis viral	0 (0.0) [0]	1 (0.0) [0]
Endometrial cancer	1 (0.0) [0]	0 (0.0) [0]
Enteritis	0 (0.0) [0]	1 (0.0) [0]
Fibula fracture	1 (0.0) [0]	0 (0.0) [0]
Foreign body trauma	0 (0.0) [0]	1 (0.0) [0]
Fractured coccyx	1 (0.0) [0]	0 (0.0) [0]
Gastroenteritis rotavirus	1 (0.0) [0]	0 (0.0) [0]
Gastrointestinal hemorrhage	1 (0.0) [0]	0 (0.0) [0]
Grand mal convulsion	1 (0.0) [0]	0 (0.0) [0]
Gynaecomastia	0 (0.0) [0]	1 (0.0) [0]
Hemothorax	0 (0.0) [0]	1 (0.0) [0]
Histrionic personality disorder	0 (0.0) [0]	1 (0.0) [0]
Humerus fracture	1 (0.0) [0]	0 (0.0) [0]
Impingement syndrome	0 (0.0) [0]	1 (0.0) [0]
Intervertebral disc protrusion	0 (0.0) [0]	1 (0.0) [0]
Iron deficiency anemia	1 (0.0) [0]	0 (0.0) [0]
Joint dislocation postoperative	0 (0.0) [0]	1 (0.0) [0]
Lacrimation increased	0 (0.0) [0]	1 (0.0) [0]
Ligament injury	1 (0.0) [0]	0 (0.0) [0]
Lipoma	0 (0.0) [0]	1 (0.0) [0]
Meningitis aseptic	0 (0.0) [0]	1 (0.0) [0]
Menometrorrhagia	0 (0.0) [0]	1 (0.0) [0]

Menorrhagia	1 (0.0) [0]	0 (0.0) [0]
Metrorrhagia	0 (0.0) [0]	1 (0.0) [0]
Mouth cyst	0 (0.0) [0]	1 (0.0) [0]
Multiple sclerosis	0 (0.0) [0]	1 (0.0) [0]
Musculoskeletal chest pain	0 (0.0) [0]	1 (0.0) [0]
Nerve compression	1 (0.0) [0]	0 (0.0) [0]
Nystagmus	0 (0.0) [0]	1 (0.0) [0]
Oophoritis	0 (0.0) [0]	1 (0.0) [0]
Open wound	1 (0.0) [0]	0 (0.0) [0]
Pancreatitis acute	0 (0.0) [0]	1 (0.0) [0]
Papillary thyroid cancer	0 (0.0) [0]	1 (0.0) [0]
Pelvic inflammatory disease	0 (0.0) [0]	1 (0.0) [0]
Pelvic pain	0 (0.0) [0]	1 (0.0) [0]
Personality disorder	1 (0.0) [0]	0 (0.0) [0]
Phimosis	0 (0.0) [0]	1 (0.0) [0]
Pneumonia	0 (0.0) [0]	1 (0.0) [0]
Pneumonia mycoplasmal	0 (0.0) [0]	1 (0.0) [0]
Pneumothorax	0 (0.0) [0]	1 (0.0) [0]
Polytraumatism	1 (0.0) [0]	0 (0.0) [0]
Postoperative hernia	0 (0.0) [0]	1 (0.0) [0]
Pyelonephritis acute	0 (0.0) [0]	1 (0.0) [0]
Retinal detachment	0 (0.0) [0]	1 (0.0) [0]
Salpingitis	0 (0.0) [0]	1 (0.0) [0]
Spinal disorder	0 (0.0) [0]	1 (0.0) [0]
Stress incontinence	0 (0.0) [0]	1 (0.0) [0]
Sympathetic posterior cervical syndrome	0 (0.0) [0]	1 (0.0) [0]
Synovial cyst	0 (0.0) [0]	1 (0.0) [0]
Synovial disorder	1 (0.0) [0]	0 (0.0) [0]
Synovitis	0 (0.0) [0]	1 (0.0) [0]
Tongue edema	0 (0.0) [0]	1 (0.0) [0]
Traumatic shock	0 (0.0) [0]	1 (0.0) [0]
Ulna fracture	0 (0.0) [0]	1 (0.0) [0]
Uterine leiomyoma	0 (0.0) [0]	1 (0.0) [0]
Varicocele	0 (0.0) [0]	1 (0.0) [0]
Varicose vein	0 (0.0) [0]	1 (0.0) [0]
Fatal SAEs	**Placebo Group N = 2066**	**Flu Group N = 4137**
Subjects with fatal SAE(s), n (%) [n related]	1 (0.0) [0]	3 (0.1) [0]
Arteriosclerosis coronary artery	0 (0.0) [0]	1 (0.0) [0]
Polytraumatism	1 (0.0) [0]	0 (0.0) [0]
Pulmonary embolism	0 (0.0) [0]	1 (0.0) [0]
Traumatic shock	0 (0.0) [0]	1 (0.0) [0]

Conclusion: During the passive and active surveillance for ILI, culture-confirmed Influenza A or B events occurred for 18 (0.9%) and 28 (0.7%) subjects in the Placebo and Flu Group, respectively. At Day 21, 97.8%, 88.1% and 95.9% of the subjects of the Flu Group had antibody titers $\geq$ 1:40 for H1N1, H3N2 and B vaccine strains, respectively. Pain at the injection site and redness were the most frequently reported solicited local symptoms. Fatigue was the most frequently reported solicited general symptom in both groups. At least one AE was reported by 32 (10.0%) and 71 (11.1%) subjects in the Placebo Group and Flu Group, respectively. SAEs were reported by 47 (2.3%) and 96 (2.3%) subjects in the Placebo Group and Flu Group, respectively. Fatal SAEs were reported for 4 subjects: 1 in the placebo Group and 3 in the Flu Group. All the SAEs reported during the course of the study were considered by the investigators to be not related to the study vaccination.

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