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.: 111295 (FLU-D-QIV-001 PRI)

Title: Immunogenicity and safety study of a GlaxoSmithKline (GSK) influenza vaccine candidate GSK 2115160A in adults.
GSK 2115160A: GSK Biologicals' influenza vaccine.

Rationale: This study was designed to evaluate the safety and immunogenicity of a quadrivalent, an adjuvanted low dose quadrivalent and adjuvanted low dose trivalent influenza vaccine candidate compared to trivalent influenza vaccine in adults.
GSK 2115160A (QIV): GSK Biologicals' quadrivalent influenza vaccine.
GSK 2115160A (LD-QIV): GSK Biologicals' adjuvanted low dose quadrivalent influenza vaccine
GSK 2115160A (LD-TIV): GSK Biologicals' adjuvanted low dose trivalent influenza vaccine
GSK 2115160A (TIV): GSK Biologicals' trivalent influenza vaccine.

Phase: I/II

Study Period: 14 July-2008
to 25 August 2008 (Day 21, end of vaccination phase)
to 28 January-2009 (Day 180, end of follow-up)

Study Design: Single-centre, single blind, randomized (1:1:1:1), controlled study in 4 parallel groups
Subjects in each group were further stratified by age: 18-49 years and 50-60 years (3:1).

Centres: 1 centre in the Czech Republic

Indication: Immunisation of healthy male and female subjects aged 18 to 60 years against influenza

Treatment: The study groups (QIV & TIV) were sub-divided into sub-groups as follows:

- QIV-1 Group: Subjects in this group received 1 full dose of QIV vaccine.
- QIV-2 Group: Subjects in this group received 1 low dose of adjuvanted QIV vaccine.
- TIV-1 Group: Subjects in this group received 1 low dose of adjuvanted TIV vaccine.
- TIV-2 Group: Subjects in this group received 1 full dose of TIV vaccine.

The vaccine was administered intramuscularly in the deltoid region of the non-dominant arm at Day 0.

Objectives:

- To assess the immunological non-inferiority Geometric Mean Titre (GMT) of the quadrivalent influenza study vaccine over the trivalent influenza vaccine for the 3 recommended interpandemic strains.
- To assess the immunological non-inferiority (GMT) of the adjuvanted low dose quadrivalent influenza study vaccine over the adjuvanted low dose trivalent influenza vaccine for the 3 recommended interpandemic strains.
- To assess the immunological superiority (GMT) of the quadrivalent influenza study vaccine over the trivalent influenza vaccine in terms of B/Jiangsu/10/2003 strain that is not included in the trivalent influenza vaccine.
- To assess the immunological superiority (GMT) of the adjuvanted low dose quadrivalent influenza study vaccine over the adjuvanted low dose trivalent influenza study vaccine in terms of B/Jiangsu/10/2003 strain that is not included in the low dose adjuvanted trivalent influenza vaccine.

Primary Outcome/Efficacy Variable:
Observed variables

- At Days 0 and 21 serum haemagglutination-inhibition (HI) antibody titre, against each of the vaccine influenza virus strains, in each group.

Derived variables

- GMTs of HI antibody titres at Days 0 and 21.

Secondary Outcome/Efficacy Variable(s):*Humoral Immune response*
Observed variables

- At Days 0 and 21 serum haemagglutination-inhibition (HI) antibody titre, against each of the vaccine influenza virus strains, in each group.

Derived variables

- Geometric mean titres (GMTs) of HI antibody titres at Days 0 and 21
- Seroconversion rates (SCR)* at Day 21
- Seroconversion factors (SCF)** at Day 21
- Seroprotection rates (SPR)*** at Days 0 and 21

*SCR defined as the percentage of vaccinees who have 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 defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.

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

Safety

- Occurrence, intensity 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 each vaccination in each group.
- Occurrence, intensity 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 each vaccination in each group.
- Occurrence and relationship to vaccination of serious adverse events (SAEs) during the entire study period in each group.
- Occurrence, intensity* and relationship to vaccination* of medically significant conditions (MSC)[£] and occurrence of Auto-immune disease (AID) throughout the study period.

*Data were not analysed.

[£]MSCs were defined as those AEs prompting emergency room visits or physician visits that were not routine visits for physical examination or vaccination.

Statistical Methods:

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

- The Total Vaccinated cohort included all subjects with a documented vaccine administration.
- 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 during the study) for whom data concerning immunogenicity outcome variables 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 based on the ATP cohort for immunogenicity.

Inferential analyses.

GMT ratios [with two-sided 95% Confidence Intervals (CIs)] related to the comparisons of interest were computed. Acceptance values of 0.67 and 1 for the lower bound of the 95% CIs were considered for non-inferiority and superiority, respectively. Adjusted GMTs were estimated using an Analysis of Covariance (ANCOVA); adjusted GMT ratios (QIV-1 over TIV-2 and QIV-2 over TIV-1) with two sided 95 % CI were computed for each strain antibody.

Descriptive analyses.

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

- Seropositivity rate and Geometric mean titre (GMT) at Day 0 and Day 21
- Seroprotection rate at Day 0 and Day 21
- Seroconversion rate at Day 21
- Seroconversion factor at Day 21

Analysis of Safety:

The analysis was based on the Total Vaccinated cohort.

For each solicited local and general symptom, the percentages of subjects with the symptom reported within 7 days (Day 0-6) following the vaccination were tabulated with exact 95% CI by group. The same calculation was performed for symptoms with intensity of grade 3, as well as for solicited general symptoms assessed by the investigator as causally related to vaccination.

The percentage of subjects with unsolicited AEs within the 21 days (Day 0-20) following the vaccination was tabulated for each group according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms. The same tabulation was performed for grade 3 unsolicited AEs and for unsolicited AEs assessed by the investigator as related to vaccination.

The occurrence of medically significant conditions (MSCs), auto-immune diseases and serious adverse events (SAEs) were tabulated according to the MedDRA preferred terms for each group during the entire study period.

Study Population: Healthy male or female between, and including, 18 and 60 years of age at the time of the vaccination who did not have confirmed influenza infection within a year preceding the study start, were enrolled in the study. Females of childbearing potential had to practice adequate contraception for 30 days prior to vaccination, had a negative pregnancy test and had agreed to continue such precautions for 2 months after vaccination. A written informed consent was obtained from the subjects prior to study entry.

Number of subjects	QIV-1 Group	QIV-2 Group	TIV-1 Group	TIV-2 Group
Planned, N	105	105	105	105
Randomised, N (Total Vaccinated Cohort)	105	105	105	105
Completed to Day 21, n (%)	105 (100)	104 (99.0)	105 (100)	105 (100)

Completed to Day 180, n (%)	105 (100)	102 (97.1)	105 (100)	104 (99.0)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	3 (2.9)	0 (0.0)	1 (1.0)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	3 (2.9)	0 (0.0)	1 (1.0)
Demographics	QIV 1 Group	QIV 2 Group	TIV 1 Group	TIV 2 Group
N (Total Vaccinated Cohort)	105	105	105	105
Females:Males	61:44	66:39	66:39	58:47
Mean Age, years (SD)	38.5 (11.85)	37.6 (12.30)	36.6 (12.87)	37.4 (12.51)
White - Caucasian / European heritage, n (%)	104 (99.0)	105 (100)	105 (100)	105 (100)

Primary Efficacy Results: Adjusted ratios for A/Solomon Islands, A/Wisconsin, B/Malaysia and B/Jiangsu GMT on Day 21 (ATP cohort for immunogenicity)

Antibody	QIV-1 Groups		TIV-2 Groups		Adjusted GMT ratio (QIV-1/TIV-2)		
	N	Adjusted GMT	N	Adjusted GMT	Value	95% CI	
						LL	UL
A/Solomon Islands	104	129.8	105	138.7	0.94	0.69	1.26
A/Wisconsin	104	161.0	105	155.6	1.03	0.83	1.30
B/Malaysia	104	184.6	105	188.5	0.98	0.74	1.29
B/Jiangsu	104	182.5	105	44.8	4.08	3.26	5.11

Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio; LL = lower limit; UL = upper limit
Non-inferiority criterion for the 3 strains contained in both vaccines: LL of 95% CI > 0.67
Superiority criterion for B/Jiangsu strain (not contained in the TIV vaccine): LL of 95% > 1.

Primary Efficacy Results: Adjusted ratios for A/Solomon Islands, A/Wisconsin, B/Malaysia and B/Jiangsu GMT on Day 21 (ATP cohort for immunogenicity)

Antibody	QIV-2 Group		TIV-1 Group		Adjusted GMT ratio (QIV-2 /TIV-1)		
	N	Adjusted GMT	N	Adjusted GMT	Value	95% CI	
						LL	UL
A/Solomon Islands	104	148.9	104	156.8	0.95	0.70	1.28
A/Wisconsin	104	195.4	104	194.1	1.01	0.80	1.26
B/Malaysia	104	214.0	104	194.5	1.10	0.84	1.45
B/Jiangsu	104	162.2	104	54.9	2.95	2.36	3.70

Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio; LL = lower limit; UL = upper limit
Non-inferiority criterion for the 3 strains contained in both vaccines: LL of 95% CI > 0.67
Superiority criterion for B/Jiangsu strain (not contained in the TIV vaccine): LL of 95% > 1.

Primary Efficacy Results: Seropositivity rates and GMTs for HI antibodies against A/Solomon Islands, A/Wisconsin, B/Malaysia and B/Jiangsu strains on 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	QIV-1	PRE	104	67	64.4	54.4	73.6	21.4	16.1	28.4
		PI(D21)	104	102	98.1	93.2	99.8	130.0	106.1	159.4
	QIV-2	PRE	104	63	60.6	50.5	70.0	22.2	16.6	29.5
		PI(D21)	104	102	98.1	93.2	99.8	150.6	118.4	191.5
	TIV-1	PRE	104	66	63.5	53.4	72.7	23.3	17.5	31.0
		PI(D21)	104	103	99.0	94.8	100	160.4	129.1	199.3
	TIV-2	PRE	105	63	60.0	50.0	69.4	18.4	14.3	23.7
		PI(D21)	105	102	97.1	91.9	99.4	133.8	105.6	169.7
A/Wisconsin	QIV-1	PRE	104	84	80.8	71.9	87.8	29.3	23.0	37.3
		PI(D21)	104	104	100	96.5	100	162.1	138.0	190.4
	QIV-2	PRE	104	77	74.0	64.5	82.1	25.7	19.8	33.3

		PI(D21)	104	104	100	96.5	100	189.5	158.9	226.0
	TIV-1	PRE	104	79	76.0	66.6	83.8	30.7	23.7	39.8
		PI(D21)	104	104	100	96.5	100	197.9	169.1	231.7
	TIV-2	PRE	105	83	79.0	70.0	86.4	29.0	22.5	37.4
		PI(D21)	105	104	99.0	94.8	100	156.3	127.5	191.6
B/Malaysia	QIV-1	PRE	104	85	81.7	72.9	88.6	32.2	24.8	41.8
		PI(D21)	104	104	100	96.5	100	192.8	159.6	232.9
	QIV-2	PRE	104	78	75.0	65.6	83.0	26.6	20.2	35.0
		PI(D21)	104	103	99.0	94.8	100	213.0	174.0	260.9
	TIV-1	PRE	104	73	70.2	60.4	78.8	23.2	17.7	30.4
		PI(D21)	104	104	100	96.5	100	187.0	151.9	230.3
	TIV-2	PRE	105	79	75.2	65.9	83.1	27.2	20.6	35.8
		PI(D21)	105	105	100	96.5	100	188.5	150.0	237.0
B/Jiangsu	QIV-1	PRE	104	73	70.2	60.4	78.8	19.6	15.6	24.8
		PI(D21)	104	104	100	96.5	100	179.1	151.4	211.9
	QIV-2	PRE	104	70	67.3	57.4	76.2	19.5	15.4	24.5
		PI(D21)	104	104	100	96.5	100	158.3	130.7	191.9
	TIV-1	PRE	104	76	73.1	63.5	81.3	23.4	18.3	29.7
		PI(D21)	104	98	94.2	87.9	97.9	59.2	47.3	74.0
	TIV-2	PRE	105	70	66.7	56.8	75.6	19.2	15.2	24.3
		PI(D21)	105	97	92.4	85.5	96.7	43.4	34.5	54.6

GMT = Geometric Mean Titre
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 blood sample at Day 0
PI(D21) = Post-vaccination blood sample at Day 21

Secondary Outcome Variable(s): Seroconversion rate (SCR) for HI antibodies against A/Solomon Islands, A/Wisconsin, B/Malaysia and B/Jiangsu strains on Day 21 (ATP cohort for immunogenicity)

Vaccine strain	Group	N	SCR			
			n	%	95% CI	
					LL	UL
A/Solomon Islands	QIV-1	104	59	56.7	46.7	66.4
	QIV-2	104	60	57.7	47.6	67.3
	TIV-1	104	57	54.8	44.7	64.6
	TIV-2	105	63	60.0	50.0	69.4
A/Wisconsin	QIV-1	104	63	60.6	50.5	70.0
	QIV-2	104	69	66.3	56.4	75.3
	TIV-1	104	67	64.4	54.4	73.6
	TIV-2	105	62	59.0	49.0	68.5
B/Malaysia	QIV-1	104	60	57.7	47.6	67.3
	QIV-2	104	68	65.4	55.4	74.4
	TIV-1	104	59	56.7	46.7	66.4
	TIV-2	105	62	59.0	49.0	68.5
B/Jiangsu	QIV-1	104	79	76.0	66.6	83.8
	QIV-2	104	82	78.8	69.7	86.2
	TIV-1	104	28	26.9	18.7	36.5
	TIV-2	105	20	19.0	12.0	27.9

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): Seroconversion factor (SCF) for HI antibodies against A/Solomon Islands, A/Wisconsin, B/Malaysia and B/Jiangsu strains on Day 21 (ATP cohort for immunogenicity)

Vaccine strain	Group	N	SCF		
			Value	95% CI	
				LL	UL
A/Solomon Islands	QIV-1	104	6.1	4.6	8.0
	QIV-2	104	6.8	5.0	9.2
	TIV-1	104	6.9	5.0	9.4
	TIV-2	105	7.3	5.3	9.9
A/Wisconsin	QIV-1	104	5.5	4.4	6.9
	QIV-2	104	7.4	5.8	9.4
	TIV-1	104	6.4	5.0	8.3
	TIV-2	105	5.4	4.1	7.0
B/Malaysia	QIV-1	104	6.0	4.7	7.7
	QIV-2	104	8.0	6.1	10.5
	TIV-1	104	8.1	5.9	11.0
	TIV-2	105	6.9	5.2	9.3
B/Jiangsu	QIV-1	104	9.1	7.2	11.5
	QIV-2	104	8.1	6.6	10.0
	TIV-1	104	2.5	2.1	3.0
	TIV-2	105	2.3	1.9	2.6

N = Number of subjects with pre- and post-vaccination results available
SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])
95% CI = 95% confidence interval; LL = Lower Limit; UL = Upper Limit

Secondary Outcome Variable(s): Seroprotection rates (SPR) for HI antibodies against A/Solomon Islands, A/Wisconsin, B/Malaysia and B/Jiangsu strains on Days 0 and 21 (ATP cohort for immunogenicity)

Vaccine strain	Group	Timing	N	SPR			
				n	%	95% CI	
						LL	UL
A/Solomon Islands	QIV-1	PRE	104	39	37.5	28.2	47.5
		PI(D21)	104	96	92.3	85.4	96.6
	QIV-2	PRE	104	44	42.3	32.7	52.4
		PI(D21)	104	92	88.5	80.7	93.9
	TIV-1	PRE	104	42	40.4	30.9	50.5
		PI(D21)	104	97	93.3	86.6	97.3
	TIV-2	PRE	105	37	35.2	26.2	45.2
		PI(D21)	105	95	90.5	83.2	95.3
A/Wisconsin	QIV-1	PRE	104	53	51.0	41.0	60.9
		PI(D21)	104	101	97.1	91.8	99.4
	QIV-2	PRE	104	48	46.2	36.3	56.2
		PI(D21)	104	102	98.1	93.2	99.8
	TIV-1	PRE	104	56	53.8	43.8	63.7
		PI(D21)	104	104	100	96.5	100
	TIV-2	PRE	105	58	55.2	45.2	65.0
		PI(D21)	105	101	96.2	90.5	99.0
B/Malaysia	QIV-1	PRE	104	53	51.0	41.0	60.9
		PI(D21)	104	101	97.1	91.8	99.4
	QIV-2	PRE	104	49	47.1	37.2	57.2
		PI(D21)	104	101	97.1	91.8	99.4
	TIV-1	PRE	104	44	42.3	32.7	52.4
		PI(D21)	104	100	96.2	90.4	98.9
	TIV-2	PRE	105	47	44.8	35.0	54.8
		PI(D21)	105	98	93.3	86.7	97.3
B/Jiangsu	QIV-1	PRE	104	33	31.7	22.9	41.6
		PI(D21)	104	102	98.1	93.2	99.8
	QIV-2	PRE	104	40	38.5	29.1	48.5
		PI(D21)	104	99	95.2	89.1	98.4
	TIV-1	PRE	104	45	43.3	33.6	53.3

		PI(D21)	104	78	75.0	65.6	83.0
	TIV-2	PRE	105	41	39.0	29.7	49.1
		PI(D21)	105	67	63.8	53.9	73.0

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 blood sample at Day 0
PI(D21) = Post-vaccination blood sample at Day 21

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

Symptom	Intensity	QIV-1 Group					QIV-2 Group					TIV-1 Group					TIV-2 Group				
		N	n	%	95 % CI		N	n	%	95 % CI		N	n	%	95 % CI		N	n	%	95 % CI	
					LL	UL				LL	UL				LL	UL				LL	UL
Pain	Any	105	76	72.4	62.8	80.7	104	79	76.0	66.6	83.8	105	74	70.5	60.8	79.0	105	52	49.5	39.6	59.5
	Grade 3	105	0	0.0	0.0	3.5	104	2	1.9	0.2	6.8	105	3	2.9	0.6	8.1	105	0	0.0	0.0	3.5
Redness	Any	105	3	2.9	0.6	8.1	104	6	5.8	2.1	12.1	105	5	4.8	1.6	10.8	105	1	1.0	0.0	5.2
	>100 mm	105	0	0.0	0.0	3.5	104	0	0.0	0.0	3.5	105	0	0.0	0.0	3.5	105	0	0.0	0.0	3.5
Swelling	Any	105	3	2.9	0.6	8.1	104	4	3.8	1.1	9.6	105	7	6.7	2.7	13.3	105	2	1.9	0.2	6.7
	>100 mm	105	0	0.0	0.0	3.5	104	0	0.0	0.0	3.5	105	0	0.0	0.0	3.5	105	0	0.0	0.0	3.5

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 specified solicited symptoms regardless of intensity grade
Grade 3 pain = Considerable pain that prevented normal activities

Secondary Outcome Variable(s): Incidence of solicited local symptoms reported by the former GSK rules of grading during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort)

Symptom	Intensity	QIV-1 Group					QIV-2 Group					TIV-1 Group					TIV-2 Group				
		N	n	%	95 % CI		N	n	%	95 % CI		N	n	%	95 % CI		N	n	%	95 % CI	
					LL	UL				LL	UL				LL	UL				LL	UL
Pain	Any	105	76	72.4	62.8	80.7	104	79	76.0	66.6	83.8	105	74	70.5	60.8	79.0	105	52	49.5	39.6	59.5
	Grade 3	105	0	0.0	0.0	3.5	104	2	1.9	0.2	6.8	105	3	2.9	0.6	8.1	105	0	0.0	0.0	3.5
Redness	Any	105	3	2.9	0.6	8.1	104	6	5.8	2.1	12.1	105	5	4.8	1.6	10.8	105	1	1.0	0.0	5.2
	>50 mm	105	1	1.0	0.0	5.2	104	2	1.9	0.2	6.8	105	1	1.0	0.0	5.2	105	0	0.0	0.0	3.5
Swelling	Any	105	3	2.9	0.6	8.1	104	4	3.8	1.1	9.6	105	7	6.7	2.7	13.3	105	2	1.9	0.2	6.7
	>50 mm	105	1	1.0	0.0	5.2	104	2	1.9	0.2	6.8	105	3	2.9	0.6	8.1	105	1	1.0	0.0	5.2

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 specified solicited symptoms regardless of intensity grade
Grade 3 pain = Symptom that prevented normal activities
Note: all solicited local symptoms were considered related to the vaccine

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

Symptom	Intensity/Relationship	QIV-1 Group					QIV-2 Group				
		N	n	%	95 % CI		N	n	%	95 % CI	
					LL	UL				LL	UL
Arthralgia	Any	105	6	5.7	2.1	12.0	104	25	24.0	16.2	33.4
	Grade 3	105	1	1.0	0.0	5.2	104	3	2.9	0.6	8.2
	Related	105	6	5.7	2.1	12.0	104	25	24.0	16.2	33.4
Fatigue	Any	105	33	31.4	22.7	41.2	104	47	45.2	35.4	55.3
	Grade 3	105	2	1.9	0.2	6.7	104	4	3.8	1.1	9.6
	Related	105	32	30.5	21.9	40.2	104	47	45.2	35.4	55.3
Headache	Any	105	25	23.8	16.0	33.1	104	36	34.6	25.6	44.6
	Grade 3	105	3	2.9	0.6	8.1	104	2	1.9	0.2	6.8
	Related	105	24	22.9	15.2	32.1	104	33	31.7	22.9	41.6
Myalgia	Any	105	17	16.2	9.7	24.7	104	40	38.5	29.1	48.5

	Grade 3	105	1	1.0	0.0	5.2	104	3	2.9	0.6	8.2
	Related	105	17	16.2	9.7	24.7	104	40	38.5	29.1	48.5
Nausea	Any	105	8	7.6	3.3	14.5	104	11	10.6	5.4	18.1
	Grade 3	105	2	1.9	0.2	6.7	104	2	1.9	0.2	6.8
	Related	105	8	7.6	3.3	14.5	104	10	9.6	4.7	17.0
Shivering	Any	105	4	3.8	1.0	9.5	104	10	9.6	4.7	17.0
	Grade 3	105	1	1.0	0.0	5.2	104	2	1.9	0.2	6.8
	Related	105	4	3.8	1.0	9.5	104	10	9.6	4.7	17.0
Temperature (Oral)	≥38°C	105	1	1.0	0.0	5.2	104	3	2.9	0.6	8.2
	≥39°C	105	0	0.0	0.0	3.5	104	0	0.0	0.0	3.5
	Related	105	1	1.0	0.0	5.2	104	3	2.9	0.6	8.2
Symptom	Intensity/Relationship	TIV-1 Group					TIV-2 Group				
		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL
Arthralgia	Any	105	13	12.4	6.8	20.2	105	12	11.4	6.0	19.1
	Grade 3	105	2	1.9	0.2	6.7	105	0	0.0	0.0	3.5
	Related	105	13	12.4	6.8	20.2	105	11	10.5	5.3	18.0
Fatigue	Any	105	36	34.3	25.3	44.2	105	34	32.4	23.6	42.2
	Grade 3	105	3	2.9	0.6	8.1	105	1	1.0	0.0	5.2
	Related	105	36	34.3	25.3	44.2	105	33	31.4	22.7	41.2
Headache	Any	105	28	26.7	18.5	36.2	105	26	24.8	16.9	34.1
	Grade 3	105	1	1.0	0.0	5.2	105	1	1.0	0.0	5.2
	Related	105	26	24.8	16.9	34.1	105	23	21.9	14.4	31.0
Myalgia	Any	105	33	31.4	22.7	41.2	105	15	14.3	8.2	22.5
	Grade 3	105	3	2.9	0.6	8.1	105	1	1.0	0.0	5.2
	Related	105	33	31.4	22.7	41.2	105	15	14.3	8.2	22.5
Nausea	Any	105	8	7.6	3.3	14.5	105	9	8.6	4.0	15.6
	Grade 3	105	2	1.9	0.2	6.7	105	1	1.0	0.0	5.2
	Related	105	8	7.6	3.3	14.5	105	8	7.6	3.3	14.5
Shivering	Any	105	9	8.6	4.0	15.6	105	4	3.8	1.0	9.5
	Grade 3	105	1	1.0	0.0	5.2	105	0	0.0	0.0	3.5
	Related	105	9	8.6	4.0	15.6	105	4	3.8	1.0	9.5
Temperature (Oral)	≥38°C	105	2	1.9	0.2	6.7	105	1	1.0	0.0	5.2
	≥39°C	105	0	0.0	0.0	3.5	105	0	0.0	0.0	3.5
	Related	105	2	1.9	0.2	6.7	105	1	1.0	0.0	5.2

N= number of subjects with the documented dose
n/%= number/percentage of subjects reporting at least once the symptom
Any = occurrence of any specified solicited symptoms regardless of intensity grade or relationship to vaccination
Grade 3 symptom = Symptom that prevented normal activities
Related = Symptom assessed by the investigator as causally related to the vaccination.
95% CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Secondary Outcome Variable(s): Incidence of solicited general symptoms reported by former GSK rules of grading during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort)

Symptom	Intensity/Relationship	QIV-1 Group					QIV-2 Group				
		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL
Arthralgia	Any	105	6	5.7	2.1	12.0	104	25	24.0	16.2	33.4
	Grade 3	105	1	1.0	0.0	5.2	104	3	2.9	0.6	8.2
	Related	105	6	5.7	2.1	12.0	104	25	24.0	16.2	33.4
Fatigue	Any	105	33	31.4	22.7	41.2	104	47	45.2	35.4	55.3
	Grade 3	105	2	1.9	0.2	6.7	104	4	3.8	1.1	9.6
	Related	105	32	30.5	21.9	40.2	104	47	45.2	35.4	55.3
Headache	Any	105	25	23.8	16.0	33.1	104	36	34.6	25.6	44.6
	Grade 3	105	3	2.9	0.6	8.1	104	2	1.9	0.2	6.8
	Related	105	24	22.9	15.2	32.1	104	33	31.7	22.9	41.6

Myalgia	Any	105	17	16.2	9.7	24.7	104	40	38.5	29.1	48.5
	Grade 3	105	1	1.0	0.0	5.2	104	3	2.9	0.6	8.2
	Related	105	17	16.2	9.7	24.7	104	40	38.5	29.1	48.5
Nausea	Any	105	8	7.6	3.3	14.5	104	11	10.6	5.4	18.1
	Grade 3	105	2	1.9	0.2	6.7	104	2	1.9	0.2	6.8
	Related	105	8	7.6	3.3	14.5	104	10	9.6	4.7	17.0
Shivering	Any	105	4	3.8	1.0	9.5	104	10	9.6	4.7	17.0
	Grade 3	105	1	1.0	0.0	5.2	104	2	1.9	0.2	6.8
	Related	105	4	3.8	1.0	9.5	104	10	9.6	4.7	17.0
Temperature (Oral)	≥37.5°C	105	1	1.0	0.0	5.2	104	2	1.9	0.2	6.8
	>39°C	105	0	0.0	0.0	3.5	104	0	0.0	0.0	3.5
	Related	105	1	1.0	0.0	5.2	104	2	1.9	0.2	6.8
Symptom	Intensity/Relationship	TIV-1 Group					TIV-2 Group				
		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL
Arthralgia	Any	105	13	12.4	6.8	20.2	105	12	11.4	6.0	19.1
	Grade 3	105	2	1.9	0.2	6.7	105	0	0.0	0.0	3.5
	Related	105	13	12.4	6.8	20.2	105	11	10.5	5.3	18.0
Fatigue	Any	105	36	34.3	25.3	44.2	105	34	32.4	23.6	42.2
	Grade 3	105	3	2.9	0.6	8.1	105	1	1.0	0.0	5.2
	Related	105	36	34.3	25.3	44.2	105	33	31.4	22.7	41.2
Headache	Any	105	28	26.7	18.5	36.2	105	26	24.8	16.9	34.1
	Grade 3	105	1	1.0	0.0	5.2	105	1	1.0	0.0	5.2
	Related	105	26	24.8	16.9	34.1	105	23	21.9	14.4	31.0
Myalgia	Any	105	33	31.4	22.7	41.2	105	15	14.3	8.2	22.5
	Grade 3	105	3	2.9	0.6	8.1	105	1	1.0	0.0	5.2
	Related	105	33	31.4	22.7	41.2	105	15	14.3	8.2	22.5
Nausea	Any	105	8	7.6	3.3	14.5	105	9	8.6	4.0	15.6
	Grade 3	105	2	1.9	0.2	6.7	105	1	1.0	0.0	5.2
	Related	105	8	7.6	3.3	14.5	105	8	7.6	3.3	14.5
Shivering	Any	105	9	8.6	4.0	15.6	105	4	3.8	1.0	9.5
	Grade 3	105	1	1.0	0.0	5.2	105	0	0.0	0.0	3.5
	Related	105	9	8.6	4.0	15.6	105	4	3.8	1.0	9.5
Temperature (Oral)	≥37.5°C	105	2	1.9	0.2	6.7	105	1	1.0	0.0	5.2
	>39°C	105	0	0.0	0.0	3.5	105	0	0.0	0.0	3.5
	Related	105	2	1.9	0.2	6.7	105	1	1.0	0.0	5.2

N= number of subjects with the documented dose
n/%= number/percentage of subjects reporting at least once the symptom
Any = occurrence of any specified solicited symptoms regardless of intensity grade or relationship to vaccination
Grade 3 symptom = Symptom that prevented normal activities
Related = Symptom assessed by the investigator as causally related to the vaccination.
95% CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Secondary Outcome Variable(s): Percentage of subjects reporting the occurrence of medically attended unsolicited adverse events (MAEs), during the entire study period (Days 0-180) (Total Vaccinated cohort)

MAE(s)	QIV-1 Group N=105	QIV-2 Group N = 105	TIV-1 Group N = 105	TIV-2 Group N = 105
Subjects with any MAE(s), n (%)	1 (1.0)	4 (3.8)	5 (4.8)	5 (4.8)
Conjunctivitis	-	-	-	1 (1.0)
Toothache	-	-	1 (1.0)	-
Cystitis	-	-	-	1 (1.0)
Pharyngitis	-	-	-	1 (1.0)
Tonsillitis	-	1 (1.0)	-	-
Vaginal infection	-	1 (1.0)	-	1 (1.0)
Fibula fracture	-	1 (1.0)	-	-
Back pain	1 (1.0)	-	-	-

Musculoskeletal pain	-	-	-	1 (1.0)
Spondylitis	-	1 (1.0)	-	-
Tendonitis	-	-	1 (1.0)	-
Metrorrhagia	-	-	1 (1.0)	-
Prurigo	-	-	1 (1.0)	-
Aborted pregnancy	-	-	1 (1.0)	-
Haemorrhage	-	-	-	1 (1.0)
-: Adverse event absent				
Secondary Outcome Variable(s): Percentage of subjects reporting the occurrence of auto-immune diseases (AID), through the entire study period (Days 0-180) (Total vaccinated cohort)				
AID(s)	QIV-1 Group N=105	QIV-2 Group N = 105	TIV-1 Group N = 105	TIV-2 Group N = 105
Subjects with any AID, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Safety Results: Number (%) of subjects reporting the occurrence of unsolicited AEs, within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort)				
Most frequent adverse events - On-Therapy (occurring within Days 0-20 following vaccination)	QIV-1 Group N = 105	QIV-2 Group N = 105	TIV-1 Group N = 105	TIV-2 Group N = 105
Subjects with any AEs, n (%)	7 (6.7)	7 (6.7)	16 (15.2)	11 (10.5)
Subjects with Grade 3 AEs, n (%)	0 (0.0)	1 (1.0)	3 (2.9)	2 (1.9)
Subjects with related AEs, n (%)	3 (2.9)	3 (2.9)	7 (6.7)	3 (2.9)
Lymphadenopathy	-	-	1 (1.0)	-
Conjunctivitis	-	-	-	1 (1.0)
Abdominal pain	-	-	1 (1.0)	-
Diarrhoea	1 (1.0)	1 (1.0)	-	1 (1.0)
Nausea	-	-	-	1 (1.0)
Toothache	-	-	4 (3.8)	
Vomiting	-	-	-	1 (1.0)
Chills	1 (1.0)	2 (1.9)	3 (2.9)	-
Injection site pruritus	-	-	1 (1.0)	-
Injection site warmth	1 (1.0)	-	-	-
Pyrexia	-	1 (1.0)	1 (1.0)	-
Swelling	-	-	-	1 (1.0)
Cystitis	-	-	-	1 (1.0)
Pharyngitis	2 (1.9)	-	-	1 (1.0)
Rhinitis	1 (1.0)	-	-	-
Tonsillitis	-	1 (1.0)	-	-
Upper respiratory tract infection	-	1 (1.0)	1 (1.0)	1 (1.0)
Vaginal infection	-	1 (1.0)	-	1(1.0)
Fibula fracture	-	1 (1.0)	-	-
Arthralgia	-	-	-	1 (1.0)
Back pain	1 (1.0)	-	-	-
Musculoskeletal pain	-	-	-	1 (1.0)
Myalgia	-	1 (1.0)	-	-
Neck pain	-	-	1 (1.0)	-
Pain in extremity	-	-	1 (1.0)	-
Tendonitis	-	-	1 (1.0)	-
Headache	-	-	2 (1.9)	2 (1.9)
Paraesthesia	1 (1.0)	-	-	-
Insomnia	-	1 (1.0)	-	-
Cough	1 (1.0)	-	-	-
Pharyngolaryngeal pain	-	-	-	1 (1.0)
-: Adverse event absent				
Safety Results: Number (%) of subjects reporting serious adverse events, during the entire study period (Days 0-180) (Total Vaccinated cohort)				

Serious adverse event, n (%) [n considered by the investigator to be related to study medication]				
All SAEs	QIV-1 Group N = 105	QIV-2 Group N = 105	TIV-1 Group N = 105	TIV-2 Group N = 105
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.0) [0]
Haemorrhage	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (1.0) [0]
Fatal SAEs	QIV-1 Group N = 105	QIV-2 Group N = 105	TIV-1 Group N = 105	TIV-2 Group N = 105
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:

At Day 0, following were the respective GMT values in QIV 1, QIV 2, TIV 1 and TIV 2 groups for HI antibodies against

- A/Solomon Islands /3/2066 (H1N1) strain: 21.4, 22.2, 23.3 and 18.4,
- A/Wisconsin/67/2005 (H3N2) strain: 29.3, 25.7, 30.7 and 29.0,
- B/Malaysia/2506/2004 strain: 32.2, 26.6, 23.2 and 27.2,
- B/Jiangsu/10/2003 strain: 19.6, 19.5, 23.4 and 19.2.

At Day 21 after vaccination, here were the respective GMT values in QIV 1, QIV 2, TIV 1 and TIV 2 groups for HI antibodies against:

- A/Solomon Islands /3/2066 (H1N1) strain: 130.0, 150.6, 160.4 and 133.8
- A/Wisconsin/67/2005 (H3N2) strain: 162.1, 189.5, 197.9 and 156.3,
- B/Malaysia/2506/2004 strain: 192.8, 213.0, 187.0 and 188,
- B/Jiangsu/10/2003 strain: 179.1, 158.3, 59.2 and 43.4.

Within the 21-day post vaccination period, 7 subjects (6.7%) in each QIV-1 & QIV-2 groups, 16 subjects (15.2%) in TIV-1 Group and 11 subjects (10.5%) in TIV-2 Group reported at least one unsolicited AE.

During the entire study period (Days 0-180), 1 SAE was reported in 1 subject from the TIV-2 Group. This SAE was assessed by the investigator to be not related to the study vaccination. No fatal SAEs were reported during the study.

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