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.

GSK Medicine: GSK218352

Study No.: 116663 (FLUARIX-071)

Title: A Phase III study for evaluation of immunogenicity and reactogenicity of *Fluarix/Influsplit SSW* 2012/2013 in people aged 18 years and above.
Fluarix/Influsplit SSW 2012-2013 – GSK218352 (FLU): GlaxoSmithKline (GSK) Biologicals' trivalent inactivated split virion influenza vaccine

Rationale: The aim of the study was to evaluate the immunogenicity and safety of the FLU vaccine containing the influenza strains recommended for 2012-2013 season. Study duration was of about 3 weeks for all subjects.

Phase: III

Study Period: 10 July 2012 to 31 July 2012.

Study Design: Open-label, non-randomized, multicentre study with 2 parallel groups.

Centres: 4 centres in Germany.

Indication: Immunization of adults against influenza.

Treatment: Study groups were as follows:

- 18-60Y Group: Subjects aged 18 to 60 years received one dose of FLU vaccine at Day 0.
- >60Y Group: Subjects aged 60 years or above received one dose of FLU vaccine at Day 0.

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

Objectives:

- To evaluate the humoral response (anti-hemagglutinin [anti-HA] antibodies tested by haemagglutination inhibition [HI]) against each vaccine strain in adults 18-60 years and > 60 years of age, 21 days after vaccination with Flu.

Primary Outcome/Efficacy Variable:
Immunogenicity

- Humoral immune response in terms of anti-HA antibodies against each of the three vaccine influenza strains.
  - At Days 0 and 21
    - Geometric mean titres (GMTs) of anti-HA antibody titres.
    - Seroprotection rates (SPR)*.
  - At Day 21
    - Seroconversion rates (SCR)£.
    - Mean geometric increase (MGI)$ also known as the seroconversion factor (SCF).
    - Seroprotection power (SPP)α.

*SPR was defined as the percentage of vaccinees with serum HI titre ≥ 1:40 (usually accepted as indicating protection in adults).
£SCR was defined as the percentage of vaccinees with either a pre-vaccination titre < 1:10 and a post-vaccination titre ≥ 1:40, or a prevaccination titre ≥ 1:10 and at least 4-fold increase in post-vaccination titre.
$MGI was defined as the fold increase in serum HI GMT post-vaccination compared to Day 0.
αSPP was defined as the percentage of vaccinees with a pre-vaccination titre < 1:40 and a post-vaccination titre ≥ 1:40.

Secondary Outcome/Efficacy Variable(s):
Immunogenicity

- Humoral immune response in terms of anti-HA antibodies against each of the three vaccine influenza strains, by influenza vaccination status in the 2011-2012 season, in subjects aged > 60 years.
  - At Days 0 and 21
    - GMTs of anti-HA antibody titres and SPRs*, by influenza vaccination status in the 2011-2012 season.
  - At Day 21
    - SCRs and MGI by influenza vaccination status in the 2011-2012 season.

Safety

- Occurrence of solicited local and general symptoms
  - Percentage, intensity and duration of solicited local symptoms during a 4-day follow-up period after vaccination (i.e. day of vaccination and 3 subsequent days).
  - Percentage, intensity, duration and relationship to vaccination of solicited general symptoms during a 4-

day follow-up period after vaccination (i.e. day of vaccination and 3 subsequent days).

- Occurrence of unsolicited symptoms
  - Percentage, intensity and relationship to vaccination of unsolicited symptoms during a 21-day follow-up period after vaccination (i.e. day of vaccination and 20 subsequent days).
- Occurrence of serious adverse events (SAEs)
  - Percentage, intensity and relationship to vaccination of SAEs during the entire study period.

Statistical Methods:

The analysis was performed on the Total Vaccinated cohort and on the According-to-Protocol (ATP) cohort for immunogenicity.

- The Total Vaccinated cohort included all subjects with vaccine administration documented.
- The ATP cohort for immunogenicity included all evaluable subjects (those who met all eligibility criteria, complied with procedures and intervals defined in the protocol, with no elimination criteria assigned during the study) for whom data concerning immunogenicity outcome measures were available.

Analysis of Immunogenicity

The analysis was performed on the ATP cohort for immunogenicity.

For each of the 3 vaccine influenza strains, and for each group the following parameters were tabulated with 95% CI:

- Seropositivity rates*, GMTs and SPR at Days 0 and 21,
- SCR, MGI and SPP at Day 21

For each of the 3 vaccine influenza strains, in the >60Y Group, the following parameters were tabulated with 95% CI by pre-vaccination status in the 2011-2012 season:

- Seropositivity rates, GMTs, and SPR at Days 0 and 21,
- SCR and MGI at Day 21.

*A seropositive/seronegative subject was a subject whose anti-HA titre was ≥ / < the 1:10 seropositivity cut-off value.

Analysis of Safety

The analysis was performed on the Total Vaccinated cohort.

The percentages of subjects reporting each individual solicited local and general symptoms during the 3-day (Days 0-4) follow-up period after vaccination were tabulated with exact 95% CI. The same tabulation was performed for grade 3 symptoms and for general symptoms with relationship to vaccination. In addition, durations of these solicited local and general symptoms were tabulated.

The percentage of subjects with at least one report of unsolicited adverse event (AE) classified by the Medical Dictionary for Regulatory Affairs (MedDRA) preferred terms during the follow-up period (Days 0-20) was tabulated. The same tabulation was performed for Grade 3 unsolicited AE and unsolicited AE assessed by the investigator as causally related to study vaccination.

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

Study Population: Healthy or with well-controlled chronic diseases male or female adults aged18 years or above at the time of the vaccination who had satisfactory baseline medical assessment by medical history and physical examination. Subjects with administration of an influenza vaccine* within the six months preceding the study vaccination were excluded from the study. Women were to be of non-childbearing potential or if of childbearing potential, had to have practiced adequate contraception for 30 days prior to vaccination, had to have a negative pregnancy test, and had to agree to continue such precautions for the entire duration of the study. Written informed consent was obtained from each subject prior to study entry.
*Note: Approximately 50% of subjects (30 subjects) in the >60Y Group and a maximum of 25% of subjects (15 subjects) in the 18-60Y Group were allowed to have had a seasonal influenza vaccination the year before (i.e. season 2011-2012).

Number of Subjects:	**18-60Y Group**	**>60Y Group**
Planned, N	60	60
Randomized, N (Total Vaccinated cohort)	60	59
Completed, n (%)	60 (100)	59 (100)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	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 (%)	0 (0.0)	0 (0.0)
Demographics	**18-60Y Group**	**>60Y Group**
N (Total Vaccinated cohort)	60	59
Females: Males	30:30	34:25
Mean Age, years (SD)	35.7 (11.98)	70.3 (5.87)

White - Caucasian/European heritage, n (%)	60 (100)	59 (100)

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

				≥ 1:10				GMT		
						95% CI			95% CI	
Strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/Christchurch/16/10 (H1N1)	18-60Y	PRE	59	39	66.1	52.6	77.9	20.57	13.98	30.27
		PI(D21)	59	59	100	93.9	100	366.04	264.22	507.09
	>60Y	PRE	58	48	82.8	70.6	91.4	19.02	14.35	25.22
		PI(D21)	58	58	100	93.8	100	110.44	79.50	153.43
Flu A/Victoria/361/11 (H3N2)	18-60Y	PRE	59	41	69.5	56.1	80.8	16.17	12.07	21.65
		PI(D21)	59	59	100	93.9	100	93.19	73.75	117.76
	>60Y	PRE	58	44	75.9	62.8	86.1	23.90	17.07	33.45
		PI(D21)	58	56	96.6	88.1	99.6	65.63	48.37	89.05
Flu B/Hubei-Wujiagang/158/09 (Yamagata)	18-60Y	PRE	59	56	94.9	85.9	98.9	68.60	50.26	93.63
		PI(D21)	59	59	100	93.9	100	431.85	332.61	560.70
	>60Y	PRE	58	58	100	93.8	100	70.19	58.98	83.53
		PI(D21)	58	58	100	93.8	100	223.56	183.62	272.19

GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
PI(D21) = Post vaccination at Day 21

Primary Efficacy Results: SPR for HI antibody titre at Days 0 and 21 (ATP cohort for immunogenicity)

				SPR			
						95% CI	
Strain	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Christchurch/16/10 (H1N1)	18-60Y	PRE	59	20	33.9	22.1	47.4
		PI(D21)	59	55	93.2	83.5	98.1
	>60Y	PRE	58	14	24.1	13.9	37.2
		PI(D21)	58	47	81.0	68.6	90.1
Flu A/Victoria/361/11 (H3N2)	18-60Y	PRE	59	15	25.4	15.0	38.4
		PI(D21)	59	51	86.4	75.0	94.0
	>60Y	PRE	58	23	39.7	27.0	53.4
		PI(D21)	58	41	70.7	57.3	81.9
Flu B/Hubei-Wujiagang/158/09 (Yamagata)	18-60Y	PRE	59	42	71.2	57.9	82.2
		PI(D21)	59	59	100	93.9	100
	>60Y	PRE	58	51	87.9	76.7	95.0
		PI(D21)	58	58	100	93.8	100

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

Primary Efficacy Results: SCR for HI antibody titre at Day 21 (ATP cohort for immunogenicity)

			SCR			
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Christchurch/16/10 (H1N1)	18-60Y	59	45	76.3	63.4	86.4
	>60Y	58	34	58.6	44.9	71.4
Flu A/Victoria/361/11 (H3N2)	18-60Y	59	34	57.6	44.1	70.4
	>60Y	58	14	24.1	13.9	37.2
Flu B/Hubei-Wujiagang/158/09 (Yamagata)	18-60Y	59	38	64.4	50.9	76.4
	>60Y	58	24	41.4	28.6	55.1

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

Primary Efficacy Results: MGI for HI antibody titre at Day 21 (ATP cohort for immunogenicity)

			MGI		
				95% CI	
Strain	**Group**	**N**	**Value**	**LL**	**UL**
Flu A/Christchurch/16/10 (H1N1)	18-60Y	59	17.8	11.5	27.6
	>60Y	58	5.8	4.2	8.0
Flu A/Victoria/361/11 (H3N2)	18-60Y	59	5.8	4.2	7.8
	>60Y	58	2.7	2.2	3.4
Flu B/Hubei-Wujiagang/158/09 (Yamagata)	18-60Y	59	6.3	4.6	8.7
	>60Y	58	3.2	2.6	3.9

MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titreN = Number of subjects with pre- and post-vaccination results available
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Primary Efficacy Results: SPP for HI antibody titre at Day 21 (ATP cohort for immunogenicity)

			SPP			
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Christchurch/16/10 (H1N1)	18-60Y	39	35	89.7	75.8	97.1
	>60Y	44	33	75.0	59.7	86.8
Flu A/Victoria/361/11 (H3N2)	18-60Y	44	36	81.8	67.3	91.8
	>60Y	35	18	51.4	34.0	68.6
Flu B/Hubei-Wujiagang/158/09 (Yamagata)	18-60Y	17	17	100	80.5	100
	>60Y	7	7	100	59.0	100

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

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibody titre at Day 0 and Day 21 by influenza vaccination status in the 2011-2012 season in subjects aged > 60 years (ATP cohort for immunogenicity)

					≥ 1:10				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu A/Christchurch/16/10 (H1N1)	>60Y	Yes	PRE	30	26	86.7	69.3	96.2	22.13	14.86	32.95
			PI(D21)	30	30	100	88.4	100	92.92	59.75	144.52
		No	PRE	28	22	78.6	59.0	91.7	16.18	10.67	24.53
			PI(D21)	28	28	100	87.7	100	132.89	79.80	221.30
Flu A/Victoria/361/11 (H3N2)	>60Y	Yes	PRE	30	24	80.0	61.4	92.3	24.02	15.11	38.17
			PI(D21)	30	28	93.3	77.9	99.2	57.22	35.97	91.03
		No	PRE	28	20	71.4	51.3	86.8	23.76	14.12	40.00
			PI(D21)	28	28	100	87.7	100	76.01	50.24	114.99
Flu B/Hubei-Wujiagang/158/09 (Yamagata)	>60Y	Yes	PRE	30	30	100	88.4	100	77.34	62.16	96.23
			PI(D21)	30	30	100	88.4	100	208.70	159.83	272.52
		No	PRE	28	28	100	87.7	100	63.26	47.63	84.01
			PI(D21)	28	28	100	87.7	100	240.65	177.18	326.87

Sub-Groups:
Yes = Subjects who received seasonal Flu vaccination in 2011-2012
No = Subjects who did not receive seasonal Flu vaccination in 2011-2012
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre equal to or above the specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0

PI(D21)= Post vaccination at Day 21

Secondary Outcome Variable(s): SPR for HI antibody titre at Day 0 and 21 by influenza vaccination status in the 2011-2012 season in subjects aged > 60 years (ATP cohort for immunogenicity)

					SPR			
							95% CI	
Strain	**Group**	**Sub-Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Christchurch/16/10 (H1N1)	>60Y	Yes	PRE	30	9	30.0	14.7	49.4
			PI(D21)	30	24	80.0	61.4	92.3
		No	PRE	28	5	17.9	6.1	36.9
			PI(D21)	28	23	82.1	63.1	93.9
Flu A/Victoria/361/11 (H3N2)	>60Y	Yes	PRE	30	12	40.0	22.7	59.4
			PI(D21)	30	21	70.0	50.6	85.3
		No	PRE	28	11	39.3	21.5	59.4
			PI(D21)	28	20	71.4	51.3	86.8
Flu B/Hubei-Wujiagang/158/09 (Yamagata)	>60Y	Yes	PRE	30	28	93.3	77.9	99.2
			PI(D21)	30	30	100	88.4	100
		No	PRE	28	23	82.1	63.1	93.9
			PI(D21)	28	28	100	87.7	100

Sub-Groups:
Yes = Subjects who received seasonal Flu vaccination in 2011-2012
No = Subjects who did not receive seasonal Flu vaccination in 2011-2012
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 at Day 0
PI(D21) = Post vaccination at Day 21

Secondary Outcome Variable(s): SCR for HI antibody titre at Day 21 by influenza vaccination status in the 2011-2012 season in subjects aged > 60 years (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Strain	**Group**	**Sub-Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/Christchurch/16/10 (H1N1)	>60Y	Yes	30	15	50.0	31.3	68.7
		No	28	19	67.9	47.6	84.1
Flu A/Victoria/361/11 (H3N2)	>60Y	Yes	30	6	20.0	7.7	38.6
		No	28	8	28.6	13.2	48.7
Flu B/Hubei-Wujiagang/158/09 (Yamagata)	>60Y	Yes	30	11	36.7	19.9	56.1
		No	28	13	46.4	27.5	66.1

Sub-Groups
Yes = Subjects who received seasonal Flu vaccination in 2011-2012
No = Subjects who did not receive seasonal Flu vaccination in 2011-2012
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): MGI for HI antibody titre at Day 21 by influenza vaccination status in the 2011-2012 season in subjects aged > 60 years (ATP cohort for immunogenicity)

				MGI		
					95% CI	
Strain	**Group**	**Sub-Group**	**N**	**Value**	**LL**	**UL**
Flu A/Christchurch/16/10 (H1N1)	>60Y	Yes	30	4.2	2.8	6.4
		No	28	8.2	5.1	13.3
Flu A/Victoria/361/11 (H3N2)	>60Y	Yes	30	2.4	1.9	3.0
		No	28	3.2	2.1	4.8
Flu B/Hubei-Wujiagang/158/09	>60Y	Yes	30	2.7	2.2	3.4

(Yamagata)		No	28	3.8	2.8	5.3

Sub-Groups:
Yes = Subjects who received seasonal Flu vaccination in 2011-2012
No = Subjects who did not receive seasonal Flu vaccination in 2011-2012
N = Number of subjects with pre- and post-vaccination results available
MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): Percentage of subjects with solicited local symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total Vaccinated cohort)

		18-60Y Group					>60Y Group				
					95 % CI					95 % CI	
Symptom	**Intensity**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Ecchymosis	Any	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
	>100 mm	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
Induration	Any	60	2	3.3	0.4	11.5	59	4	6.8	1.9	16.5
	>100 mm	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
Pain	Any	60	33	55.0	41.6	67.9	59	23	39.0	26.5	52.6
	Grade 3	60	1	1.7	0.0	8.9	59	0	0.0	0.0	6.1
Redness	Any	60	6	10.0	3.8	20.5	59	7	11.9	4.9	22.9
	>100 mm	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
Swelling	Any	60	6	10.0	3.8	20.5	59	5	8.5	2.8	18.7
	>100 mm	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1

N = number of subjects with the documented 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 = occurrence of any local symptom regardless of their intensity grade
Grade 3 pain = pain that prevented normal, everyday activities

Secondary Outcome Variable(s): Number of days of local symptoms during the 4-day (Days 0-3) post-vaccination period (Total Vaccinated cohort)

Solicited Symptom	**Group**	**N**	**Mean**	**Median**
Induration	18-60Y	2	2.5	2.5
	>60Y	4	1.8	2.0
Pain	18-60Y	33	2.2	2.0
	>60Y	23	1.9	2.0
Redness	18-60Y	6	2.5	2.5
	>60Y	7	2.1	2.0
Swelling	18-60Y	6	2.2	2.0
	>60Y	5	1.8	2.0

N = Number of subjects with the symptom and without the missing confirmed grade

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

		18-60Y Group					>60Y Group				
					95 % CI					95 % CI	
Symptom	**Intensity/Relationship**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Arthralgia	Any	60	2	3.3	0.4	11.5	59	4	6.8	1.9	16.5
	Grade 3	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
	Related	60	2	3.3	0.4	11.5	59	1	1.7	0.0	9.1
Fatigue	Any	60	11	18.3	9.5	30.4	59	14	23.7	13.6	36.6
	Grade 3	60	1	1.7	0.0	8.9	59	0	0.0	0.0	6.1
	Related	60	7	11.7	4.8	22.6	59	10	16.9	8.4	29.0
Gastrointestinal symptoms	Any	60	4	6.7	1.8	16.2	59	3	5.1	1.1	14.1
	Grade 3	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
	Related	60	2	3.3	0.4	11.5	59	3	5.1	1.1	14.1
Headache	Any	60	15	25.0	14.7	37.9	59	7	11.9	4.9	22.9
	Grade 3	60	1	1.7	0.0	8.9	59	1	1.7	0.0	9.1
	Related	60	11	18.3	9.5	30.4	59	6	10.2	3.8	20.8

Myalgia	Any	60	11	18.3	9.5	30.4	59	7	11.9	4.9	22.9
	Grade 3	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
	Related	60	11	18.3	9.5	30.4	59	5	8.5	2.8	18.7
Shivering	Any	60	1	1.7	0.0	8.9	59	2	3.4	0.4	11.7
	Grade 3	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
	Related	60	1	1.7	0.0	8.9	59	1	1.7	0.0	9.1
Sweating increase	Any	60	8	13.3	5.9	24.6	59	9	15.3	7.2	27.0
	Grade 3	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
	Related	60	6	10.0	3.8	20.5	59	6	10.2	3.8	20.8
Temperature (Axillary)	≥37.5ºC	60	2	3.3	0.4	11.5	59	1	1.7	0.0	9.1
	>39.0ºC	60	0	0.0	0.0	6.0	59	0	0.0	0.0	6.1
	Related	60	2	3.3	0.4	11.5	59	1	1.7	0.0	9.1

N = number of subjects with the documented 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 = occurrence of any general symptom regardless of their intensity grade or relationship to vaccination
Grade 3 = general symptom that prevented normal activity
Related = general symptom assessed by the investigator as causally related to the study vaccination
Gastrointestinal symptoms included nausea, vomiting, diarrhoea and/or abdominal pain.

Secondary Outcome Variable(s): Number of days of general symptoms during the 4-day (Days 0-3) post-vaccination period (Total Vaccinated cohort)

Solicited Symptom	**Group**	**N**	**Mean**	**Median**
Arthralgia	18-60Y	2	2.5	2.5
	>60Y	4	2.8	3.0
Fatigue	18-60Y	11	1.4	1.0
	>60Y	14	1.9	2.0
Gastrointestinal symptoms	18-60Y	4	1.3	1.0
	>60Y	3	1.3	1.0
Headache	18-60Y	15	1.7	1.0
	>60Y	7	1.0	1.0
Myalgia	18-60Y	11	1.5	1.0
	>60Y	7	1.7	1.0
Sweating increase	18-60Y	8	1.5	1.0
	>60Y	9	1.8	2.0
Shivering	18-60Y	1	1.0	1.0
	>60Y	2	1.5	1.5
Temperature (Axillary)	18-60Y	2	1.0	1.0
	>60Y	1	4.0	4.0

N = Number of subjects with the symptom and without the missing confirmed grade

Safety Results: Number (%) of subjects with unsolicited AEs (Total Vaccinated cohort)

Most frequent adverse events – On-Therapy (occurring within Days 0-20 following vaccination)	**18-60Y Group N = 60**	**>60Y Group N = 59**
Subjects with any unsolicited AE(s), n (%)	8 (13.3)	11 (18.6)
Subjects with grade 3 unsolicited AE(s), n (%)	0 (0.0)	1 (1.7)
Subjects with related unsolicited AE(s), n (%)	4 (6.7)	3 (5.1)
Injection site pruritus	3 (5.0)	2 (3.4)
Back pain	1 (1.7)	1 (1.7)
Diarrhoea	-	1 (1.7)
Dysaesthesia	-	1 (1.7)
Ear pain	-	1 (1.7)
Exostosis	-	1 (1.7)
Gastroenteritis	1 (1.7)	-
Herpes zoster	1 (1.7)	-
Hypertension	-	1 (1.7)
Insomnia	-	1 (1.7)
Lymphadenopathy	1 (1.7)	-

Musculoskeletal stiffness	-	1 (1.7)
Myalgia	-	1 (1.7)
Respiratory tract infection viral	1 (1.7)	-
Viral infection	-	1 (1.7)
- : AE absent. Grade 3 = AE which prevented normal activities Related = AE assessed by the investigator as causally related to vaccination		
Safety results: Number (%) of subjects with SAEs during the entire study period (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	**18-60Y Group N = 60**	**>60Y Group N = 59**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**18-60Y Group N = 60**	**>60Y Group N = 59**
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:

Pre-vaccination, at Day 0, GMTS for antibodies against the H1N1, H3N2 and Yamagata strains were 20.57, 16.17 and 68.60 in the 18-60Y Group, respectively. At that same time point, in the >60Y Group, GMTs for antibodies against the H1N1, H3N2 and Yamagata strains were 19.02, 23.90 and 70.19, respectively. At Day 21, GMTS for antibodies against the H1N1, H3N2 and Yamagata strains were 366.04, 93.19, and 431.85 in the 18-60Y Group, respectively. At that same time point, in the >60Y Group, GMTS for antibodies against the H1N1, H3N2 and Yamagata strains were 110.44, 65.63, and 223.56, respectively.

At Day 0, 33.9%, 25.4% and 71.2% of subjects in the 18-60Y Group and 24.1%, 39.7% and 87.9% of subjects in the >60Y Group were seroprotected against the H1N1, H3N2 and Yamagata strains, respectively. At Day 21, 93.2%, 86.4% and 100% of subjects in the 18-60Y Group and 81.0%, 70.7% and 100% of subjects in the >60Y Group were seroprotected against the H1N1, H3N2 and Yamagata strains, respectively.

At Day 21, 76.3%, 57.6% and 64.4% of subjects in the 18-60Y Group and 58.6%, 24.1% and 41.4% of subjects in the >60Y Group were seroconverted against the H1N1, H3N2 and Yamagata strains, respectively.

At Day 21, MGI for antibody titre against the H1N1, H3N2 and Yamagata strains was 17.8, 5.8 and 6.3 in the 18-60Y Group and 5.8, 2.7 and 3.2 in the >60Y Group, respectively.

In the 18-60Y Group the seroprotection power was, 89.7%, 81.8% and 100% at Day 21 against the H1N1, H3N2 and Yamagata strains, respectively. In the >60Y Group seroprotection power was, 75.0%, 51.4% and 100% at Day 21 against the H1N1, H3N2 and Yamagata strains, respectively.

During the 21-day follow-up period after vaccination, at least one unsolicited AE was reported for 8 (13.3%) subjects in the 18-60Y Group and for 11 (18.6%) subjects in the >60Y Group. During that period, no Grade 3 unsolicited AE was reported in the 18-60Y Group and at least one Grade 3 unsolicited AE was reported for one (1.7%) subject in the >60Y Group. During that same period, at least one unsolicited AE assessed by the investigator as related causally related to study vaccination was reported for 4 (6.7%) subjects in the 18-60Y Group and 3 (5.1%) subjects in the >60Y Group. No SAEs were reported during the entire study period.

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