Clinical trial results:
A phase III, observer-blind, multi-centre, multi-country, randomized study to evaluate the immunogenicity and safety of thimerosal-free (TF) Fluarix™ (GSK Biologicals) compared with Fluzone® (Sanofi Pasteur) administered intramuscularly in children (6 to 35 months of age)

Summary

EudraCT number	2015-001258-13
Trial protocol	Outside EU/EEA
Global end of trial date	01 June 2009

Results information

Result version number	v1
This version publication date	04 May 2016
First version publication date	18 July 2015

Trial information

Trial identification

Sponsor protocol code	111751

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00764790
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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 September 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 March 2009
Global end of trial reached?	Yes
Global end of trial date	01 June 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To demonstrate the immunological non-inferiority (in terms of GMTs and seroconversion rates) of TF Fluarix (0.5mL) versus Fluzone (0.25mL) in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial IM vaccination.
•To demonstrate the immunological non-inferiority (in terms of GMTs and seroconversion rates) of TF Fluarix (0.25mL) versus Fluzone (0.25mL) in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial IM 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	01 October 2008
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	United States: 1289
Country: Number of subjects enrolled	Taiwan: 177
Country: Number of subjects enrolled	Thailand: 275
Country: Number of subjects enrolled	Mexico: 1297
Country: Number of subjects enrolled	Hong Kong: 280
Worldwide total number of subjects	3318
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 months)	2212
Children (2-11 years)	1106
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: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Fluarix Dose A Group

Arm description:

Subjects were administered 1 or 2 doses* of Fluarix vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age).

* Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Arm type	Experimental
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:

One (Day 0) or two (Day 0 and Day 28) doses by intramuscular injection. Two different doses were tested.

Arm title	Fluarix Dose B Group

Arm description:

Subjects were administered 1 or 2 doses*, half the volume of dose A, of Fluarix vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age).

* Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Arm type	Experimental
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:

One (Day 0) or two (Day 0 and Day 28) doses by intramuscular injection. Two different doses were tested.

Arm title	Fluzone Group

Arm description:

Subjects were administered 1 or 2 doses* of Fluzone vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age).

* Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Arm type	Active comparator
Investigational medicinal product name	Fluzone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One (Day 0) or two (Day 0 and Day 28) doses by intramuscular injection.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: This is an observer-blind study which means that during the course of the study, the vaccine recipient (subject) and those responsible for the evaluation of any study endpoint, were all unaware of which vaccine was administered to a particular subject. To do so, vaccine preparation and vaccination was done by authorized medical personnel who did not participate in any of the study clinical evaluation (i.e. carer and assessor).

Number of subjects in period 1[2]	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group
Started	1107	1106	1104
Completed	1069	1065	1074
Not completed	38	41	30
Consent withdrawn by subject	10	12	6
Protocol violation	-	-	1
Migrated/moved from study area	4	3	5
Lost to follow-up	24	26	18

Notes:

[2] - 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: 1 subject enrolled in the study was allocated a subject number but the study vaccine dose was not administered.

Baseline characteristics

Reporting groups	
Reporting group title	Fluarix Dose A Group

Reporting group description:

Subjects were administered 1 or 2 doses* of Fluarix vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age).

* Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Reporting group title	Fluarix Dose B Group

Reporting group description:

Subjects were administered 1 or 2 doses*, half the volume of dose A, of Fluarix vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age).

* Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Reporting group title	Fluzone Group

Reporting group description:

Subjects were administered 1 or 2 doses* of Fluzone vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age).

* Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Reporting group values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group
Number of subjects	1107	1106	1104
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: months			
arithmetic mean	20.9	20.9	21
standard deviation	± 8.07	± 8.42	± 8.23
Gender categorical Units: Subjects			
Female	539	517	560
Male	568	589	544

Reporting group values	Total		

Number of subjects	3317		
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			
standard deviation	-		
Gender categorical Units: Subjects			
Female	1616		
Male	1701		

End points

End points reporting groups

Reporting group title	Fluarix Dose A Group

Reporting group description:

Subjects were administered 1 or 2 doses* of Fluarix vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age).

* Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Reporting group title	Fluarix Dose B Group

Reporting group description:

Subjects were administered 1 or 2 doses*, half the volume of dose A, of Fluarix vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age).

* Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Reporting group title	Fluzone Group

Reporting group description:

Subjects were administered 1 or 2 doses* of Fluzone vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age).

* Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Primary: Geometric Mean Titer (GMT) of serum anti-hemagglutinin (HA) antibodies against each of the influenza vaccine strains

End point title	Geometric Mean Titer (GMT) of serum anti-hemagglutinin (HA) antibodies against each of the influenza vaccine strains

End point description:

GMTs and their 95% confidence interval are presented for all 3 viral strains comprised in the vaccine.
Post-vaccination timepoints: Day 28 for primed or Day 56 for unprimed subjects

End point type	Primary

End point timeframe:

Day 0 (PRE), Day 28 or Day 56 (POST)

End point values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1018	1016	1031	
Units: titre				
geometric mean (confidence interval 95%)				
A/Brisbane (PRE) (N=1017; 1013; 1030)	10.4 (9.7 to 11.1)	10.6 (9.8 to 11.4)	10.9 (10.1 to 11.7)	
A/Brisbane (POST) (N=1018; 1016; 1031)	106.1 (93.8 to 120.1)	131.6 (116.3 to 148.9)	232.4 (214 to 252.3)	
A/Uruguay (PRE) (N=1017; 1013; 1030)	12.1 (11.1 to 13.2)	11.2 (10.2 to 12.2)	11.6 (10.7 to 12.7)	

A/Uruguay (POST) (N=1018; 1016; 1031)	125.6 (113.3 to 139.3)	158.7 (143.9 to 175.2)	280.3 (260.3 to 301.9)	
B/Florida (PRE) (N=1017; 1013; 1030)	8.4 (7.9 to 9)	8.9 (8.3 to 9.6)	8.3 (7.7 to 8.8)	
B/Florida (POST) (N=1018; 1016; 1031)	113 (103.4 to 123.4)	164.4 (150.2 to 180.1)	176.4 (162.3 to 191.7)	

Statistical analyses

Statistical analysis title	Adjusted GMT ratio anti-A/Brisbane Fluzone/Fluarix

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of geometric mean titers [GMTs] of Fluarix (Dose B) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluarix Dose B Group v Fluzone Group
Number of subjects included in analysis	2047
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Adjusted GMT ratio
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	1.98

Notes:

[1] - The non-inferiority of the Fluarix Dose B Group as compared to the Fluzone Group was concluded if the upper limit of two-sided 95% CI of the GMT ratio (Fluzone Group over Fluarix Dose B Group) was ≤ 1.50 in terms of anti-A/Brisbane titers.

Statistical analysis title	Adjusted GMT ratio anti-A/Uruguay Fluzone/Fluarix

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of geometric mean titers [GMTs] of Fluarix (Dose B) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluarix Dose B Group v Fluzone Group
Number of subjects included in analysis	2047
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Adjusted GMT ratio
Point estimate	1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	1.89

Notes:

[2] - The non-inferiority of the Fluarix Dose B Group as compared to the Fluzone Group was concluded if the upper limit of two-sided 95% CI of the GMT ratio (Fluzone Group over Fluarix Dose B Group) was ≤ 1.50 in terms of anti-A/Uruguay titers.

Statistical analysis title	Adjusted GMT ratio anti-B/Florida Fluzone/Fluarix

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of geometric mean titers [GMTs] of Fluarix

(Dose B) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluzone Group v Fluarix Dose B Group
Number of subjects included in analysis	2047
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Adjusted GMT ratio
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.25

Notes:

[3] - The non-inferiority of the Fluarix Dose B Group as compared to the Fluzone Group was concluded if the upper limit of two-sided 95% CI of the GMT ratio (Fluzone Group over Fluarix Dose B Group) was ≤ 1.50 in terms of anti-B/Florida titers.

Statistical analysis title	Adjusted GMT ratio anti-A/Brisbane Fluzone/Fluarix

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of geometric mean titers [GMTs] of Fluarix (Dose A) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluzone Group v Fluarix Dose A Group
Number of subjects included in analysis	2049
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Adjusted GMT ratio
Point estimate	2.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.86
upper limit	2.4

Notes:

[4] - The non-inferiority of the Fluarix Dose A Group as compared to the Fluzone Group was concluded if the upper limit of two-sided 95% CI of the GMT ratio (Fluzone Group over Fluarix Dose A Group) was ≤ 1.50 in terms of anti-A/Brisbane titers.

Statistical analysis title	Adjusted GMT ratio anti-A/Uruguay Fluzone/Fluarix

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of geometric mean titers [GMTs] of Fluarix (Dose A) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluzone Group v Fluarix Dose A Group
Number of subjects included in analysis	2049
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Adjusted GMT ratio
Point estimate	2.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.08
upper limit	2.52

Notes:

[5] - The non-inferiority of the Fluarix Dose A Group as compared to the Fluzone Group was concluded if the upper limit of two-sided 95% CI of the GMT ratio (Fluzone Group over Fluarix Dose A Group) was ≤ 1.50 in terms of anti-A/Uruguay titers.

Statistical analysis title	Adjusted GMT ratio anti-B/Florida Fluzone/Fluarix

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of geometric mean titers [GMTs] of Fluarix (Dose A) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluzone Group v Fluarix Dose A Group
Number of subjects included in analysis	2049
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Adjusted GMT ratio
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.42
upper limit	1.76

Notes:

[6] - The non-inferiority of the Fluarix Dose A Group as compared to the Fluzone Group was concluded if the upper limit of two-sided 95% CI of the GMT ratio (Fluzone Group over Fluarix Dose A Group) was ≤ 1.50 in terms of anti-B/Florida titers.

Primary: Number of subjects seroconverted for the 3 Flu strains

End point title	Number of subjects seroconverted for the 3 Flu strains

End point description:

Seroconversion rate was defined as the number of subjects with either a pre-vaccination anti-HA titer < 1:10 and a post-vaccination titer ≥ 1:40, or a pre-vaccination titer ≥ 1:10 and a minimum 4-fold increase at post-vaccination titer. Post-vaccination timepoints: Day 28 for primed or Day 56 for unprimed subjects

End point type	Primary

End point timeframe:

Day 28 or Day 56

End point values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1017	1013	1030	
Units: Subjects				
A/Brisbane	636	699	929	
A/Uruguay	747	808	988	
B/Florida	812	864	904	

Statistical analyses

Statistical analysis title	SCR difference A/Brisbane Fluzone/Fluarix Dose B

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of seroconversion rates [SCRs]) of Fluarix (Dose B) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluarix Dose B Group v Fluzone Group
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	SCR difference
Point estimate	21.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.82
upper limit	24.58

Notes:

[7] - The non-inferiority of the Fluarix Dose B Group as compared to the Fluzone Group was concluded if the upper limit of the two-sided 95% CI for the difference (Fluzone Group minus Fluarix Dose B Group) in SCR was ≤ 10% for the 3 strains.

Statistical analysis title	SCR difference A/Uruguay Fluzone/Fluarix Dose B

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of seroconversion rates [SCRs]) of Fluarix (Dose B) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluarix Dose B Group v Fluzone Group
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	SCR difference
Point estimate	16.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.46
upper limit	18.98

Notes:

[8] - The non-inferiority of the Fluarix Dose B Group as compared to the Fluzone Group was concluded if the upper limit of the two-sided 95% CI for the difference (Fluzone Group minus Fluarix Dose B Group) in SCR was ≤ 10% for the 3 strains.

Statistical analysis title	SCR difference B/Florida Fluzone/Fluarix Dose B

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of seroconversion rates [SCRs]) of Fluarix (Dose B) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluarix Dose B Group v Fluzone Group
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	SCR difference
Point estimate	2.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	5.45

Notes:

[9] - The non-inferiority of the Fluarix Dose B Group as compared to the Fluzone Group was concluded if the upper limit of the two-sided 95% CI for the difference (Fluzone Group minus Fluarix Dose B Group) in SCR was ≤ 10% for the 3 strains.

Statistical analysis title	SCR difference A/Brisbane Fluzone/Fluarix Dose A

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of seroconversion rates [SCRs]) of Fluarix (Dose A) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluzone Group v Fluarix Dose A Group
Number of subjects included in analysis	2047
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	SCR difference
Point estimate	27.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.16
upper limit	31.14

Notes:

[10] - The non-inferiority of the Fluarix Dose A Group as compared to the Fluzone Group was concluded if the upper limit of the two-sided 95% CI for the difference (Fluzone Group minus Fluarix Dose A Group) in SCR was ≤ 10% for the 3 strains.

Statistical analysis title	SCR difference A/Uruguay Fluzone/Fluarix Dose A

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of seroconversion rates [SCRs]) of Fluarix (Dose A) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluzone Group v Fluarix Dose A Group
Number of subjects included in analysis	2047
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	SCR difference
Point estimate	22.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.54
upper limit	25.49

Notes:

[11] - The non-inferiority of the Fluarix Dose A Group as compared to the Fluzone Group was concluded if the upper limit of the two-sided 95% CI for the difference (Fluzone Group minus Fluarix Dose A Group) in SCR was ≤ 10% for the 3 strains.

Statistical analysis title	SCR difference B/Florida Fluzone/Fluarix Dose A

Statistical analysis description:

To demonstrate the immunological non-inferiority (in terms of seroconversion rates [SCRs]) of Fluarix (Dose A) vaccine versus Fluzone vaccine in subjects (6 to 35 months) at approximately 28 days (for

primed subjects) or 56 days (for unprimed subjects) following initial intramuscular vaccination.

Comparison groups	Fluarix Dose A Group v Fluzone Group
Number of subjects included in analysis	2047
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	SCR difference
Point estimate	7.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.75
upper limit	11.12

Notes:

[12] - The non-inferiority of the Fluarix Dose A Group as compared to the Fluzone Group was concluded if the upper limit of the two-sided 95% CI for the difference (Fluzone Group minus Fluarix Dose A Group) in SCR was ≤ 10% for the 3 strains.

Secondary: Number of Seroprotected Subjects for the 3 Flu strains

End point title	Number of Seroprotected Subjects for the 3 Flu strains

End point description:

A seroprotected subject is a subject with a serum anti-HA titer ≥ 1:40 Post-vaccination timepoints: Day 28 for primed or Day 56 for unprimed subjects

End point type	Secondary

End point timeframe:

Day 0 (PRE), Day 28 or Day 56 (POST)

End point values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1018	1016	1031	
Units: Subjects				
A/Brisbane (PRE) (N=1017; 1013; 1030)	185	186	206	
A/Brisbane (POST) (N=1018; 1016; 1031)	699	754	986	
A/Uruguay (PRE) (N=1017; 1013; 1030)	222	193	214	
A/Uruguay (POST) (N=1018; 1016; 1031)	788	846	1012	
B/Florida (PRE) (N=1017; 1013; 1030)	171	181	166	
B/Florida (POST) (N=1018; 1016; 1031)	872	902	935	

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion factor

End point title	Seroconversion factor

End point description:

Seroconversion factor is defined as the fold increase in serum anti-HA GMTs post-vaccination (Day 28 or 56) compared to pre-vaccination (Day 0). Post-vaccination timepoints: Day 28 for primed or Day 56 for unprimed subjects

End point type	Secondary

End point timeframe:

Day 28 or Day 56

End point values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1017	1013	1030	
Units: fold increase				
geometric mean (confidence interval 95%)				
A/Brisbane	10.2 (9.2 to 11.4)	12.4 (11.2 to 13.7)	21.4 (19.9 to 23.1)	
A/Uruguay	10.4 (9.6 to 11.3)	14.2 (13.1 to 15.4)	24.1 (22.6 to 25.7)	
B/Florida	13.4 (12.4 to 14.5)	18.4 (17 to 20)	21.4 (19.7 to 23.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms

End point title	Number of subjects reporting solicited local symptoms

End point description:

Solicited local symptoms assessed included pain, redness and swelling.

End point type	Secondary

End point timeframe:

During a 4-day follow-up period after vaccination

End point values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1081	1086	1090	
Units: Subjects				
Pain	403	406	363	
Redness	259	249	253	
Swelling	152	170	129	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general symptoms

End point title	Number of subjects reporting solicited general symptoms

End point description:

Solicited general symptoms assessed included drowsiness, irritability, loss of appetitie, and temperature.

End point type	Secondary

End point timeframe:

During a 4-day follow-up period after vaccination

End point values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1080	1086	1090	
Units: Subjects				
Drowsiness	293	317	298	
Irritability	386	387	375	
Loss of appetite	281	273	270	
Temperature	67	69	72	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events (AE)

End point title	Number of subjects reporting unsolicited adverse events (AE)

End point description:

An AE is 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

End point type	Secondary

End point timeframe:

During a 28-day follow-up period after vaccination

End point values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1107	1106	1104	
Units: Subjects				
Unsolicited adverse events (AE)	565	541	562	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAE) and new onset of chronic diseases (NOCD)

End point title	Number of subjects reporting serious adverse events (SAE) and new onset of chronic diseases (NOCD)

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above. NOCDs assessed include for example: diabetes, asthma, allergies, autoimmune disease, cancer, neuropathic disorders

End point type	Secondary

End point timeframe:

During the entire study (Day 0 until Month 6)

End point values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1107	1106	1104	
Units: Subjects				
SAE	35	29	31	
NOCD	10	8	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting rare serious events

End point title	Number of subjects reporting rare serious events

End point description:

Rare serious events have an occurrence rate of 1/300 (0.3%).

End point type	Secondary

End point timeframe:

During the entire study (Day 0 until Month 6)

End point values	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1107	1106	1104	
Units: Subjects				
Pneumonia	0	0	3	
Bronchiolitis	0	3	3	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: Day 0 to Month 6; Unsolicted AEs: During the 28-day post-vaccination period; Solicited local and general symptoms: During the 4-day post-vaccination period.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Fluarix Dose A Group

Reporting group description:

Subjects were administered 1 or 2 doses* of Fluarix vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age). * Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Reporting group title	Fluarix Dose B Group

Reporting group description:

Subjects were administered 1 or 2 doses*, half the volume of dose A, of Fluarix vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age). * Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Reporting group title	Fluzone Group

Reporting group description:

Subjects were administered 1 or 2 doses* of Fluzone vaccine (at Day 0 or at Days 0 and 28) intramuscularly, in the non-dominant upper arm (children >12 months of age) or in the anterolateral thigh (children <12 months of age). * Only those subjects who had no history of prior influenza vaccination (i.e. unprimed subjects) received 2 doses.

Serious adverse events	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 1107 (3.16%)	29 / 1106 (2.62%)	31 / 1104 (2.81%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electric shock			

subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body trauma			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	1 / 1107 (0.09%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury corneal			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	2 / 1107 (0.18%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			

subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	2 / 1104 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Coarctation of the aorta			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cyanosis			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Adverse drug reaction			

subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	2 / 1107 (0.18%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception			
subjects affected / exposed	0 / 1107 (0.00%)	2 / 1106 (0.18%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	2 / 1107 (0.18%)	1 / 1106 (0.09%)	2 / 1104 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Asthmatic crisis			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Idiopathic urticaria			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute sinusitis			

subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute tonsillitis			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	4 / 1107 (0.36%)	3 / 1106 (0.27%)	3 / 1104 (0.27%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 1107 (0.09%)	2 / 1106 (0.18%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			
subjects affected / exposed	1 / 1107 (0.09%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	6 / 1107 (0.54%)	4 / 1106 (0.36%)	2 / 1104 (0.18%)
occurrences causally related to treatment / all	0 / 6	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			

subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	2 / 1107 (0.18%)	0 / 1106 (0.00%)	4 / 1104 (0.36%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	2 / 1104 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			

subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	4 / 1107 (0.36%)	4 / 1106 (0.36%)	3 / 1104 (0.27%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia primary atypical			
subjects affected / exposed	1 / 1107 (0.09%)	0 / 1106 (0.00%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 1107 (0.09%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	2 / 1104 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	7 / 1107 (0.63%)	4 / 1106 (0.36%)	4 / 1104 (0.36%)
occurrences causally related to treatment / all	0 / 7	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral rash			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	2 / 1104 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 1107 (0.00%)	0 / 1106 (0.00%)	1 / 1104 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 1107 (0.00%)	1 / 1106 (0.09%)	0 / 1104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Fluarix Dose A Group	Fluarix Dose B Group	Fluzone Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	565 / 1107 (51.04%)	541 / 1106 (48.92%)	562 / 1104 (50.91%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	53 / 1107 (4.79%)	52 / 1106 (4.70%)	62 / 1104 (5.62%)
occurrences (all)	53	52	62
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	403 / 1107 (36.40%)	406 / 1106 (36.71%)	363 / 1104 (32.88%)
occurrences (all)	403	406	363
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	259 / 1107 (23.40%)	249 / 1106 (22.51%)	253 / 1104 (22.92%)
occurrences (all)	259	249	253
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	152 / 1107 (13.73%)	170 / 1106 (15.37%)	129 / 1104 (11.68%)
occurrences (all)	152	170	129
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	293 / 1107 (26.47%)	317 / 1106 (28.66%)	298 / 1104 (26.99%)
occurrences (all)	293	317	298
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	386 / 1107 (34.87%)	387 / 1106 (34.99%)	375 / 1104 (33.97%)
occurrences (all)	386	387	375
Loss of appetite			
alternative assessment type: Systematic			

subjects affected / exposed	281 / 1107 (25.38%)	273 / 1106 (24.68%)	270 / 1104 (24.46%)
occurrences (all)	281	273	270
Temperature			
alternative assessment type: Systematic			
subjects affected / exposed	67 / 1107 (6.05%)	69 / 1106 (6.24%)	72 / 1104 (6.52%)
occurrences (all)	67	69	72
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	62 / 1107 (5.60%)	42 / 1106 (3.80%)	60 / 1104 (5.43%)
occurrences (all)	62	42	60
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	59 / 1107 (5.33%)	70 / 1106 (6.33%)	60 / 1104 (5.43%)
occurrences (all)	59	70	60
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	135 / 1107 (12.20%)	116 / 1106 (10.49%)	139 / 1104 (12.59%)
occurrences (all)	135	116	139
Nasopharyngitis			
subjects affected / exposed	139 / 1107 (12.56%)	119 / 1106 (10.76%)	123 / 1104 (11.14%)
occurrences (all)	139	119	123
Pharyngitis			
subjects affected / exposed	49 / 1107 (4.43%)	60 / 1106 (5.42%)	52 / 1104 (4.71%)
occurrences (all)	49	60	52

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 August 2008	The rationale for this amendment was to include respiratory rate and heart rate measures at visit Day 0, change in the number of subjects planned (from 150 to 300) for interim analyses and recruitment plan was changed as enrollment plan was not available.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported