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.: 111454 (FLU-AS25-026 PRI)

Title: Non-inferiority study of GlaxoSmithKline Biologicals' influenza vaccine GSK576389A using different formulations. FluAS25: GlaxoSmithKline (GSK) Biologicals' AS25 adjuvanted influenza vaccine.

Rationale: The aim of this study was to assess the immunological non-inferiority of the thiomersal-free (TF) FluAS25 adjuvanted vaccine as compared to the thiomersal reduced (TR) FluAS25 adjuvanted vaccine.

Phase: II

Study Period: 03 March 2008 to 11 April 2008.

Study Design: A multi-center, double-blind, randomized study with 2 parallel groups (1:1).

Centers: 3 study centers in Estonia.

Indication: Immunization against influenza disease in an elderly population aged over 65 years.

Treatment: The study groups were as follows:

- TF-FluAS25 Group: subjects received 1 dose of TF FluAS25 adjuvanted vaccine.
- TR-FluAS25 Group: subjects received 1 dose of TR FluAS25 adjuvanted vaccine.

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

Objectives:

- To demonstrate the immunological non-inferiority (in terms of haemagglutination inhibition (HI) antibody geometric mean titers (GMT)) of the TF FluAS25 adjuvanted influenza vaccine compared to the TR FluAS25 adjuvanted influenza vaccine 21 days after vaccination in subjects aged ≥ 65 years.

Criterion to demonstrate the non-inferiority: The non-inferiority was demonstrated if the upper limits (UL) of the two-sided 95% confidence intervals (CI) of the GMT ratio (TR-FluAS25 over TF-FluAS25) were below 1.5 in terms of antibody titers for each of the 3 vaccine strains.

Primary Outcome/Efficacy Variable:

Immunogenicity

Observed variable

- At Days 0 and 21, serum HI antibody titer, against the 3 vaccine strains, in the TF-FluAS25 and the TR-FluAS25 groups

Derived variable:

- GMTs of HI antibody titers at Days 0 and 21

Secondary Outcome/Efficacy Variable(s):

Immunogenicity

Observed variable

- At Days 0 and 21: serum HI antibody titer, against each of the 3 vaccine strains in both groups.

Derived variables:

- Seropositivity rates* at Days 0 and 21, in each group.
- Seroconversion rates (SCR)** at Day 21, in each group.
- Seroconversion factors (SCF)*** at Day 21, in each group.
- Seroprotection rates (SPR)**** at Days 0 and 21, in each group.

* Seropositivity is defined as the percentage of vaccinees with a serum HI titers ≥ 1:10

** Seroconversion rate is defined as the percentage of vaccinees who have either a pre-vaccination titer < 1:10 and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least a four-fold increase in post-vaccination titer.

***Seroconversion factor is defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.

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

Safety

- Occurrence, intensity, duration and relationship to vaccination of solicited local and general signs and symptoms during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after vaccination, in each group.
- Occurrence, intensity, duration* and relationship to vaccination of unsolicited adverse events (AEs) during a 21-day follow-up period (i.e. day of vaccination and 20 subsequent days) after vaccination, in each group.
- Occurrence, intensity, duration* and relationship to vaccination of medically significant conditions$ prompting emergency room visits, hospitalizations or physician visits that are not routine visits for physical examination or vaccination, during a 21-day follow-up period (i.e. day of vaccination and 20 subsequent days) after vaccination, in

each group.

- Occurrence and relationship to vaccination of serious adverse events (SAEs) during the entire study period (up to Day 21) in each group.

*Duration data were not analysed for these AEs.

$It was decided to analyze the medically significant conditions as all unsolicited adverse events that resulted in a medically attended visit.

Statistical Methods:

The analyses were performed on the Total Vaccinated cohort and on the According-To-Protocol (ATP) cohort for immunogenicity.

- The Total Vaccinated cohort included all subjects with study vaccine administered.
- The ATP cohort for immunogenicity included all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures and intervals defined in the protocol, with no elimination criteria) who had received the study vaccine according to their random assignment, for whom administration site of study vaccine was known, for whom the randomization code had not been broken and for whom data concerning immunogenicity outcome measures were available. These included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination.

Analysis of immunogenicity

The analysis was performed on the ATP cohort for immunogenicity.

To demonstrate the immunological non-inferiority of the TF-FluAS25 adjuvant influenza vaccine compared to the TR-FluAS25 adjuvant influenza vaccine 21 days after vaccination, the 95% CIs of the group GMT ratio (TR-FluAS25 group over TF-FluAS25 group) were computed for each strain using an ANCOVA model.

For each group and each antibody, the following parameters were also tabulated with 95% CI:

- Seropositivity rates and GMTs at Day 0 and Day 21
- SCR at Day 21
- SCF at Day 21
- SPR at Day 0 and Day 21

Analysis of safety

The analysis was performed on the Total Vaccinated cohort.

The percentages of subjects reporting each individual solicited local and general symptom during the 7-day (Days 0-6) solicited follow-up period were tabulated with exact 95% CI for each vaccine group. The same tabulation was performed for grade 3 symptoms and for general symptoms with relationship to vaccination. All local symptoms were considered as related to the study vaccination. The duration of each solicited local and general symptom reported during the 7-day solicited follow-up period was tabulated.

The percentage of subjects with at least one report of unsolicited AEs reported within the 21 days (Days 0-20) after vaccination and classified by the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms was tabulated. The same tabulation was performed for grade 3 AEs and for AEs with a relationship to vaccination.

The percentage of subjects with unsolicited AE that resulted in a medically attended visit classified by MedDRA preferred terms and reported within the 21 days after vaccination was tabulated. The same tabulation was done for grade 3 AE and those with a relationship to vaccination.

The occurrence of SAEs during the entire study period was also tabulated according to MedDRA preferred terms.

Study Population: Healthy male or female aged 65 years or older at the time of vaccination who were free of an acute aggravation of the health status as established by clinical evaluation before entering into the study. Subjects with a history of hypersensitivity to a previous dose of influenza vaccine and with a previous vaccination against influenza with any seasonal vaccine since July 2007 were excluded from the study. Written informed consent was obtained from the subject before study enrolment.

Number of Subjects:	**TF-FluAS25 Group**	**TR-FluAS25 Group**
Planned, N	355	355
Randomized, N (Total Vaccinated cohort)	360	360
Completed, n (%)	359 (99.7)	360 (100)
Total Number Subjects Withdrawn, n (%)	1 (0.3)	0 (0.0)
Withdrawn due to Adverse Events, n (%)	1 (0.3)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	0 (0.0)
Demographics	**TF-FluAS25 Group**	**TR-FluAS25 Group**
N (Total Vaccinated cohort)	360	360

Females: Males	263:97	257:103
Mean Age, years (SD)	72 (5.02)	71.7 (4.88)
White-Caucasian / European heritage, n (%)	359 (99.7)	359 (99.7)

Primary Efficacy Results: Adjusted ratios of HI antibody GMTs at Day 21 (ATP cohort for immunogenicity)

Vaccine strains	TR-FluAS25 Group		TF-FluAS25 Group		Adjusted GMT ratio (TR-FluAS25 Group / TF-FluAS25 Group)		
					Value	95% CI	
	N	Adjusted GMT	N	Adjusted GMT		LL	UL*
A/Solomon Islands	360	93.4	357	86.2	1.08	0.89	1.31
A/Wisconsin	360	525.8	357	605.5	0.87	0.73	1.03
B/Malaysia	360	265.7	357	286.6	0.93	0.80	1.08

Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the GMT ratio, LL = Lower Limit, UL = Upper Limit
**Criterion of non-inferiority: UL of the 2-sided 95% CI of the GMT ratio < 1.5 for each of the 3 vaccine strains*

Primary Efficacy Results: Seropositivity rates and GMTs for HI antibody titer at Days 0 and 21 (ATP cohort for immunogenicity)

Antibody	Group	Timing	N	≥ 1:10				GMT*		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
A/Solomon Islands	TF-FluAS25	PRE	357	67	18.8	14.9	23.2	6.0	5.7	6.4
		PI(D21)	357	342	95.8	93.2	97.6	86.5	75.8	98.8
	TR-FluAS25	PRE	360	62	17.2	13.5	21.5	6.0	5.7	6.3
		PI(D21)	360	338	93.9	90.9	96.1	93.1	80.5	107.6
A/Wisconsin	TF-FluAS25	PRE	357	209	58.5	53.2	63.7	15.9	13.9	18.1
		PI(D21)	357	357	100	99.0	100	613.2	540.1	696.1
	TR-FluAS25	PRE	360	199	55.3	50.0	60.5	14.9	13.1	17.0
		PI(D21)	360	359	99.7	98.5	100	519.3	451.5	597.3
B/Malaysia	TF-FluAS25	PRE	357	215	60.2	54.9	65.3	13.2	11.9	14.7
		PI(D21)	357	355	99.4	98.0	99.9	287.5	255.9	323.1
	TR-FluAS25	PRE	360	208	57.8	52.5	62.9	13.0	11.7	14.5
		PI(D21)	360	357	99.2	97.6	99.8	264.9	235.5	297.9

GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n (%) = number (percentage) of seropositive subjects (HI titer ≥ 1:10)
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination
PI(D21) = post-vaccination Dose 1 at Day 21
*Primary outcome variable

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

Vaccine strain	Group	N	SCR			
			n	%	95% CI	
					LL	UL
A/Solomon Islands	TF-FluAS25	357	278	77.9	73.2	82.1
	TR-FluAS25	360	281	78.1	73.4	82.2
A/Wisconsin	TF-FluAS25	357	336	94.1	91.1	96.3
	TR-FluAS25	360	337	93.6	90.6	95.9
B/Malaysia	TF-FluAS25	357	332	93.0	89.8	95.4
	TR-FluAS25	360	335	93.1	89.9	95.5

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

N = number of subjects with pre- and post-vaccination results available
n (%) = number (percentage) of seroconverted subjects

95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): SCF for HI antibody titer at Day 21 (ATP cohort for immunogenicity)

Vaccine strain	Group	N	SCF		
			Value	95% CI	
				LL	UL
A/Solomon Islands	TF-FluAS25	357	14.3	12.6	16.3
	TR-FluAS25	360	15.6	13.5	18.1
A/Wisconsin	TF-FluAS25	357	38.7	33.6	44.5
	TR-FluAS25	360	34.8	30.0	40.3
B/Malaysia	TF-FluAS25	357	21.8	19.3	24.6
	TR-FluAS25	360	20.3	18.0	22.9

N = number of subjects with pre- and post-vaccination results available
SCF = seroconversion factor of the within-subject ratios of the post-vaccination reciprocal HI titer to the Day 0 reciprocal HI titer
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): SPR for HI antibody titer at Days 0 and 21 (ATP cohort for immunogenicity)

Vaccine strain	Group	Timing	N	SPR			
				n	%	95% CI	
						LL	UL
A/Solomon Islands	TF-FluAS25	PRE	357	10	2.8	1.4	5.1
		PI(D21)	357	280	78.4	73.8	82.6
	TR-FluAS25	PRE	360	6	1.7	0.6	3.6
		PI(D21)	360	287	79.7	75.2	83.8
A/Wisconsin	TF-FluAS25	PRE	357	112	31.4	26.6	36.5
		PI(D21)	357	350	98.0	96.0	99.2
	TR-FluAS25	PRE	360	97	26.9	22.4	31.8
		PI(D21)	360	348	96.7	94.2	98.3
B/Malaysia	TF-FluAS25	PRE	357	74	20.7	16.6	25.3
		PI(D21)	357	349	97.8	95.6	99.0
	TR-FluAS25	PRE	360	75	20.8	16.8	25.4
		PI(D21)	360	351	97.5	95.3	98.9

N = Number of subjects with available results
n (%) = number (percentage) of seroprotected subjects (HI titer $\geq$ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination
PI(D21) = post-vaccination Dose 1 at Day 21

Secondary Outcome Variable(s): Percentage of subjects reporting solicited local symptoms during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort.)

Symptom	Intensity	TF-FluAS25 Group					TR-FluAS25Group				
		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL
Ecchymosis	>20 mm	360	7	1.9	0.8	4.0	360	6	1.7	0.6	3.6
	>100 mm	360	0	0.0	0.0	1.0	360	0	0.0	0.0	1.0
Pain	Any	360	237	65.8	60.7	70.7	360	246	68.3	63.3	73.1
	Grade 3	360	2	0.6	0.1	2.0	360	1	0.3	0.0	1.5
Redness	>20 mm	360	152	42.2	37.1	47.5	360	161	44.7	39.5	50.0
	>100 mm	360	10	2.8	1.3	5.0	360	12	3.3	1.7	5.8
Swelling	>20 mm	360	74	20.6	16.5	25.1	360	90	25.0	20.6	29.8
	>100 mm	360	1	0.3	0.0	1.5	360	4	1.1	0.3	2.8

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

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

period (Total Vaccinated cohort.)

Symptom	Group	N	Mean	Median
Ecchymosis	TF-FluAS25	7	4.6	4.0
	TR-FluAS25	6	3.3	3.0
Pain	TF-FluAS25	237	2.7	3.0
	TR-FluAS25	246	2.8	3.0
Redness	TF-FluAS25	152	3.5	3.0
	TR-FluAS25	161	3.6	4.0
Swelling	TF-FluAS25	74	3.6	3.5
	TR-FluAS25	90	3.5	3.5

N = number of subjects with the symptom

Secondary Outcome Variable(s): Percentage of subjects reporting solicited general symptoms during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort.)

Symptom	Intensity/ Relationship	TF-FluAS25 Group					TR-FluAS25 Group				
		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL
Arthralgia	Any	360	78	21.7	17.5	26.3	360	87	24.2	19.8	28.9
	Grade 3	360	1	0.3	0.0	1.5	360	2	0.6	0.1	2.0
	Related	360	75	20.8	16.8	25.4	360	85	23.6	19.3	28.3
Fatigue	Any	360	139	38.6	33.6	43.9	360	143	39.7	34.6	45.0
	Grade 3	360	2	0.6	0.1	2.0	360	0	0.0	0.0	1.0
	Related	360	139	38.6	33.6	43.9	360	141	39.2	34.1	44.4
Headache	Any	360	109	30.3	25.6	35.3	360	107	29.7	25.0	34.7
	Grade 3	360	3	0.8	0.2	2.4	360	1	0.3	0.0	1.5
	Related	360	109	30.3	25.6	35.3	360	105	29.2	24.5	34.2
Myalgia	Any	360	111	30.8	26.1	35.9	360	101	28.1	23.5	33.0
	Grade 3	360	1	0.3	0.0	1.5	360	3	0.8	0.2	2.4
	Related	360	111	30.8	26.1	35.9	360	99	27.5	23.0	32.4
Nausea	Any	360	38	10.6	7.6	14.2	360	43	11.9	8.8	15.8
	Grade 3	360	1	0.3	0.0	1.5	360	1	0.3	0.0	1.5
	Related	360	37	10.3	7.3	13.9	360	42	11.7	8.5	15.4
Shivering	Any	360	45	12.5	9.3	16.4	360	43	11.9	8.8	15.8
	Grade 3	360	1	0.3	0.0	1.5	360	0	0.0	0.0	1.0
	Related	360	45	12.5	9.3	16.4	360	43	11.9	8.8	15.8
Fever (Orally)	≥ 38.0°C	360	34	9.4	6.6	12.9	360	38	10.6	7.6	14.2
	≥ 39.0°C	360	0	0.0	0.0	1.0	360	1	0. 3	0.0	1. 5
	Related	360	34	9.4	6.6	12.9	360	38	10.6	7.6	14.2

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

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

Symptom	Group	N	Mean	Median
Arthralgia	TF-FluAS25	78	2.3	2.0
	TR-FluAS25	87	2.6	2.0
Fatigue	TF-FluAS25	139	2.3	2.0
	TR-FluAS25	143	2.6	2.0
Headache	TF-FluAS25	109	2.1	2.0
	TR-FluAS25	107	2.2	2.0
Myalgia	TF-FluAS25	111	2.0	2.0
	TR-FluAS25	101	2.4	2.0
Nausea	TF-FluAS25	38	1.7	1.0

	TR-FluAS25	43	1.9	1.0
Shivering	TF-FluAS25	45	1.5	1.0
	TR-FluAS25	43	2.1	1.0
Fever	TF-FluAS25	26	1.0	1.0
	TR-FluAS25	25	1.2	1.0

N = number of subjects with the symptom

Secondary Outcome Variable(s): Number (%) of subjects with Medically Significant Conditions (MSC), i.e. unsolicited AEs that resulted in a medically attended visit within the 21-day post-vaccination period (Total Vaccinated cohort.)

All MSCs	**TF-AS25 Group N = 360**	**TR-AS25 Group N = 360**
Subjects with any AE(s), n (%)	9 (2.5)	5 (1.4)
Subjects with grade 3 AE(s), n (%)	3 (0.8)	0 (0.0)
Subjects with related AE(s), n (%)	1 (0.3)	1 (0.3)
Thrombocytopenia	1 (0.3)	-
Arrhythmia	1 (0.3)	-
Atrial fibrillation	1 (0.3)	-
Myocardial infarction	1 (0.3)	-
Tachycardia	-	1 (0.3)
Vomiting	1 (0.3)	-
Inflammation	1 (0.3)	-
Influenza like illness	1 (0.3)	-
Bronchitis	-	1 (0.3)
Erysipelas	-	1 (0.3)
Herpes zoster	-	1 (0.3)
Sinusitis	1 (0.3)	1 (0.3)
Blood glucose decreased	1 (0.3)	-
Cough	1 (0.3)	-
Circulatory collapse	1 (0.3)	-
Hypertension	1 (0.3)	-

-: Adverse event absent
Grade 3 = symptom that prevented normal activities
Related = general symptom assessed by the investigator as causally related to the study vaccination

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

Most frequent adverse events–On-Therapy (occurring within Days 0-20 following vaccination)	**TF-FluAS25 Group N = 360**	**TR-FluAS25 Group N = 360**
Subjects with any AE(s), n (%)	83 (23.1)	71 (19.7)
Subjects with grade 3 AE(s), n (%)	3 (0.8)	0 (0.0)
Subjects with related AE(s), n (%)	61 (16.9)	53 (14.7)
Injection site pruritus	34 (9.4)	30 (8.3)
Injection site induration	22 (6.1)	19 (5.3)
Rhinitis	7 (1.9)	3 (0.8)
Cough	4 (1.1)	3 (0.8)
Dizziness	4 (1.1)	1 (0.3)
Pharyngolaryngeal pain	2 (0.6)	3 (0.8)
Arrhythmia	2 (0.6)	1 (0.3)
Arthralgia	2 (0.6)	1 (0.3)
Diarrhoea	-	3 (0.8)
Discomfort	2 (0.6)	1 (0.3)
Headache	2 (0.6)	1 (0.3)
Injection site warmth	2 (0.6)	1 (0.3)
Pain in extremity	2 (0.6)	1 (0.3)
Pyrexia	2 (0.6)	1 (0.3)
Angina pectoris	-	2 (0.6)
Asthenopia	2 (0.6)	-
Ear pain	-	2 (0.6)

Eye pain	2 (0.6)	-
Pain of skin	2 (0.6)	-
Anxiety	-	1 (0.3)
Bronchitis	-	1 (0.3)
Chest pain	-	1 (0.3)
Dermatitis	-	1 (0.3)
Diastolic hypertension	-	1 (0.3)
Erysipelas	-	1 (0.3)
Feeling cold	-	1 (0.3)
Flatulence	-	1 (0.3)
Frequent bowel movements	-	1 (0.3)
Herpes zoster	-	1 (0.3)
Hyperhidrosis	-	1 (0.3)
Influenza like illness	-	1 (0.3)
Injection site haematoma	-	1 (0.3)
Insomnia	-	1 (0.3)
Intercostal neuralgia	-	1 (0.3)
Muscle spasms	-	1 (0.3)
Myalgia	-	1 (0.3)
Ocular hyperaemia	-	1 (0.3)
Oral herpes	-	1 (0.3)
Periorbital oedema	-	1 (0.3)
Radiculitis cervical	-	1 (0.3)
Sinusitis	-	1 (0.3)
Sluggishness	-	1 (0.3)
Tachycardia	-	1 (0.3)
Urticaria	-	1 (0.3)
Vertigo	-	1 (0.3)
Vocal cord inflammation	-	1 (0.3)
Vomiting	-	1 (0.3)
Counting rule applied: As there were more than 30 subjects per treatment group and ≤ 3 groups, only the 10 most frequent events in each treatment group are to be listed. -: Implies that adverse event was not reported in the particular group or that the adverse event was reported in the particular group but did not fall within the pre-defined counting rule of 10 most frequent events for that group Grade 3 = symptom that prevented normal activities Related = general symptom assessed by the investigator as causally related to the study vaccination		
Safety results: Number (%) of subjects with SAEs throughout the study period (Total Vaccinated cohort.)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	**TF-FluAS25 Group N=360**	**TR-FluAS25 Group N=360**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	3 (0.8) [0]	0 (0.0) [0]
Arterial fibrillation	1 (0.3) [0]	0 (0.0) [0]
Circulatory collapse	1 (0.3) [0]	0 (0.0) [0]
Myocardial infarction	1 (0.3) [0]	0 (0.0) [0]
Thrombocytopenia	1 (0.3) [0]	0 (0.0) [0]
Fatal SAEs	**TF-FluAS25 Group N=360**	**TR-FluAS25 Group N=360**
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	1 (0.3) [0]	0 (0.0) [0]
Circulatory collapse	1 (0.3) [0]	0 (0.0) [0]
Myocardial infarction	1 (0.3) [0]	0 (0.0) [0]

Conclusion: Before vaccination, GMTs values of HI antibody titers for both groups were at least 6.0, 14.9 and 13.0 against the A/Solomon Islands, A/Wisconsin and B/Malaysia vaccine strains, respectively. At Day 21 after vaccination, GMTs

values of HI antibody titers for both groups were at least 86.5, 519.3 and 264.9 against the A/Solomon Islands, A/Wisconsin and B/Malaysia vaccine strains, respectively.
Within the 21-day follow-up period after vaccination, at least one unsolicited AE was reported by 83 (23.1%) subjects in the TF-FluAS25 Group and 71 (19.7%) subjects in the TR-FluAS25 Group. Throughout the entire study period, SAEs were reported in 3 (0.8%) subjects in the TF-FluAS25 Group; all were assessed by the investigators as not causally related to the study vaccination.
Fatal SAEs were reported in 1 subject from the TF-FluAS25 Group; they were assessed by the investigator as not causally related to the study vaccination.

Date updated: 08-September-2014