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.: 107507 (Flu-063)

Title: A Phase III study for evaluation of immunogenicity and reactogenicity of Fluarix™ (Influsplit SSW®) 2006/2007 in people aged 18 years or above
Influsplit SSW® 2006/2007 *(Fluarix™):* GSK Biologicals' inactivated influenza split vaccine

Rationale: To evaluate immunogenicity and safety of the influenza split vaccine containing the strains recommended for the 2006-2007 season (Northern Hemisphere).

Phase: III

Study Period: 27 July 2006 to 28 August 2006

Study Design: Open, non-randomized, multi-centric study with 2 parallel age-groups

Centres: Multicenter (4 centres in Germany)

Indication: Seasonal vaccination against influenza virus in subjects 18 years or older.

Treatment: All subjects received one dose of the influenza vaccine. The study group was sub-divided into 2 age groups:

- Subjects aged 18-60 years
- Subjects aged >60 years.

The vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.

Objectives: To evaluate the humoral response (anti-haemagglutinin antibody tested by haemagglutination inhibition - HI) against each vaccine strain in adults aged 18 years or above, 21 days after vaccination with the influenza vaccine.

Primary Outcome/Efficacy Variable: Evaluation of the humoral immune response in terms of anti-HA antibodies against each of the three vaccine influenza strains. The following parameters were calculated with 95% confidence intervals:

- Geometric mean titres (GMTs) of anti-HA antibodies at Days 0 and 21.
- Seroconversion factors at Day 21.
- Seroconversion rates at Day 21.
- Seroprotection rates at Days 0 and 21.
- Seroprotection power at Day 21.

Seroconversion factor was defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.
Seroconversion rate was defined as the percentage of vaccinees who had either a prevaccination titre < 1:10 and a post-vaccination titre ≥ 1:40 or a pre-vaccination titre ≥ 1:10 and at least a fourfold increase in post-vaccination titre.
Seroprotection rate was defined as the percentage of vaccinees with a serum HI titre ≥1:40 that is usually accepted as indicating protection.
Seroprotection power was defined as the percentage of subjects who had a prevaccination titre <1:40 and a post-vaccination titre ≥ 1:40.

Secondary Outcome/Efficacy Variable(s):

- Percentage, intensity and relationship to vaccination of solicited local and general signs and symptoms during a 4-day follow-up period (Day 0-3) after vaccination.
- Percentage, intensity and relationship to vaccination of unsolicited adverse events (AEs) during the 30 days following the vaccination (Day 0-29).
- Percentage, intensity and relationship to vaccination of serious adverse events (SAEs) during the entire study period.

Statistical Methods:
The analyses were performed on the Total Vaccinated Cohort and the 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., who met all eligibility criteria, who complied with the protocol procedures, with no elimination criteria assigned during the study) of the immunogenicity subset for whom data concerning immunogenicity results were available. This 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.
For the humoral immune response in terms of anti-HA antibodies against each of the three vaccine influenza strains, Geometric mean titres (GMTs) and seroprotection rates of anti-HA antibody titres at Days 0 and 21, seroconversion rates, seroconversion factors and seroprotection power at Day 21 were calculated with 95% Confidence Intervals (CIs) for each age group.

Analysis of Safety:
The analysis was performed on the Total Vaccinated Cohort.
The percentage of subjects with each individual solicited local and general symptom (any and Grade 3) during the 4-day solicited follow-up period (Day 0-3) was tabulated with exact 95% CI for each age group. The same tabulation was performed for solicited general symptoms with relationship to vaccination. The percentage of subjects reporting unsolicited AEs during the 30-day follow-up period (Day 0 – 29) after vaccine administration, their intensity and relationship to vaccination was summarized by age group according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms. The occurrence of SAEs throughout the entire study was tabulated per age group according to MedDRA preferred terms.

Study Population: Male or female aged 18 years or above at the time of enrolment. Healthy subjects or with well-controlled chronic diseases as established by medical history and clinical examination before entering into the study. If the subject was female and of childbearing potential, she had to be abstinent or to have used contraceptive precautions for 30 days prior to vaccination; she was to have a negative pregnancy test at study entry and had to agree to continue contraceptive precautions during the study period. Written informed consent was obtained from each subject prior to the performance of any study-specific procedures.

Number of Subjects:	**18-60 years Group**	**>60 years Group**
Planned, N	60	60
Randomised, N (Total Vaccinated Cohort)	62	55
Completed, n (%)	61 (98.4)	55 (100)
Total Number Subjects Withdrawn, n (%)	1 (1.6)	0 (0.0)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not Applicable	Not Applicable
Withdrawn for other reasons, n (%)	1	0 (0.0)
Demographics	**18-60 years Group**	**>60 years Group**
N, (Total Vaccinated Cohort)	62	55
Females: Males	31:31	29:26
Mean Age, years (SD)	35.7 (13.74)	68.8 (6.54)
White/Caucasian, n (%)	60 (96.8)	54 (98.2)

Primary Efficacy Results: GMTs for HI antibodies (ATP Cohort for immunogenicity)

Antibody	**Group**	**Timing**	**N**	**GMT**		
				Value	**95% CI**	
					LL	**UL**
A/New Caledonia	18-60 years	PRE	61	35.1	23.8	51.5
		PI(D21)	61	417.8	292.1	597.6
	>60 years	PRE	55	35.2	26.1	47.6
		PI(D21)	55	145.5	105.7	200.4
A/Wisconsin	18-60 years	PRE	61	12.7	9.8	16.5
		PI(D21)	61	282.4	209.3	381.1
	>60 years	PRE	55	24.3	16.9	34.9
		PI(D21)	55	173.6	127.9	235.7
B/Malaysia	18-60 years	PRE	61	25.1	18.4	34.1
		PI(D21)	61	257.7	197.3	336.6
	>60 years	PRE	55	42.8	31.6	58.1
		PI(D21)	55	209.7	163.5	269.0

N = Number of subjects with available results
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination; PI(D21) = 21 days after vaccination

Primary Efficacy Results: Seroconversion factor for HI antibody titre at Day 21 (ATP Cohort for immunogenicity)

Vaccine strain	**Group**	**N**	**SCF**		
			Value	**95%CI**	
				LL	**UL**
A/New Caledonia	18-60 years	61	11.9	7.7	18.5
	>60 years	55	4.1	2.8	6.2
A/Wisconsin	18-60 years	61	22.3	16.8	29.6
	>60 years	55	7.2	4.9	10.5
B/Malaysia	18-60 years	61	10.3	7.2	14.6

	>60 years	55	4.9	3.5	6.8	

N = Number of subjects with available results
SCF = Seroconversion Factor or geometric mean ratio
95% CI = 95% confidence interval
LL = Lower Limit, UL = Upper Limit

Primary Efficacy Results: Seroconversion rates for HI antibody titre at Day 21 (ATP Cohort for immunogenicity)

Vaccine Strain	Group	N	n	%	95%CI	
					LL	UL
A/New Caledonia	18-60 years	61	40	65.6	52.3	77.3
	>60 years	55	20	36.4	23.8	50.4
A/Wisconsin	18-60 years	61	59	96.7	88.7	99.6
	>60 years	55	37	67.3	53.3	79.3
B/Malaysia	18-60 years	61	45	73.8	60.9	84.2
	>60 years	55	28	50.9	37.1	64.6

N = number of subjects with available results
n(%) = number(percentage) who seroconverted at Day 21
95% CI = 95% confidence interval
LL = Lower Limit, UL = Upper Limit

Primary Efficacy Results: Seroprotection rates at Days 0 and 21 (ATP Cohort for immunogenicity)

Vaccine strain	Group	Timing	N	SP			
				n	%	95%CI	
						LL	UL
A/New Caledonia	18-60 years	PRE	61	23	37.7	25.61	51.04
		PI(D21)	61	59	96.7	88.65	99.60
	>60 years	PRE	55	28	50.9	37.07	64.65
		PI(D21)	55	50	90.9	80.05	96.98
A/Wisconsin	18-60 years	PRE	61	14	23.0	13.15	35.50
		PI(D21)	61	60	98.4	91.20	99.96
	>60 years	PRE	55	21	38.2	25.41	52.27
		PI(D21)	55	52	94.5	84.88	98.86
B/Malaysia	18-60 years	PRE	61	27	44.3	31.55	57.55
		PI(D21)	61	57	93.4	84.05	98.18
	>60 years	PRE	55	34	61.8	47.73	74.59
		PI(D21)	55	53	96.4	87.47	99.56

PRE = Pre-vaccination; PI(D21)= 21 days after vaccination
SP = Seroprotection
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

Primary Efficacy Results: Seroprotection powers for HI antibody titre at Day 21 (ATP Cohort for immunogenicity)

Vaccine Strain	Group	N	n	%	95%CI	
					LL	UL
A/New Caledonia	18-60 years	38	36	94.7	82.3	99.4
	>60 years	27	23	85.2	66.3	95.8
A/Wisconsin	18-60 years	47	46	97.9	88.7	99.9
	>60 years	34	32	94.1	80.3	99.3
B/Malaysia	18-60 years	34	31	91.2	76.3	98.1
	>60 years	21	20	95.2	76.2	99.9

N = number of subjects unprotected at pre-vaccination and with available results
n(%) = number(percentage) of subjects unprotected at PRE and protected at Day 21
95% CI = 95% confidence interval
LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): Seropositivity rates for HI antibodies (ATP Cohort for immunogenicity)

Vaccine	Group	Timing	N	≥ 10 1/DIL

strain				n	%	95% CI	
						LL	UL
A/New Caledonia	18-60 years	PRE	61	54	88.5	77.8	95.3
		PI(D21)	61	61	100	94.1	100
	>60 years	PRE	55	50	90.9	80.0	97.0
		PI(D21)	55	55	100	93.5	100
A/Wisconsin	18-60 years	PRE	61	37	60.7	47.3	72.9
		PI(D21)	61	61	100	94.1	100
	>60 years	PRE	55	42	76.4	63.0	86.8
		PI(D21)	55	54	98.2	90.3	100
B/Malaysia	18-60 years	PRE	61	48	78.7	66.3	88.1
		PI(D21)	61	61	100	94.1	100
	>60 years	PRE	55	51	92.7	82.4	98.0
		PI(D21)	55	55	100	93.5	100

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; PI(D21) = 21 days after vaccination

Secondary Outcome Variable(s): Number (percentage) of subjects with solicited local symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total vaccinated Cohort)

		18-60 years Group					>60 years Group				
					95 % CI					95 % CI	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Induration	Any	62	12	19.4	10.4	31.4	55	3	5.5	1.1	15.1
	>50 mm	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
Pain	Any	62	37	59.7	46.4	71.9	55	9	16.4	7.8	28.8
	Grade 3	62	1	1.6	0.0	8.7	55	0	0.0	0.0	6.5
Redness	Any	62	11	17.7	9.2	29.5	55	4	7.3	2.0	17.6
	>50 mm	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
Swelling	Any	62	6	9.7	3.6	19.9	55	2	3.6	0.4	12.5
	>50 mm	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5

N= number of subjects with an administered dose
n(%)= Number(percentage) of subjects reporting the specified symptom
Any: any solicited local symptom irrespective of intensity grade
Grade 3 pain: pain that prevented normal activity
95%CI= Exact 95% confidence interval
LL = lower limit, UL = upper limit

Secondary Outcome Variable(s): Number (percentage) of subjects with solicited general symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total vaccinated Cohort)

		18-60 years Group					>60 years Group				
					95 % CI					95 % CI	
Symptom	**Intensity/ relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Arthralgia	Any	62	4	6.5	1.8	15.7	55	1	1.8	0.0	9.7
	Grade 3	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
	Related	62	1	1.6	0.0	8.7	55	0	0.0	0.0	6.5
Fatigue	Any	62	12	19.4	10.4	31.4	55	1	1.8	0.0	9.7
	Grade 3	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
	Related	62	3	4.8	1.0	13.5	55	1	1.8	0.0	9.7
Fever/ (Axillary)	≥ 37.5 °C	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
	> 39.0 °C	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
	Related	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
Headache	Any	62	9	14.5	6.9	25.8	55	3	5.5	1.1	15.1
	Grade 3	62	1	1.6	0.0	8.7	55	0	0.0	0.0	6.5
	Related	62	1	1.6	0.0	8.7	55	0	0.0	0.0	6.5

Myalgia	Any	62	5	8.1	2.7	17.8	55	3	5.5	1.1	15.1
	Grade 3	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
	Related	62	0	0.0	0.0	5.8	55	2	3.6	0.4	12.5
Shivering	Any	62	3	4.8	1.0	13.5	55	0	0.0	0.0	6.5
	Grade 3	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
	Related	62	1	1.6	0.0	8.7	55	0	0.0	0.0	6.5
Sweating	Any	62	6	9.7	3.6	19.9	55	1	1.8	0.0	9.7
	Grade 3	62	0	0.0	0.0	5.8	55	0	0.0	0.0	6.5
	Related	62	1	1.6	0.0	8.7	55	0	0.0	0.0	6.5

N= number of subjects with an administered dose
n(%)= Number(percentage) of subjects reporting the symptom at least once
Any : any solicited general symptom irrespective of intensity grade or relationship to vaccination
Grade 3 symptom: prevented normal activity
Related : symptoms considered by the investigator to have a causal relationship to vaccination
95%CI= Exact 95% confidence interval
LL = lower limit, UL = upper limit

Safety results: Number (%) of subjects with unsolicited adverse events (Total Vaccinated Cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-29 following vaccination)	**18-60 years Group N = 62**	**>60 years Group N = 55**
Subjects with any AE(s), n (%)	3 (4.8)	1 (1.8)
Subjects with severe AEs, n (%)	2 (3.2)	0 (0.0)
Subjects with related AEs, n (%)	2 (3.2)	0 (0.0)
Gastritis	1 (1.6)	0 (0.0)
Pharyngolaryngeal pain	1 (1.6)	0 (0.0)
Abdominal pain	1 (1.6)	0 (0.0)
Abdominal pain upper	0 (0.0)	1 (1.8)
Axillary pain	0 (0.0)	1 (1.8)
Back pain	1 (1.6)	0 (0.0)
Circulatory collapse	1 (1.6)	0 (0.0)
Cough	1 (1.6)	0 (0.0)
Ear pain	1 (1.6)	0 (0.0)
Haematoma	1 (1.6)	0 (0.0)
Hand fracture	1 (1.6)	0 (0.0)
Hypermetropia	1 (1.6)	0 (0.0)
Influenza like illness	0 (0.0)	1 (1.8)
Injection site pruritus	0 (0.0)	1 (1.8)
Injection site warmth	1 (1.6)	0 (0.0)
Intercostal neuralgia	1 (1.6)	0 (0.0)
Migraine	1 (1.6)	0 (0.0)
Myalgia	1 (1.6)	0 (0.0)
Nasopharyngitis	1 (1.6)	0 (0.0)
Rhinitis	1 (1.6)	0 (0.0)
Tonsillitis	1 (1.6)	0 (0.0)
Urogenital disorder	1 (1.6)	0 (0.0)

Safety results: Number (%) of subjects with serious adverse events (Total Vaccinated Cohort)

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

All SAEs	**18-60 years Group N=62**	**>60 years Group N=55**
Subjects with any SAE(s), n (%) [n related]	0 (0.0)	0 (0.0)
Fatal SAEs	**18-60 years Group N=62**	**>60 years Group N=55**
Subjects with fatal SAE(s), n (%) [n related]	0 (0.0)	0 (0.0)

Conclusion: On Day 21, the GMTs for HI antibodies were at least 145.5 for A/New Caledonia strain, 173.6 for A/Wisconsin strain and 209.7 for B/Malaysia strain; at least 90.9%, 94.5% and 93.4% of subjects had HI antibody titres ≥

1:40 against A/ New Caledonia, A/Wisconsin and B/Malaysia, respectively.
For the 18-60 years group pain and fatigue were the most frequently reported solicited local and general symptoms, respectively. For the >60 years group pain was the most frequently reported solicited local symptom while headache and myalgia were the most frequently reported solicited general symptoms. A total of 20 (17.1%) subjects reported unsolicited adverse events: 17 (27.4%) in the 18-60 years group and 3 (5.5%) in the >60 years group. No SAEs were reported during the study period.

Date Updated: 11-August-2014