



Clinical trial results:

A phase II, double-blind, multicenter, randomized study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza candidate vaccine GSK2321138A compared with GSK Biologicals' trivalent influenza vaccine, Fluarix™, administered intramuscularly in children (18-47 months of age) in both unprimed subjects and in primed subjects who previously participated in the 111751 study

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2012-002587-27
Trial protocol	Outside EU/EEA
Global end of trial date	21 May 2010

Results information

Result version number	v2
This version publication date	22 May 2016
First version publication date	15 July 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Data correction due to a system error in EudraCT – Results (Primary endpoint) Data (typos) were corrected for 1 secondary endpoint

Trial information

Trial identification

Sponsor protocol code	113237
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00985790
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, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 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?	Yes
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Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 September 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2010
Global end of trial reached?	Yes
Global end of trial date	21 May 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the immunological non-inferiority in terms of Geometric Mean Titers (GMTs) of the quadrivalent influenza study vaccine (FLU D-QIV) compared to the trivalent influenza vaccine (Fluarix™) in primed and unprimed subjects for the three recommended seasonal strains, 28 days after the last vaccination.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 October 2009
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	Mexico: 599
Worldwide total number of subjects	599
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	299

months)	
Children (2-11 years)	300
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 599 subjects were enrolled in the study, and assigned to either the GSK2321138A Group (298 subjects) or the Fluarix Group (301 subjects). Duration of study was of approximately 6 months for each subject.

Pre-assignment

Screening details:

For demography and safety, results are presented as per the main study groups. For some outcome measures and where relevant, subjects as in these 2 main groups are split according to their priming status at study entry.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK2321138A Group

Arm description:

Subjects aged between 18 and 47 months received the GSK2321138A. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the GSK2321138A-Primed Group) received 1 dose of GSK2321138A vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the GSK2321138A-Unprimed Group) received 2 doses of GSK2321138A vaccine at Days 0 and 28. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

Arm type	Experimental
Investigational medicinal product name	FLU D-QIV
Investigational medicinal product code	GSK2321138A
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccines were given intramuscularly in the deltoid of the right arm

Arm title	Fluarix Group
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Arm description:

Subjects aged between 18 and 47 months received the Fluarix™ vaccine. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the Fluarix-Primed Group) received 1 dose of Fluarix™ vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the Fluarix-Unprimed Group) received 2 doses of Fluarix™ vaccine at Days 0 and 28. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

Arm type	Active comparator
Investigational medicinal product name	Fluarix™
Investigational medicinal product code	
Other name	Trivalent Inactivated Influenza Vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

Number of subjects in period 1	GSK2321138A Group	Fluarix Group
Started	298	301
Completed	291	293
Not completed	7	8
Consent withdrawn by subject	1	1
Lost to follow-up	6	7

Baseline characteristics

Reporting groups

Reporting group title	GSK2321138A Group
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Reporting group description:

Subjects aged between 18 and 47 months received the GSK2321138A. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the GSK2321138A-Primed Group) received 1 dose of GSK2321138A vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the GSK2321138A-Unprimed Group) received 2 doses of GSK2321138A vaccine at Days 0 and 28. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

Reporting group title	Fluarix Group
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Reporting group description:

Subjects aged between 18 and 47 months received the Fluarix™ vaccine. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the Fluarix-Primed Group) received 1 dose of Fluarix™ vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the Fluarix-Unprimed Group) received 2 doses of Fluarix™ vaccine at Days 0 and 28. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

Reporting group values	GSK2321138A Group	Fluarix Group	Total
Number of subjects	298	301	599
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: months			
arithmetic mean	31.4	31.6	
standard deviation	± 8.46	± 8.29	-
Gender categorical Units: Subjects			
Female	138	147	285
Male	160	154	314

End points

End points reporting groups

Reporting group title	GSK2321138A Group
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Reporting group description:

Subjects aged between 18 and 47 months received the GSK2321138A. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the GSK2321138A-Primed Group) received 1 dose of GSK2321138A vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the GSK2321138A-Unprimed Group) received 2 doses of GSK2321138A vaccine at Days 0 and 28. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

Reporting group title	Fluarix Group
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Reporting group description:

Subjects aged between 18 and 47 months received the Fluarix™ vaccine. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the Fluarix-Primed Group) received 1 dose of Fluarix™ vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the Fluarix-Unprimed Group) received 2 doses of Fluarix™ vaccine at Days 0 and 28. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

Subject analysis set title	GSK2321138A-Primed Group
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Subjects in this group were the primed subjects from the GSK2321138A Group, aged between 18 and 47 months, who received 1 dose of GSK2321138A vaccine at Day 0, and who had previously received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

Subject analysis set title	GSK2321138A-Unprimed Group
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Subjects in this group were the unprimed subjects from the GSK2321138A Group, aged between 18 and 47 months, who received 2 doses of GSK2321138A vaccine at Days 0 and 28, and who had not received any 2-dose priming influenza immunization in any previous year. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

Subject analysis set title	Fluarix-Primed Group
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Subjects in this group were the primed subjects from the Fluarix Group, aged between 18 and 47 months, who received 1 dose of Fluarix™ vaccine at Day 0, and who had previously received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

Subject analysis set title	Fluarix-Unprimed Group
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Subjects in this group were the unprimed subjects from the Fluarix Group, aged between 18 and 47 months, who received 2 doses of Fluarix™ vaccine at Days 0 and 28, and who had not received any 2-dose priming influenza immunization in any previous year. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

Primary: Titers for serum Hemagglutination Inhibition (HI) antibodies against the 3 Fluarix vaccine strains.

End point title	Titers for serum Hemagglutination Inhibition (HI) antibodies against the 3 Fluarix vaccine strains.
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End point description:

Titers are presented as geometric mean titers (GMTs). The reference cut-off value was 1:10. The 3 influenza strains assessed were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2) and Flu B/Brisbane/60/08 Victoria (VICT).The POST results were the primary outcome variables.

End point type	Primary
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End point timeframe:

At Day 0 [PRE] and at 28 days post last vaccination (Day 28 or Day 56) [POST]

End point values	GSK2321138A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	193	193		
Units: titers				
geometric mean (confidence interval 95%)				
H1N1, PRE [N=189;192]	22.2 (17.2 to 28.7)	21.6 (16.7 to 28)		
H1N1, POST [N=193;193]	173.8 (141.4 to 213.5)	176.9 (143.3 to 218.5)		
H3N2, PRE [N=190;192]	18.6 (14.9 to 23.2)	20.8 (16.5 to 26.2)		
H3N2, POST [N=193;193]	120.7 (101.2 to 143.9)	130.4 (108 to 157.5)		
VICT, PRE [N=190;192]	8.7 (7.3 to 10.2)	9 (7.7 to 10.6)		
VICT, POST [N=192;193]	61.9 (48.7 to 78.6)	66.6 (52.4 to 84.7)		

Statistical analyses

Statistical analysis title	Adjusted GMT ratio for FLU A/Bri/59/07 H1N1
Statistical analysis description: To assess the immunological non-inferiority in terms of Geometric Mean Titers (GMTs) of the GSK2321138A vaccine compared to the Fluarix vaccine in primed and unprimed subjects for the three recommended seasonal strains, 28 days after the last vaccination.	
Comparison groups	GSK2321138A Group v Fluarix Group
Number of subjects included in analysis	386
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
Parameter estimate	Adjusted GMT ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.33

Notes:

[1] - Non-inferiority criterion: UL of the two-sided 95% CI on GMT ratio < 2.

Statistical analysis title	Adjusted GMT ratio for Flu A/Uru/716/07 H3N2
Statistical analysis description: To assess the immunological non-inferiority in terms of Geometric Mean Titers (GMTs) of the GSK2321138A vaccine compared to the Fluarix vaccine in primed and unprimed subjects for the three recommended seasonal strains, 28 days after the last vaccination.	
Comparison groups	GSK2321138A Group v Fluarix Group

Number of subjects included in analysis	386
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
Parameter estimate	Adjusted GMT ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.23

Notes:

[2] - Non-inferiority criterion: UL of the two-sided 95% CI on GMT ratio < 2.

Statistical analysis title	Adjusted GMT ratio for FluB/Bri/60/08 Victoria
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Statistical analysis description:

To assess the immunological non-inferiority in terms of Geometric Mean Titers (GMTs) of the GSK2321138A vaccine compared to the Fluarix vaccine in primed and unprimed subjects for the three recommended seasonal strains, 28 days after the last vaccination.

Comparison groups	GSK2321138A Group v Fluarix Group
Number of subjects included in analysis	386
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Parameter estimate	Adjusted GMT ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.37

Notes:

[3] - Non-inferiority criterion: UL of the two-sided 95% CI on GMT ratio < 2.

Secondary: Titers for serum Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.

End point title	Titers for serum Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.
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End point description:

Titers are presented as geometric mean titers (GMTs). The reference cut-off value was 1:10. The 4 influenza strains assessed were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups.

End point type	Secondary
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End point timeframe:

At Days 0 and 28.

End point values	GSK2321138A-Primed Group	Fluarix-Primed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	95		
Units: titers				
geometric mean (confidence interval 95%)				
H1N1, Day 0	40.3 (27 to 60.2)	36.5 (24.3 to 54.9)		
H1N1, Day 28	117 (83.2 to 164.5)	124.4 (89.8 to 172.4)		
H3N2, Day 0	22.8 (16.7 to 31.2)	21.7 (16 to 29.5)		
H3N2, Day 28	85.2 (64.8 to 112)	83 (63.6 to 108.2)		
VICT, Day 0	8.9 (7.2 to 11)	9.7 (7.7 to 12.4)		
VICT, Day 28	38.7 (26.2 to 57.1)	44 (29.6 to 65.2)		
YAMA, Day 0	29.3 (23 to 37.4)	37.7 (29.8 to 47.8)		
YAMA, Day 28	243.6 (198.1 to 299.6)	127.2 (106.1 to 152.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for serum Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.

End point title	Titers for serum Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.
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End point description:

Titers are presented as geometric mean titers (GMTs). The reference cut-off value was 1:10. The 4 influenza strains assessed were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups.

End point type	Secondary
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End point timeframe:

At Days 0, 28 and Day 56

End point values	GSK2321138A-Unprimed Group	Fluarix-Unprimed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	192	198		
Units: titers				
geometric mean (confidence interval 95%)				
H1N1, Day 0 [N=190;198]	14.7 (11.8 to 18.4)	12.8 (10.5 to 15.7)		
H1N1, Day 28 [N=97;101]	173.1 (113.1 to 264.8)	161.6 (103.9 to 251.4)		

H1N1, Day 56 [N=99;98]	253.1 (203.4 to 314.8)	249 (192.5 to 321.9)		
H3N2, Day 0 [N=192;197]	17.7 (14.1 to 22.1)	17.9 (14.1 to 22.6)		
H3N2, Day 28 [N=96;101]	99.3 (64.8 to 152.2)	84.2 (54.1 to 131.2)		
H3N2, Day 56 [N=99;98]	168.1 (136.6 to 206.7)	202.1 (158.6 to 257.5)		
VICT, Day 0 [N=190;198]	7.8 (6.7 to 9.2)	8.7 (7.5 to 10.3)		
VICT, Day 28 [N=95;101]	26.5 (17.7 to 39.7)	34.6 (22.4 to 53.6)		
VICT, Day 56 [N=98;98]	97.2 (74.9 to 126.1)	99.6 (76.7 to 129.4)		
YAMA, Day 0 [N=188;198]	9.1 (7.7 to 10.7)	9.9 (8.4 to 11.8)		
YAMA, Day 28 [N=97;102]	97 (64.7 to 145.4)	30 (21.3 to 42.1)		
YAMA, Day 56 [N=99;98]	311.1 (255.4 to 379.1)	42.2 (30.6 to 58.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects against 4 strains of influenza disease.

End point title	Number of seropositive subjects against 4 strains of influenza disease.
End point description: A seropositive subject was defined as a vaccinated subject with serum Hemagglutination Inhibition (HI) titer $\geq 1:10$. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups.	
End point type	Secondary
End point timeframe: At Days 0 and 28	

End point values	GSK2321138A-Primed Group	Fluarix-Primed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	95		
Units: Subjects				
H1N1, Day 0	58	54		
H1N1, Day 28	83	87		
H3N2, Day 0	60	59		
H3N2, Day 28	88	87		
VICT, Day 0	26	28		
VICT, Day 28	62	66		
YAMA, Day 0	73	80		
YAMA, Day 28	93	94		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects against 4 strains of influenza disease.

End point title	Number of seropositive subjects against 4 strains of influenza disease.
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End point description:

A seropositive subject was defined as a vaccinated subject with serum Hemagglutination Inhibition (HI) titer $\geq 1:10$. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups.

End point type	Secondary
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End point timeframe:

At Days 0, 28 and 56

End point values	GSK2321138A- Unprimed Group	Fluarix- Unprimed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	192	198		
Units: Subjects				
H1N1, Day 0 [N=190;198]	75	71		
H1N1, Day 28 [N=97;101]	83	84		
H1N1, Day 56 [N=99;98]	99	96		
H3N2, Day 0 [N=192;197]	85	82		
H3N2, Day 28 [N=96;101]	74	78		
H3N2, Day 56 [N=99;98]	99	98		
VICT, Day 0 [N=190; 198]	30	42		
VICT, Day 28 [N=95; 101]	51	61		
VICT, Day 56 [N=98; 98]	96	94		
YAMA, Day 0 [N=188;198]	45	57		
YAMA, Day 28 [N=97;102]	75	57		
YAMA, Day 56 [N=99;98]	98	70		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects against 4 strains of influenza disease.

End point title	Number of seroconverted subjects against 4 strains of influenza disease.
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End point description:

A seroconverted subject was defined as a vaccinated subject who had either a pre-vaccination titer <1:10 and a post-vaccination titer \geq 1:40 or a pre-vaccination titer \geq 1:10 and at least a four-fold increase in post-vaccination titer. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups.

End point type	Secondary
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End point timeframe:

At Day 28

End point values	GSK2321138A-Primed Group	Fluarix-Primed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	95		
Units: Subjects				
H1N1, Day 28	30	39		
H3N2, Day 28	48	46		
VICT, Day 28	46	42		
YAMA, Day 28	82	40		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects against 4 strains of influenza disease.

End point title	Number of seroconverted subjects against 4 strains of influenza disease.
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End point description:

A seroconverted subject was defined as a vaccinated subject who had either a pre-vaccination titer <1:10 and a post-vaccination titer \geq 1:40 or a pre-vaccination titer \geq 1:10 and at least a four-fold increase in post-vaccination titer. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups.

End point type	Secondary
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End point timeframe:

At Days 28 and 56

End point values	GSK2321138A-Unprimed Group	Fluarix-Unprimed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96	101		
Units: Subjects				
H1N1, Day 28 [N=95;101]	63	74		
H1N1, Day 56 [N=95;97]	81	89		
H3N2, Day 28 [N=96;100]	55	54		
H3N2, Day 56 [N=96;97]	79	75		

VICT, Day 28 [N=94;101]	34	40		
VICT, Day 56 [N=95;97]	77	85		
YAMA, Day 28 [N=93;101]	59	40		
YAMA, Day 56 [N=95;97]	90	42		

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion factor for Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.

End point title	Seroconversion factor for Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.
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End point description:

The seroconversion factor (SCF) was defined as the fold increase in serum Hemagglutination Inhibition (HI) geometric mean titers (GMTs) post vaccination compared to Day 0. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups.

End point type	Secondary
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End point timeframe:

At Day 28

End point values	GSK2321138A-Primed Group	Fluarix-Primed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	95		
Units: fold increase				
geometric mean (confidence interval 95%)				
H1N1, Day 28	2.9 (2.3 to 3.6)	3.4 (2.7 to 4.2)		
H3N2, Day 28	3.7 (3.1 to 4.5)	3.8 (3.1 to 4.7)		
VICT, Day 28	4.4 (3.3 to 5.8)	4.5 (3.4 to 6)		
YAMA, Day 28	8.3 (6.8 to 10.1)	3.4 (2.8 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion factor for Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.

End point title	Seroconversion factor for Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.
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End point description:

The seroconversion factor (SCF) was defined as the fold increase in serum Hemagglutination Inhibition (HI) geometric mean titers (GMTs) post vaccination compared to Day 0. The 4 assessed influenza

strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups.

End point type	Secondary
End point timeframe:	
At Days 28 and 56	

End point values	GSK2321138A- Unprimed Group	Fluarix- Unprimed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96	101		
Units: fold increase				
geometric mean (confidence interval 95%)				
H1N1, Day 28 [N=95;101]	9.9 (7 to 14.1)	12.7 (9.1 to 17.7)		
H1N1, Day 56 [N=95;97]	19.8 (15.4 to 25.6)	19.2 (15.2 to 24.2)		
H3N2, Day 28 [N=96;100]	4.9 (3.7 to 6.3)	5.1 (3.9 to 6.7)		
H3N2, Day 56 [N=96;97]	11.1 (9 to 13.7)	10.3 (8.3 to 12.9)		
VICT, Day 28 [N=94;101]	3.6 (2.7 to 5)	3.8 (2.9 to 5)		
VICT, Day 56 [N=95;97]	11.3 (9.4 to 13.6)	12.1 (9.8 to 14.8)		
YAMA, Day 28 [N=93;101]	9.9 (6.9 to 14)	3.4 (2.5 to 4.5)		
YAMA, Day 56 [N=95;97]	35.1 (27.6 to 44.6)	3.7 (2.9 to 4.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against 4 strains of influenza disease.

End point title	Number of seroprotected subjects against 4 strains of influenza disease.
End point description:	
A seroprotected subject was defined as a vaccinated subject with serum Hemagglutination Inhibition (HI) titer $\geq 1:40$. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups.	
End point type	Secondary
End point timeframe:	
At Days 0 and 28	

End point values	GSK2321138A- Primed Group	Fluarix-Primed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	95		
Units: Subjects				
H1N1, Day 0	48	45		
H1N1, Day 28	73	78		
H3N2, Day 0	39	36		
H3N2, Day 28	75	80		
VICT, Day 0	16	20		
VICT, Day 28	50	52		
YAMA, Day 0	56	62		
YAMA, Day 28	91	90		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against 4 strains of influenza disease.

End point title	Number of seroprotected subjects against 4 strains of influenza disease.
End point description:	
A seroprotected subject was defined as a vaccinated subject with serum Hemagglutination Inhibition (HI) titer $\geq 1:40$. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups.	
End point type	Secondary
End point timeframe:	
At Days 0, 28 and 56	

End point values	GSK2321138A- Unprimed Group	Fluarix- Unprimed Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	192	198		
Units: Subjects				
H1N1, Day 0 [N=190;198]	58	54		
H1N1, Day 28 [N=97;101]	76	78		
H1N1, Day 56 [N=99;98]	95	94		
H3N2, Day 0 [N=192;197]	74	70		
H3N2, Day 28 [N=96;101]	64	61		
H3N2, Day 56 [N=99;98]	96	94		
VICT, Day 0 [N=190;198]	25	35		
VICT, Day 28 [N=95;101]	36	41		
VICT, Day 56 [N=98;98]	84	88		
YAMA, Day 0 [N=188;198]	37	40		
YAMA, Day 28 [N=97;102]	67	53		
YAMA, Day 56 [N=99;98]	98	59		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and grade 3 solicited local symptoms.

End point title	Number of subjects with any and grade 3 solicited local symptoms.
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End point description:

Assessed solicited local symptoms were pain, redness and swelling at the injection site. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 50 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

During the 7-day follow-up period (Days 0 to 6) after any vaccination

End point values	GSK2321138A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	298		
Units: Subjects				
Any Pain	125	116		
Grade 3 Pain	4	1		
Any Redness	31	34		
Redness >50 mm	0	0		
Any Swelling	27	24		
Swelling >50 mm	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms.

End point title	Number of subjects with any, grade 3 and related solicited general symptoms.
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End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and temperature (defined as axillary temperature equal to or above 37.5 degrees Celsius). For other symptoms: Any = any solicited general symptom reported irrespective of intensity and relationship to vaccination. Related = symptoms assessed by the investigator as related to vaccination. Grade 3 drowsiness = prevented normal activity. Grade 3 loss of appetite = not eating at all. Grade 3 irritability= crying that could not be comforted/prevented normal activity. Grade 3 temperature: $\geq 39.0^{\circ}\text{C}$.

End point type	Secondary
End point timeframe:	
During the 7-day follow-up period (Days 0 to 6) after any vaccination	

End point values	GSK2321138A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	298		
Units: Subjects				
Any Drowsiness	70	62		
Grade 3 Drowsiness	2	0		
Related Drowsiness	64	57		
Any Irritability	90	87		
Grade 3 Irritability	4	2		
Related Irritability	83	78		
Any Loss of appetite	89	86		
Grade 3 Loss of appetite	4	3		
Related Loss of appetite	79	68		
Temperature $\geq 37.5^{\circ}\text{C}$	74	79		
Temperature $> 39.0^{\circ}\text{C}$	3	3		
Related Temperature	63	62		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related unsolicited adverse events (AEs).

End point title	Number of subjects with any, grade 3 and related unsolicited adverse events (AEs).
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End point description:

An unsolicited AE covers any untoward medical occurrence in a 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 = occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to vaccination.

End point type	Secondary
End point timeframe:	
During the 28-day follow-up period (Days 0 to 27) after vaccination	

End point values	GSK2321138A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	298	301		
Units: Subjects				
Subjects with any AE(s)	116	118		
Subjects with Grade 3 AE(s)	10	12		
Subjects with related AE(s)	7	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and related serious adverse events (SAEs).

End point title	Number of subjects with any and related serious adverse events (SAEs).
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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. Any was defined as occurrence of any symptom regardless of intensity grade and related was an event assessed by the investigator as causally related to the study vaccination.

End point type	Secondary
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End point timeframe:

From Day 0 to Day 180 (study conclusion)

End point values	GSK2321138A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	298	301		
Units: Subjects				
Any SAE(s)	0	2		
Related SAE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any adverse events of specific interest (AESIs).

End point title	Number of subjects with any adverse events of specific interest (AESIs).
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End point description:

An AESI was defined as an AE including autoimmune diseases and other mediated inflammatory disorders and assessed by the investigator as specific to the treatment administration.

End point type	Secondary
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End point timeframe:

From Day 0 to Day 180 (study conclusion)

End point values	GSK2321138A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	298	301		
Units: Subjects				
Subjects with any AESI(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAE(s): during the entire study period (Day 0 - Day 180); Unsolicited AE(s): during the 28-day follow-up period (Days 0 to 27) after any vaccination; Solicited local and general symptoms: during the 7-day (Days 0-6) follow-up period after any vaccination.

Adverse event reporting additional description:

The number of occurrences reported for solicited symptoms, adverse events, and serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Fluarix Group
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Reporting group description:

Subjects aged between 18 and 47 months received the Fluarix™ vaccine. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the Fluarix-Primed Group) received 1 dose of Fluarix™ vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the Fluarix-Unprimed Group) received 2 doses of Fluarix™ vaccine at Days 0 and 28. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

Reporting group title	GSK2321138A Group
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Reporting group description:

Subjects aged between 18 and 47 months received the GSK2321138A. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the GSK2321138A-Primed Group) received 1 dose of GSK2321138A vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the GSK2321138A-Unprimed Group) received 2 doses of GSK2321138A vaccine at Days 0 and 28. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

Serious adverse events	Fluarix Group	GSK2321138A Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 301 (0.66%)	0 / 298 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 301 (0.33%)	0 / 298 (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			
Bronchopneumonia			

subjects affected / exposed	1 / 301 (0.33%)	0 / 298 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fluarix Group	GSK2321138A Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 301 (38.54%)	125 / 298 (41.95%)	
General disorders and administration site conditions			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed ^[1]	62 / 298 (20.81%)	70 / 293 (23.89%)	
occurrences (all)	62	70	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed ^[2]	87 / 298 (29.19%)	90 / 293 (30.72%)	
occurrences (all)	87	90	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed ^[3]	86 / 298 (28.86%)	89 / 293 (30.38%)	
occurrences (all)	86	89	
Temperature			
alternative assessment type: Systematic			
subjects affected / exposed ^[4]	79 / 298 (26.51%)	74 / 293 (25.26%)	
occurrences (all)	79	74	
Pain			
alternative assessment type: Systematic			
subjects affected / exposed ^[5]	116 / 298 (38.93%)	125 / 293 (42.66%)	
occurrences (all)	116	125	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed ^[6]	34 / 298 (11.41%)	31 / 293 (10.58%)	
occurrences (all)	34	31	

Swelling alternative assessment type: Systematic subjects affected / exposed ^[7] occurrences (all)	24 / 298 (8.05%) 24	27 / 293 (9.22%) 27	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all)	69 / 301 (22.92%) 69 21 / 301 (6.98%) 21	72 / 298 (24.16%) 72 20 / 298 (6.71%) 20	

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: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[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: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[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: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[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: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[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: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[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: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[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: The analysis was performed on Total Vaccinated cohort which included all subjects with the

vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported