



Clinical trial results:

A phase III, randomized, open-label, multicentre clinical trial to assess the immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A when co-administered with GSK Biologicals' quadrivalent influenza vaccine FLU-D-QIV (GSK2321138A) versus separate administration of the two vaccines in adults aged 50 years and older.

Summary

EudraCT number	2013-000372-15
Trial protocol	DE
Global end of trial date	20 March 2015

Results information

Result version number	v1
This version publication date	02 April 2016
First version publication date	02 April 2016

Trial information

Trial identification

Sponsor protocol code	117036
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01954251
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 March 2015
Global end of trial reached?	Yes
Global end of trial date	20 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the vaccine response rate (VRR) to the HZ/su vaccine (based on the humoral immune response) one month after the last vaccine dose in the HZ/su-FLU-D-QIV co-administration group.

To demonstrate non-inferiority in terms of humoral immune response of two doses of the HZ/su vaccine when FLU-D-QIV vaccine is co-administered with the first HZ/su vaccine dose compared to two doses of HZ/su vaccine given alone, one month after the last vaccine dose.

To demonstrate non-inferiority (in terms of HI antibody Geometric mean titres (GMTs)) of one dose of FLU-D-QIV vaccine when co-administered with the first HZ/su vaccine dose compared to one dose of FLU-D-QIV vaccine given alone, for the four strains included in FLU-D-QIV vaccine, at Day 21 post vaccination.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for 30 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 565
Country: Number of subjects enrolled	Canada: 132
Country: Number of subjects enrolled	United States: 132
Worldwide total number of subjects	829
EEA total number of subjects	565

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	465
From 65 to 84 years	364
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of the 829 subjects enrolled in this trial, 1 subject did not receive vaccination even though subject number had been allocated, hence he/she was excluded from study start.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK1437173A + GSK2321138A Group

Arm description:

The subjects assigned to the Co-Ad group received one injection of the FLU-D-QIV vaccine and one injection of the HZ/su study vaccine during the first visit and a second injection of the HZ/su study vaccine during the third visit, two months later.

Arm type	Experimental
Investigational medicinal product name	Herpes Zoster vaccine GSK 1437173A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses administered intramuscularly (IM) in the deltoid region of the non-dominant arm.

Investigational medicinal product name	GSK Biologicals' quadrivalent seasonal influenza vaccine FLU-D-QIV GSK2321138A
Investigational medicinal product code	
Other name	Influsplit™ Tetra (Germany); Fluarix™ Quadrivalent (United States)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses administered intramuscularly (IM) in the deltoid region of the dominant arm.

Arm title	Control Group
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Arm description:

The subjects assigned to the Control group received all vaccines separately: one injection of the FLU-D-QIV vaccine at the first visit, one injection of the HZ/su study vaccine at the third visit and a second injection of the HZ/su study vaccine at the fourth visit, all two months apart.

Arm type	Active comparator
Investigational medicinal product name	Herpes Zoster vaccine GSK 1437173A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses administered intramuscularly (IM) in the deltoid region of the non-dominant arm.

Investigational medicinal product name	GSK Biologicals' quadrivalent seasonal influenza vaccine FLU-D-QIV GSK2321138A
Investigational medicinal product code	
Other name	Influsplit™ Tetra (Germany); Fluarix™ Quadrivalent (United States)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses administered intramuscularly (IM) in the deltoid region of the dominant arm.

Number of subjects in period 1^[1]	GSK1437173A + GSK2321138A Group	Control Group
Started	413	415
Completed	400	396
Not completed	13	19
Adverse event, serious fatal	4	5
Consent withdrawn by subject	2	6
Adverse event, non-fatal	1	2
Lost to follow-up	6	6

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of the 829 subjects enrolled in this trial, 1 subject did not receive vaccination even though subject number had been allocated, hence he/she was excluded from study start.

Baseline characteristics

Reporting groups

Reporting group title	GSK1437173A + GSK2321138A Group
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Reporting group description:

The subjects assigned to the Co-Ad group received one injection of the FLU-D-QIV vaccine and one injection of the HZ/su study vaccine during the first visit and a second injection of the HZ/su study vaccine during the third visit, two months later.

Reporting group title	Control Group
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Reporting group description:

The subjects assigned to the Control group received all vaccines separately: one injection of the FLU-D-QIV vaccine at the first visit, one injection of the HZ/su study vaccine at the third visit and a second injection of the HZ/su study vaccine at the fourth visit, all two months apart.

Reporting group values	GSK1437173A + GSK2321138A Group	Control Group	Total
Number of subjects	413	415	828
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	63.4	63.4	
standard deviation	± 8.3	± 8.8	-
Gender categorical Units: Subjects			
Female	211	218	429
Male	202	197	399

End points

End points reporting groups

Reporting group title	GSK1437173A + GSK2321138A Group
Reporting group description: The subjects assigned to the Co-Ad group received one injection of the FLU-D-QIV vaccine and one injection of the HZ/su study vaccine during the first visit and a second injection of the HZ/su study vaccine during the third visit, two months later.	
Reporting group title	Control Group
Reporting group description: The subjects assigned to the Control group received all vaccines separately: one injection of the FLU-D-QIV vaccine at the first visit, one injection of the HZ/su study vaccine at the third visit and a second injection of the HZ/su study vaccine at the fourth visit, all two months apart.	

Primary: Number of subjects with vaccine response to anti-gE antibodies

End point title	Number of subjects with vaccine response to anti-gE
End point description: The vaccine response (VRR) for anti-gE humoral immunogenicity, as determined by enzyme-linked immunosorbent assay (ELISA), was assessed only in subjects from the GSK1437173A + GSK2321138A Group. The VRR for anti-gE was defined as the percentage of subjects who had at least: a 4-fold increase in the post-dose 2 anti-gE antibody concentration as compared to the pre-vaccination anti-gE antibody concentration, for subjects who were seropositive at baseline (cut-off ≥ 97 mIU/ml), or, a 4-fold increase in the post dose 2 anti-gE antibody concentrations as compared to the anti-gE antibodies cut-off value for seropositivity, for subjects who were seronegative at baseline (cut-off < 97 mIU/ml).	
End point type	Primary
End point timeframe: At one month post-dose 2 (Month 3)	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: This outcome was descriptive, hence no statistical analyses were required. [2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome was descriptive, hence no statistical analyses were required.	

End point values	GSK1437173A + GSK2321138A Group			
Subject group type	Reporting group			
Number of subjects analysed	382			
Units: Subjects	366			

Statistical analyses

No statistical analyses for this end point

Primary: Vaccine response for anti-gE humoral immunogenicity

End point title	Vaccine response for anti-gE humoral immunogenicity ^{[3][4]}
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End point description:

The vaccine response (VRR) for anti-gE humoral immunogenicity, as determined by enzyme-linked immunosorbent assay (ELISA), was assessed only in subjects from the GSK1437173A + GSK2321138A Group. The VRR for anti-gE was defined as the percentage of subjects who had at least: a 4-fold increase in the post-dose 2 anti-gE antibody concentration as compared to the pre-vaccination anti-gE antibody concentration, for subjects who were seropositive at baseline (cut-off ≥ 97 mIU/ml), or, a 4-fold increase in the post dose 2 anti-gE antibody concentrations as compared to the anti-gE antibodies cut-off value for seropositivity, for subjects who were seronegative at baseline (cut-off < 97 mIU/ml). Criterion used: the objective was met if the Lower Limit (LL) of the 95% confidence interval (CI) of the VRR for anti-gE antibody concentrations was at least 60%.

End point type	Primary
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End point timeframe:

At one month post-dose 2 (Month 3)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This outcome was descriptive, hence no statistical analyses were required.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to different number of vaccine doses administered, the results for the two groups were presented separately.

End point values	GSK1437173A + GSK2321138A Group			
Subject group type	Reporting group			
Number of subjects analysed	382			
Units: Percentage				
number (confidence interval 95%)	95.8 (93.3 to 97.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Adjusted geometric mean ELISA concentrations of anti-gE antibodies

End point title	Adjusted geometric mean ELISA concentrations of anti-gE antibodies
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End point description:

Geometric means (GMs) of post-vaccination concentrations (Month 3 for GSK1437173A + GSK2321138A group and Month 5 for Control group) was calculated conditionally to the means of the pre-vaccination log-transformed concentrations for anti-gE (Month 0 for GSK1437173A + GSK2321138A group and Month 2 for Control group). Adjusted Least Squares (LS) means and difference of LS means between the groups were calculated together with 2-sided 95% CIs and back-transformed to the original units to provide GMCs.

End point type	Primary
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End point timeframe:

At one month post-dose 2 (Month 3 for GSK1437173A + GSK2321138A group and Month 5 for Control group)

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	382	388		
Units: mIU/mL				
geometric mean (confidence interval 95%)	52151.6 (48356 to 56245.2)	56247.4 (52177.3 to 60634.9)		

Statistical analyses

Statistical analysis title	Adjusted GMC rate 1 of anti-gE antibodies
Statistical analysis description:	
Adjusted ratios of Control group over GSK1437173A + GSK2321138A group in anti-gE antibody ELISA concentrations GMCs at one month after last vaccine dose. An Analysis of Covariance (ANCOVA) model was used to analyse post-vaccination log-transformed concentrations of anti-gE. The fixed-effect model included the minimisation variable (age cohorts) and the treatment as fixed effect. The pre-vaccination log-transformed concentrations were included as continuous covariate.	
Comparison groups	GSK1437173A + GSK2321138A Group v Control Group
Number of subjects included in analysis	770
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[5]
Method	ANCOVA
Parameter estimate	Adjusted Geometric mean concentration ra
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.2

Notes:

[5] - Comparison at one month after the last dose of HZ/su was performed between the Control group and GSK1437173A + GSK2321138A group. The GSK1437173A + GSK2321138A group was considered as statistically significant non-inferior compared to the Control group in terms of immunogenicity if the UL of the 2-sided 95% CI of the ratio of GMs between the Control and the Co-Ad group (Control over GSK1437173A + GSK2321138A) was below 1.5.

Primary: FLU Haemagglutination inhibition (HI) antibodies titers

End point title	FLU Haemagglutination inhibition (HI) antibodies titers
End point description:	
For each strain included in the FLU-D-QIV vaccine, an ANOVA model was used to analyze post-vaccination log-transformed titers. The fixed-effect model included the minimization variable (age cohorts) and the treatment as fixed effect. The pre-vaccination log-transformed concentrations were included as continuous covariate. Geometric Means (GM) of post-vaccination titers (Day 21) were calculated conditionally to the means of the pre-vaccination log-transformed titers (Month 0) for each strain. Adjusted GMTs (GMTs adjusted for baseline titers) and Adjusted GMT ratios were calculated together with 2-sided 95% CIs.	
End point type	Primary
End point timeframe:	
At Day 21 post vaccination	

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	394		
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/California/7/2009 H1N1 HI Day 21	187.5 (166.7 to 210.8)	194.3 (173 to 218.1)		
Flu A/Texas/50/2012 H3N2 HI Day 21	63.7 (58.3 to 69.7)	65.9 (60.3 to 72)		
Flu B/Brisbane/60/2008 Victoria HI Day 21	170.2 (156.1 to 185.6)	181.6 (166.7 to 197.8)		
Flu B/Massachusetts/2/2012 Yamagata HI Day 21	423.5 (392 to 457.5)	413.9 (383.4 to 446.8)		

Statistical analyses

Statistical analysis title	Adjusted GMT ratio 1 of HI antibodies
Statistical analysis description:	
For the Flu A/California/7/2009 H1N1 strain ,an ANOVA model was used to analyze post-vaccination log-transformed titers. The fixed-effect model included the minimization variable (age cohorts) and the treatment as fixed effect. The pre-vaccination log-transformed concentrations were included as continuous covariate. GMs of post-vaccination titers (Day 21) were calculated conditionally to the means of the pre-vaccination log-transformed titers (Month 0) for this strain.	
Comparison groups	GSK1437173A + GSK2321138A Group v Control Group
Number of subjects included in analysis	778
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[6]
Method	ANOVA
Parameter estimate	Adjusted geometric mean Titer ratio
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.22

Notes:

[6] - Comparisons at Day 21 after the FLU-D-QIV dose were performed between the Control group and GSK1437173A + GSK2321138A group. The GSK1437173A + GSK2321138A group was considered as statistically significant non inferior compared to the Control group in terms of immunogenicity (for each strain) if the UL of 2-sided 95% CI of the ratio of GMTs between the Control and the GSK1437173A + GSK2321138A (Control/ GSK1437173A + GSK2321138A) group is below 1.5.

Statistical analysis title	Adjusted GMT ratio 2 of HI antibodies
Statistical analysis description:	
For the Flu A/Texas/50/2012 H3N2 strain ,an ANOVA model was used to analyze post-vaccination log-transformed titers. The fixed-effect model included the minimization variable (age cohorts) and the treatment as fixed effect. The pre-vaccination log-transformed concentrations were included as	

continuous covariate. GMs of post-vaccination titers (Day 21) were calculated conditionally to the means of the pre-vaccination log-transformed titers (Month 0) for this strain.

Comparison groups	GSK1437173A + GSK2321138A Group v Control Group
Number of subjects included in analysis	778
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[7]
Method	ANOVA
Parameter estimate	Adjusted geometric mean Titer ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.17

Notes:

[7] - Comparisons at Day 21 after the FLU-D-QIV dose were performed between the Control group and GSK1437173A + GSK2321138A group. The GSK1437173A + GSK2321138A group was considered as statistically significant non inferior compared to the Control group in terms of immunogenicity (for each strain) if the UL of 2-sided 95% CI of the ratio of GMTs between the Control and the GSK1437173A + GSK2321138A (Control/ GSK1437173A + GSK2321138A) group is below 1.5.

Statistical analysis title	Adjusted GMT ratio 3 of HI antibodies
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Statistical analysis description:

For the Flu B/Brisbane/60/2008 Victoria strain ,an ANOVA model was used to analyze post-vaccination log-transformed titers. The fixed-effect model included the minimization variable (age cohorts) and the treatment as fixed effect. The pre-vaccination log-transformed concentrations were included as continuous covariate. GMs of post-vaccination titers (Day 21) were calculated conditionally to the means of the pre-vaccination log-transformed titers (Month 0) for this strain.

Comparison groups	GSK1437173A + GSK2321138A Group v Control Group
Number of subjects included in analysis	778
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[8]
Method	ANOVA
Parameter estimate	Adjusted geometric mean Titer ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.2

Notes:

[8] - Comparisons at Day 21 after the FLU-D-QIV dose were performed between the Control group and GSK1437173A + GSK2321138A group. The GSK1437173A + GSK2321138A group was considered as statistically significant non inferior compared to the Control group in terms of immunogenicity (for each strain) if the UL of 2-sided 95% CI of the ratio of GMTs between the Control and the GSK1437173A + GSK2321138A (Control/ GSK1437173A + GSK2321138A) group is below 1.5.

Statistical analysis title	Adjusted GMT ratio 4 of HI antibodies
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Statistical analysis description:

For the Flu B/Massachusetts/2/2012 Yamagata strain ,an ANOVA model was used to analyze post-vaccination log-transformed titers. The fixed-effect model included the minimization variable (age cohorts) and the treatment as fixed effect. The pre-vaccination log-transformed concentrations were included as continuous covariate. GMs of post-vaccination titers (Day 21) were calculated conditionally to the means of the pre-vaccination log-transformed titers (Month 0) for this strain.

Comparison groups	Control Group v GSK1437173A + GSK2321138A Group
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Number of subjects included in analysis	778
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[9]
Method	ANOVA
Parameter estimate	Adjusted geometric mean Titer ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.09

Notes:

[9] - Comparisons at Day 21 after the FLU-D-QIV dose were performed between the Control group and GSK1437173A + GSK2321138A group. The GSK1437173A + GSK2321138A group was considered as statistically significant non inferior compared to the Control group in terms of immunogenicity (for each strain) if the UL of 2-sided 95% CI of the ratio of GMTs between the Control and the GSK1437173A + GSK2321138A (Control/ GSK1437173A + GSK2321138A) group is below 1.5.

Secondary: Number of subjects with FLU HI antibodies $\geq 1:10$

End point title	Number of subjects with FLU HI antibodies $\geq 1:10$
End point description:	
FLU HI antibodies were assessed in four strains: Flu A/California/7/2009 H1N1, Flu A/Texas/50/2012 H3N2, Flu B/Brisbane/60/2008 Victoria and Flu B/Massachusetts/2/2012 Yamagata (Yamag). Cut-off titer for seropositivity was 1:10.	
End point type	Secondary
End point timeframe:	
At Days 0 and 21 post vaccination	

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386	395		
Units: Subjects				
Flu A/California/7/2009 H1N1 Day 0 [N=386,395]	288	294		
Flu A/California/7/2009 H1N1Day 21 [N=384,394]	381	389		
Flu A/Texas/50/2012 H3N2 Day 0 [N=386,395]	283	300		
Flu A/Texas/50/2012 H3N2 Day 21 [N=384,394]	380	392		
Flu B/Brisbane/60/2008 Victoria Day 0 [N=386,395]	365	375		
Flu B/Brisbane/60/2008 Victoria Day 21 [N=384,394]	383	394		
Flu B/Massachusetts/2/2012 Yamag Day 0 [N=386,395]	376	389		
Flu B/Massachusetts/2/2012 Yamag Day21 [N=384,394]	384	394		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects with HI antibody concentrations \geq 1:40

End point title	Number of seroprotected subjects with HI antibody concentrations \geq 1:40
End point description: Seroprotection rate is defined as the percentage of vaccines with a serum HI titer \geq 1:40 that usually was accepted as indicating protection.	
End point type	Secondary
End point timeframe: At Day 0 (PRE) and at Day 21 post vaccination	

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386	395		
Units: Subjects				
Flu A/California/7/2009 H1N1 HI Day 0 [N=386,395]	185	161		
Flu A/California/7/2009 H1N1 HI Day 21 [N=384,394]	347	360		
Flu A/Texas/50/2012 H3N2 HI Day 0 [N=386,395]	134	121		
Flu A/Texas/50/2012 H3N2 HI Day 21 [N=384,394]	292	295		
Flu B/Brisbane/60/2008 Vic HI Day 0 [N=386,395]	279	271		
Flu B/Brisbane/60/2008 Vic HI Day 21 [N=384,394]	372	382		
Flu B/Massach/2/2012 Yama HI Day 0 [N=386,395]	351	361		
Flu B/Massach/2/2012 Yama HI Day 21 [N=384,394]	383	393		

Statistical analyses

No statistical analyses for this end point

Secondary: FLU Haemagglutination inhibition (HI) antibody titers

End point title	FLU Haemagglutination inhibition (HI) antibody titers
End point description: HI antibody titres against the four influenza vaccine strains Flu A/California/7/2009, Flu A/Texas/50/2012, Flu B/Brisbane/60/2008 Victoria and Flu B/Massachusetts/2/2012 Yamagata were expressed as geometric mean titers (GMTs).	
End point type	Secondary

End point timeframe:
At Day 0 (PRE) and Day 21 post vaccination

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386	395		
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/California/7/2009 H1N1 HI Day 0	29 (25.1 to 33.5)	24.9 (21.8 to 28.5)		
Flu A/California/7/2009 H1N1 HI Day 21	196.2 (172.2 to 223.5)	193.2 (170.2 to 219.4)		
Flu A/Texas/50/2012 H3N2 HI Day 0	19.6 (17.5 to 21.9)	19 (17.1 to 21.1)		
Flu A/Texas/50/2012 H3N2 HI Day 21	65.4 (59 to 72.5)	66.8 (60.4 to 74)		
Flu B/Brisbane/60/2008 Victoria HI Day 0	52.2 (46.9 to 58.1)	48.6 (43.7 to 54)		
Flu B/Brisbane/60/2008 Victoria HI Day 21	177.2 (161.6 to 194.2)	185.2 (168 to 204.1)		
Flu B/Massachusetts/2/2012 Yamagata HI Day 0	128.8 (115.7 to 143.4)	127 (114.9 to 140.3)		
Flu B/Massachusetts/2/2012 Yamagata HI Day 21	433.7 (401.3 to 468.7)	423.3 (388 to 461.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects in terms of HI antibodies

End point title	Number of seroconverted subjects in terms of HI antibodies
End point description: The number of seroconverted subjects was assessed in terms of HI antibodies against the four influenza vaccine strains Flu A/California/7/2009, Flu A/Texas/50/2012, Flu B/Brisbane/60/2008 Victoria and Flu B/Massachusetts/2/2012 Yamagata.	
End point type	Secondary
End point timeframe: At Day 21 post vaccination	

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	394		
Units: Subjects				
Flu A/California/7/2009 H1N1 HI	232	240		
Flu A/Texas/50/2012 H3N2 HI	136	139		
Flu B/Brisbane/60/2008 Victoria HI	143	169		
Flu B/Massachusetts/2/2012 Yamagata HI	154	148		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean ratio for Flu HI antibodies post-vaccination titer

End point title	Geometric mean ratio for Flu HI antibodies post-vaccination titer
End point description:	
The geometric mean ratio for Flu HI antibodies against the four influenza vaccine strains Flu A/California/7/2009, Flu A/Texas/50/2012, Flu B/Brisbane/60/2008 Victoria and Flu B/Massachusetts/2/2012 Yamagata was defined as the geometric mean of the within subject ratios of the post-vaccination reciprocal HI titer to the Day 0 reciprocal HI titer.	
End point type	Secondary
End point timeframe:	
At Day 21 post vaccination	

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	394		
Units: Ratio				
geometric mean (confidence interval 95%)				
Flu A/California/7/2009 H1N1 HI	6.8 (5.9 to 7.8)	7.7 (6.7 to 9)		
Flu A/Texas/50/2012 H3N2 HI	3.4 (3 to 3.7)	3.5 (3.2 to 4)		
Flu B/Brisbane/60/2008 Victoria HI	3.4 (3 to 3.8)	3.8 (3.4 to 4.3)		
Flu B/Massachusetts/2/2012 Yamagata HI	3.4 (3 to 3.7)	3.3 (3 to 3.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms ^[10]
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site.

Relationship analysis was not performed. Since this group only received GSK2321138A vaccine at Dose 1 (D1) and GSK1437173A vaccine at Dose 1 and Dose 2 (D2), only the results for the respective doses and vaccine administrations were available.

End point type	Secondary
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End point timeframe:

Within 7 days (Days 0-6) after each vaccine dose

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to different number of vaccine doses administered, the results for the two groups were presented separately.

End point values	GSK1437173A + GSK2321138A Group			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: Subjects				
Any Pain D1 GSK 2321138A [N=410]	140			
Grade3 Pain D1 GSK 2321138A [N=410]	7			
Any Redness D1 GSK 2321138A [N=410]	31			
Grade3 Redness D1 GSK 2321138A [N=410]	1			
Any Swelling D1 GSK 2321138A [N=410]	16			
Grade3 Swelling D1 GSK 2321138A [N=410]	0			
Any Pain D1 GSK 1437173A [N=410]	292			
Grade3 Pain D1 GSK 1437173A [N=410]	31			
Any Redness D1 GSK 1437173A [N=410]	112			
Grade3 Redness D1 GSK 1437173A [N=410]	4			
Any Swelling D1 GSK 1437173A [N=410]	64			
Grade3 Swelling D1 GSK 1437173A [N=410]	0			
Any Pain D2 GSK 1437173A [N=403]	290			
Grade3 Pain D2 GSK 1437173A [N=403]	32			
Any Redness D2 GSK 1437173A [N=403]	103			
Grade3 Redness D2 GSK 1437173A [N=403]	5			
Any Swelling D2 GSK 1437173A [N=403]	64			
Grade3 Swelling D2 GSK 1437173A [N=403]	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms ^[11]
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site. Relationship analysis was not performed.

End point type	Secondary
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End point timeframe:

Within 7 days (Days 0-6) after each vaccine dose

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to different number of vaccine doses administered, the results for the two groups were presented separately.

End point values	Control Group			
Subject group type	Reporting group			
Number of subjects analysed	412			
Units: Subjects				
Any Pain, Dose 1 [N=412]	112			
Grade 3 Pain, Dose 1 [N=412]	4			
Any Redness, Dose 1 [N=412]	37			
Grade 3 Redness, Dose 1 [N=412]	2			
Any Swelling, Dose 1 [N=412]	18			
Grade 3 Swelling, Dose 1 [N=412]	1			
Any Pain, Dose 2 [N=405]	280			
Grade 3 Pain, Dose 2 [N=405]	25			
Any Redness, Dose 2 [N=405]	91			
Grade 3 Redness, Dose 2 [N=405]	6			
Any Swelling, Dose 2 [N=405]	47			
Grade 3 Swelling, Dose 2 [N=405]	0			
Any Pain, Dose 3 [N=402]	269			
Grade 3 Pain, Dose 3 [N=402]	25			
Any Redness, Dose 3 [N=402]	100			
Grade 3 Redness, Dose 3 [N=402]	7			
Any Swelling, Dose 3 [N=402]	50			
Grade 3 Swelling, Dose 3 [N=402]	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site. Relationship analysis was not performed.

End point type	Secondary
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End point timeframe:

Within 7 days (Days 0-6) across doses

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	413		
Units: Subjects				
Any Pain Across Doses	344	318		
Grade 3 Pain Across Doses	55	40		
Any Redness Across Doses	153	144		
Grade 3 Redness Across Doses	9	14		
Any Swelling Across Doses	99	86		
Grade 3 Swelling Across Doses	0	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms ^[12]
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End point description:

Assessed solicited general symptoms were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, shivering and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

Within 7 days (Days 0-6) after each vaccine dose

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to different number of vaccine doses administered, the results for the two groups were presented separately.

End point values	GSK1437173A + GSK2321138A Group			
Subject group type	Reporting group			
Number of subjects analysed	409			
Units: Subjects				
Any Arthralgia Dose 1 [N=409;411]	89			
Grade 3 Arthralgia Dose 1 [N=409;411]	8			
Related Arthralgia Dose 1 [N=409;411]	67			
Any Fatigue Dose 1 [N=409;411]	150			
Grade 3 Fatigue Dose 1 [N=409;411]	15			
Related Fatigue Dose 1 [N=409;411]	107			
Any Gastrointestinal Dose 1 [N=409;411]	57			
Grade 3 Gastrointestinal Dose 1 [N=409;411]	5			
Related Gastrointestinal Dose 1 [N=409;411]	28			
Any Headache Dose 1 [N=409;411]	122			
Grade 3 Headache Dose 1 [N=409;411]	5			
Related Headache Dose 1 [N=409;411]	80			
Any Myalgia Dose 1 [N=409;411]	135			
Grade 3 Myalgia Dose 1 [N=409;411]	11			
Related Myalgia Dose 1 [N=409;411]	105			
Any Shivering Dose 1 [N=409;411]	101			
Grade 3 Shivering Dose 1 [N=409;411]	12			
Related Shivering Dose 1 [N=409;411]	86			
Any Temperature Dose 1 [N=409;411]	63			
Grade 3 Temperature Dose 1 [N=409;411]	1			
Related Temperature Dose 1 [N=409;411]	53			
Any Arthralgia Dose 2 [N=402;405]	114			
Grade 3 Arthralgia Dose 2 [N=402;405]	16			
Related Arthralgia Dose 2 [N=402;405]	94			
Any Fatigue Dose 2 [N=402;405]	167			
Grade 3 Fatigue Dose 2 [N=402;405]	23			
Related Fatigue Dose 2 [N=402;405]	138			
Any Gastrointestinal Dose 2 [N=402;405]	47			
Grade 3 Gastrointestinal Dose 2 [N=402;405]	3			
Related Gastrointestinal Dose 2 [N=402;405]	32			
Any Headache Dose 2 [N=402;405]	136			
Grade 3 Headache Dose 2 [N=402;405]	16			
Related Headache Dose 2 [N=402;405]	109			
Any Myalgia Dose 2 [N=402;405]	157			
Grade 3 Myalgia Dose 2 [N=402;405]	18			
Related Myalgia Dose 2 [N=402;405]	135			
Any Shivering Dose 2 [N=402;405]	142			
Grade 3 Shivering Dose 2 [N=402;405]	30			
Related Shivering Dose 2 [N=402;405]	122			
Any Temperature Dose 2 [N=402;405]	74			

Grade 3 Temperature Dose 2 [N=402;405]	1			
Related Temperature Dose 2 [N=402;405]	63			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms ^[13]
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End point description:

Assessed solicited general symptoms were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, shivering and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

Within 7 days (Days 0-6) after each vaccine dose

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to different number of vaccine doses administered, the results for the two groups were presented separately.

End point values	Control Group			
Subject group type	Reporting group			
Number of subjects analysed	411			
Units: Subjects				
Any Arthralgia, Dose 1 [N=411]	37			
Grade 3 Arthralgia, Dose 1 [N=411]	8			
Related Arthralgia, Dose 1 [N=411]	25			
Any Fatigue, Dose 1 [N=411]	52			
Grade 3 Fatigue, Dose 1 [N=411]	4			
Related Fatigue, Dose 1 [N=411]	33			
Any Gastrointestinal, Dose 1 [N=411]	32			
Grade 3 Gastrointestinal, Dose 1 [N=411]	2			
Related Gastrointestinal, Dose 1 [N=411]	16			
Any Headache, Dose 1 [N=411]	57			
Grade 3 Headache, Dose 1 [N=411]	2			
Related Headache, Dose 1 [N=411]	31			
Any Myalgia, Dose 1 [N=411]	55			
Grade 3 Myalgia, Dose 1 [N=411]	4			
Related Myalgia, Dose 1 [N=411]	45			
Any Shivering, Dose 1 [N=411]	30			
Grade 3 Shivering, Dose 1 [N=411]	0			
Related Shivering, Dose 1 [N=411]	25			
Any Temperature, Dose 1 [N=411]	18			

Grade 3 Temperature, Dose 1 [N=411]	0			
Related Temperature, Dose 1 [N=411]	15			
Any Arthralgia, Dose 2 [N=405]	67			
Grade 3 Arthralgia, Dose 2 [N=405]	6			
Related Arthralgia, Dose 2 [N=405]	51			
Any Fatigue, Dose 2 [N=405]	108			
Grade 3 Fatigue, Dose 2 [N=405]	9			
Related Fatigue, Dose 2 [N=405]	87			
Any Gastrointestinal, Dose 2 [N=405]	37			
Grade 3 Gastrointestinal, Dose 2 [N=405]	1			
Related Gastrointestinal, Dose 2 [N=405]	28			
Any Headache, Dose 2 [N=405]	87			
Grade 3 Headache, Dose 2 [N=405]	8			
Related Headache, Dose 2 [N=405]	70			
Any Myalgia, Dose 2 [N=405]	135			
Grade 3 Myalgia, Dose 2 [N=405]	7			
Related Myalgia, Dose 2 [N=405]	115			
Any Shivering, Dose 2 [N=405]	87			
Grade 3 Shivering, Dose 2 [N=405]	10			
Related Shivering, Dose 2 [N=405]	75			
Any Temperature, Dose 2 [N=405]	44			
Grade 3 Temperature, Dose 2 [N=405]	1			
Related Temperature, Dose 2 [N=405]	34			
Any Arthralgia, Dose 3 [N=402]	95			
Grade 3 Arthralgia, Dose 3 [N=402]	18			
Related Arthralgia, Dose 3 [N=402]	79			
Any Fatigue, Dose 3 [N=402]	149			
Grade 3 Fatigue, Dose 3 [N=402]	31			
Related Fatigue, Dose 3 [N=402]	120			
Any Gastrointestinal, Dose 3 [N=402]	63			
Grade 3 Gastrointestinal, Dose 3 [N=402]	6			
Related Gastrointestinal, Dose 3 [N=402]	46			
Any Headache, Dose 3 [N=402]	133			
Grade 3 Headache, Dose 3 [N=402]	23			
Related Headache, Dose 3 [N=402]	111			
Any Myalgia, Dose 3 [N=402]	138			
Grade 3 Myalgia, Dose 3 [N=402]	24			
Related Myalgia, Dose 3 [N=402]	121			
Any Shivering, Dose 3 [N=402]	147			
Grade 3 Shivering, Dose 3 [N=402]	23			
Related Shivering, Dose 3 [N=402]	131			
Any Temperature, Dose 3 [N=402]	87			
Grade 3 Temperature, Dose 3 [N=402]	2			
Related Temperature, Dose 3 [N=402]	70			

Statistical analyses

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms
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End point description:

Assessed solicited general symptoms were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, shivering and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

Within 7 days (Days 0-6) across doses

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	413		
Units: Subjects				
Any Arthralgia, Across Doses	154	135		
Grade 3 Arthralgia, Across Doses	23	24		
Related Arthralgia, Across Doses	121	110		
Any Fatigue, Across Doses	224	186		
Grade 3 Fatigue, Across Doses	30	38		
Related Fatigue, Across Doses	175	151		
Any Gastrointestinal, Across Doses	90	92		
Grade 3 Gastrointestinal, Across Doses	6	9		
Related Gastrointestinal, Across Doses	49	66		
Any Headache, Across Doses	183	170		
Grade 3 Headache, Across Doses	20	28		
Related Headache, Across Doses	140	142		
Any Myalgia, Across Doses	201	201		
Grade 3 Myalgia, Across Doses	27	30		
Related Myalgia, Across Doses	167	177		
Any Shivering, Across Doses	174	181		
Grade 3 Shivering, Across Doses	35	30		
Related Shivering, Across Doses	151	159		
Any Temperature, Across Doses	107	119		
Grade 3 Temperature, Across Doses	2	3		
Related Temperature, Across Doses	90	96		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)
End point description:	
An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.	
End point type	Secondary
End point timeframe:	
During 30 days (Days 0-29) after vaccination	

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	413	415		
Units: Subjects				
Any AEs	110	162		
Grade 3 AEs	17	29		
Related AEs	18	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)
End point description:	
Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.	
End point type	Secondary
End point timeframe:	
From first vaccination up to Month 18 (study end)	

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	413	415		
Units: Subjects				
Any SAEs	42	39		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential immune-mediated diseases (pIMDs)

End point title	Number of subjects with potential immune-mediated diseases (pIMDs)
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End point description:

pIMDs are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

End point type	Secondary
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End point timeframe:

From first vaccination up to Month 18 (study end)

End point values	GSK1437173A + GSK2321138A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	413	415		
Units: Subjects				
Any pIMDs	4	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Systematically-assessed symptoms: Days 0-7 post each vaccine dose; AEs: Days 0-29 post each vaccine dose; SAEs: from Day 0 to Month 18

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	GSK1437173A + GSK2321138A Group
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Reporting group description:

The subjects assigned to the Co-Ad group received one injection of the FLU-D-QIV vaccine and one injection of the HZ/su study vaccine during the first visit and a second injection of the HZ/su study vaccine during the third visit, two months later.

Reporting group title	Control Group
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Reporting group description:

The subjects assigned to the Control group received all vaccines separately: one injection of the FLU-D-QIV vaccine at the first visit, one injection of the HZ/su study vaccine at the third visit and a second injection of the HZ/su study vaccine at the fourth visit, all two months apart.

Serious adverse events	GSK1437173A + GSK2321138A Group	Control Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 413 (10.17%)	39 / 415 (9.40%)	
number of deaths (all causes)	3	5	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	1 / 413 (0.24%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adrenal adenoma			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			

subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic cancer metastatic			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung adenocarcinoma metastatic			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 413 (0.24%)	2 / 415 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			

subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death (unknown causes)			
subjects affected / exposed	0 / 413 (0.00%)	2 / 415 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Asthenia			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic lung injury			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	3 / 413 (0.73%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 413 (0.24%)	2 / 415 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 413 (0.24%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	2 / 413 (0.48%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 413 (0.24%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aortic valve stenosis			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			

subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	3 / 413 (0.73%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 413 (0.48%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired syringomyelia			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dementia			

subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Occipital neuralgia			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Hypochromic anaemia			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			

subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 413 (0.24%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 413 (0.00%)	2 / 415 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 413 (0.24%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Calculus urethral			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 413 (0.24%)	3 / 415 (0.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 413 (0.24%)	2 / 415 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal discomfort			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rheumatoid arthritis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 413 (0.73%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 413 (0.24%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	2 / 413 (0.48%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Abscess			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cellulitis			

subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis pharyngeal			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	0 / 413 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	GSK1437173A + GSK2321138A Group	Control Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	344 / 413 (83.29%)	318 / 415 (76.63%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed ^[1]	344 / 411 (83.70%)	318 / 413 (77.00%)	
occurrences (all)	344	318	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed ^[2]	153 / 411 (37.23%)	144 / 413 (34.87%)	
occurrences (all)	153	144	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed ^[3]	99 / 411 (24.09%)	86 / 413 (20.82%)	
occurrences (all)	99	86	
Arthralgia			
subjects affected / exposed ^[4]	154 / 411 (37.47%)	135 / 413 (32.69%)	
occurrences (all)	154	135	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed ^[5]	224 / 411 (54.50%)	186 / 413 (45.04%)	
occurrences (all)	224	186	
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed ^[6]	90 / 411 (21.90%)	92 / 413 (22.28%)	
occurrences (all)	90	92	
Headache			

alternative assessment type: Systematic subjects affected / exposed ^[7] occurrences (all)	183 / 411 (44.53%) 183	170 / 413 (41.16%) 170	
Myalgia alternative assessment type: Systematic subjects affected / exposed ^[8] occurrences (all)	201 / 411 (48.91%) 201	201 / 413 (48.67%) 201	
Shivering alternative assessment type: Systematic subjects affected / exposed ^[9] occurrences (all)	174 / 411 (42.34%) 174	181 / 413 (43.83%) 181	
Temperature/(Oral) alternative assessment type: Systematic subjects affected / exposed ^[10] occurrences (all)	107 / 411 (26.03%) 107	119 / 413 (28.81%) 119	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	14 / 413 (3.39%) 14	22 / 415 (5.30%) 22	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2013	<p>Amendment 1</p> <p>Addressing a request from the US Food and Drug Administration Center for Biologics Evaluation and Research (CBER), a secondary objective has been added for an evaluation of the difference between the Seroconversion Rates (SCR) for each influenza strain when administered either concomitantly with or separately from the HZ/su vaccine. Following CBER's recommendation, the upper limit of the two-sided 95% Confidence Interval (CI) between the SCR of each strain should not exceed 10%.</p> <p>As a consequence, the sample size has been increased in order to ensure adequate power for this additional secondary objective. The overall power to reach the co-primary objectives has been corrected with the new sample size determination.</p> <p>As per CBER's request, it was added in the secondary objective that the immunogenicity of the FLU-D-QIV vaccine will be assessed according to the CBER criteria for determination of immunogenicity (SCR and SPR) as described in Section III, B1b-FDA Guidance to Industry, Clinical Data Needed to Support the Licensure of Seasonal Inactivated Influenza Vaccines, May 2007. The nominal powers have been calculated in order to respond to this request, assuming 393 subjects are available in each arm.</p> <p>As per CBER's request, Section 6.5 has been amended to indicate that any medical condition including the occurrence of a new pIMD or the exacerbation of an existing pIMD that, in the opinion of the investigator, exposes the subject to unacceptable risk from subsequent vaccination, constitutes absolute contraindications to further administration of HZ/su vaccine. The change is not in response to any safety concern identified by GSK arising from an event or series of events in any completed or ongoing clinical studies that have been or are being conducted as part of GSK's Zoster vaccine program.</p>
16 May 2014	<p>Amendment 2</p> <p>The cut-off of the gE-specific ELISA assay has been changed from 18 to 97 mIU/mL. Background signal has been measured with the anti-gE ELISA on samples from Varicella Zoster Virus (VZV) naïve paediatric subjects. This observation of background signal on VZV naïve samples was not part of the original validation of the assay and establishment of the assay cut-off. Background signal measured with the anti-gE ELISA has no impact on Zoster project clinical conclusions as the vast majority of the samples (at all timepoints) have high titers well above the unspecific response level measured on VZV naïve samples from Measles, Mumps, Rubella and Varicella (MMRV) studies and Zoster vaccine responses are very robust. However this finding triggered re-evaluation of the assay cut-off. Based on complementary validation experiments performed in line with Clinical and Laboratory Standards Institute (CLSI) guidelines and taking into account internal company guidelines the technical and seropositivity cut-off has been set at 97 mIU/mL.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

