Clinical trial results:
A Phase 3, Randomized, Multicenter, Observer-Blinded, Noninferiority Study to Evaluate the Immunogenicity and Safety of a Seqirus Quadrivalent Inactivated Influenza Virus Vaccine (Seqirus QIV) with a US-Licensed 2015-2016 Quadrivalent Inactivated Comparator Influenza Vaccine (Comparator QIV) in a Pediatric Population Aged 5 Through 17 Years of Age.

Summary

EudraCT number	2016-004133-25
Trial protocol	Outside EU/EEA
Global end of trial date	13 June 2016

Results information

Result version number	v1 (current)
This version publication date	29 March 2017
First version publication date	29 March 2017

Trial information

Trial identification

Sponsor protocol code	CSLCT-QIV-13-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02545543
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Seqirus
Sponsor organisation address	45 Sidney Street, Cambridge MA, United States, 02139
Public contact	Seqirus Clinical Trials, Seqirus, Seqirus.ClinicalTrials@Seqirus.com
Scientific contact	Seqirus Clinical Trials, Seqirus, Seqirus.ClinicalTrials@Seqirus.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001894-PIP01-15
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that vaccination with Seqirus QIV elicits an immune response that is not inferior to that of a US licensed comparator QIV containing the same virus strains as Seqirus QIV, among a pediatric population 5 through 17 years of age.

Protection of trial subjects:

This clinical study was designated, implemented and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations, and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 September 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	10 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 2278
Worldwide total number of subjects	2278
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)	0
Children (2-11 years)	655

Adolescents (12-17 years)	1623
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First Patient In: 14-SEP-2015, Last Patient Last Visit: 13-JUN-2016. Number of activated sites that enrolled subjects: 32 (all based in USA)

Pre-assignment

Screening details:

Number of subjects screened: 2349. Number of subjects randomized: 2278

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Seqirus Quadrivalent Influenza Vaccine

Arm description:

The Seqirus study vaccine is a sterile, thiomersal-free suspension containing 60 mcg total hemagglutinin antigen per 0.5 mL dose (15 mcg each of the four recommended influenza strains for the Northern Hemisphere 2015/2016 influenza season).

Arm type	Experimental
Investigational medicinal product name	Seqirus Quadrivalent Inactivated Influenza Vaccine (Seqirus QIV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Seqirus QIV, inactivated, split-virion, thimerosal-free, quadrivalent influenza vaccine, administered as a 0.5 mL intramuscular dose. The vaccine is presented in a prefilled needleless syringe.

Arm title	Comparator Quadrivalent Influenza Vaccine

Arm description:

The Comparator Quadrivalent Inactivated Influenza vaccine is a US-licensed product containing four recommended influenza strains for the Northern Hemisphere 2015/2016 influenza season.

Arm type	Active comparator
Investigational medicinal product name	Comparator Quadrivalent Influenza Vaccine (Comparator QIV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The US-licensed Comparator QIV, inactivated, split-virion, thimerosal-free, quadrivalent influenza vaccine, administered as a 0.5 mL intramuscular dose. The vaccine is presented in a prefilled needleless syringe.

Number of subjects in period 1	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine
Started	1709	569
Number of subjects in period 1	1692	560
Completed	1628	535
Not completed	81	34
Consent withdrawn by subject	9	8
Physician decision	3	-
Lost to follow-up	67	25
Enrollment of subject at >1 study site	1	1
Noncompliance	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Seqirus Quadrivalent Influenza Vaccine
Reporting group description:	
The Seqirus study vaccine is a sterile, thiomersal-free suspension containing 60 mcg total hemagglutinin antigen per 0.5 mL dose (15 mcg each of the four recommended influenza strains for the Northern Hemisphere 2015/2016 influenza season).	
Reporting group title	Comparator Quadrivalent Influenza Vaccine
Reporting group description:	
The Comparator Quadrivalent Inactivated Influenza vaccine is a US-licensed product containing four recommended influenza strains for the Northern Hemisphere 2015/2016 influenza season.	

Reporting group values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine	Total
Number of subjects	1709	569	2278
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	9.5	9.5	
standard deviation	± 3.49	± 3.46	-
Gender categorical Units: Subjects			
Female	825	267	1092
Male	884	302	1186

End points

End points reporting groups

Reporting group title	Seqirus Quadrivalent Influenza Vaccine

Reporting group description:

The Seqirus study vaccine is a sterile, thiomersal-free suspension containing 60 mcg total hemagglutinin antigen per 0.5 mL dose (15 mcg each of the four recommended influenza strains for the Northern Hemisphere 2015/2016 influenza season).

Reporting group title	Comparator Quadrivalent Influenza Vaccine

Reporting group description:

The Comparator Quadrivalent Inactivated Influenza vaccine is a US-licensed product containing four recommended influenza strains for the Northern Hemisphere 2015/2016 influenza season.

Subject analysis set title	Per-protocol population
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol Population comprised all subjects in the Evaluable Population who did not have any protocol deviations that were medically assessed as potentially impacting on immunogenicity results.

Primary: The Geometric Mean Titre (GMT) ratio of each virus strain (Comparator QIV over Seqirus QIV)

End point title	The Geometric Mean Titre (GMT) ratio of each virus strain (Comparator QIV over Seqirus QIV)[1]

End point description:

Noninferiority of Seqirus QIV compared to comparator QIV was assessed by the eight co-primary endpoints of hemagglutination inhibition (HI) antibody geometric mean titer (GMT) and seroconversion rate (SCR) for each viral strain included in the vaccines. The GMT ratio is defined as the geometric mean of the postvaccination HI titer for the US-licensed comparator QIV over the geometric mean of the postvaccination HI titer for Seqirus QIV.

The noninferiority criterion for the GMT ratio (adjusted analysis) was that the upper bound of the two-sided 95% CI of the GMT ratio for the Comparator QIV GMT, divided by the bioCSL QIV GMT, should not exceed 1.5.

Analysis Population Description: The Per Protocol Population was used for the primary and secondary analysis of immunogenicity data and included subjects in the Evaluable Population minus any subjects with deviations that were thought to potentially affect the immunogenicity results, following medical review prior to unblinding.

End point type	Primary

End point timeframe:

28 days after last vaccination

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Noninferiority analysis by GMT Ratios: The noninferiority criterion for the GMT ratio was that the upper bound of the two-sided 95% CI of the GMT ratio for the Comparator QIV GMT, divided by the Seqirus QIV GMT, should not exceed 1.5.

End point values	Per-protocol population			
Subject group type	Subject analysis set			
Number of subjects analysed	2133			
Units: Titer Ratios				
geometric mean (confidence interval 95%)				
A/H1N1	1.01 (0.93 to 1.09)			
A/H3N2	1.05 (0.96 to 1.15)			

B/YAM	0.89 (0.81 to 0.98)			
B/VIC	0.92 (0.83 to 1.02)			

Statistical analyses

No statistical analyses for this end point

Primary: The difference in Seroconversion Rates (SCR) for each virus strain (Comparator QIV minus Seqirus QIV)

End point title	The difference in Seroconversion Rates (SCR) for each virus strain (Comparator QIV minus Seqirus QIV)[2]

End point description:

Noninferiority of Seqirus QIV compared to Comparator QIV was assessed by the eight co-primary endpoints of HI geometric mean titer (GMT) and seroconversion rate (SCR) for each viral strain. The rate of SCR is defined as the percentage of subjects with either a prevaccination HI titer < 1:10 and a postvaccination HI titer ≥ 1:40, or a prevaccination HI titer ≥ 1:10 and a ≥ 4-fold increase in postvaccination HI titer. For the SCR comparison, the difference between the SCR for each virus strain will be determined.

The noninferiority criterion for the SCR difference was that the upper bound of the two-sided 95% CI on the difference between SCRs for Comparator QIV minus the bioCSL QIV SCR should not exceed 10%.

Analysis Population Description: The Per Protocol Population was used for the primary and secondary analysis of immunogenicity data and included subjects in the Evaluable Population minus any subjects with deviations that were thought to potentially affect the immunogenicity r

End point type	Primary

End point timeframe:

28 days after last vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Noninferiority analysis by Seroconversion Rates: The noninferiority criterion for the SCR difference was that the upper bound of the two-sided 95% CI on the difference between SCRs for Comparator QIV minus the Seqirus QIV SCR should not exceed 10%.

End point values	Per-protocol population			
Subject group type	Subject analysis set			
Number of subjects analysed	2133			
Units: Percentage point				
number (confidence interval 95%)				
A/H1N1	-3.1 (-8 to 1.8)			
A/H3N2	0.4 (-4.5 to 5.3)			
B/YAM	-3.4 (-8.3 to 1.5)			
B/VIC	-2 (-6.9 to 2.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: The Frequency and Severity of Solicited Local Adverse Reactions (AEs)

End point title	Safety Endpoint: The Frequency and Severity of Solicited Local Adverse Reactions (AEs)

End point description:

Frequency and severity of solicited local adverse reactions (AEs) for 7 days (ie, day of vaccination and 6 subsequent days) after each vaccination dose

Analysis Population Description: The Solicited Safety Population comprises all subjects in the FAS who received at least one dose or partial dose of Study Vaccine and provided any evaluable data on solicited events.

End point type	Secondary

End point timeframe:

7 days after each vaccination

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1621	535		
Units: participants				
number (not applicable)				
Frequency of Solicited Local AEs	909	279		
Severe (Grade 3) Solicited Local AEs	71	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: The Frequency and Severity of Solicited Systemic Adverse Events (AEs).

End point title	Safety Endpoint: The Frequency and Severity of Solicited Systemic Adverse Events (AEs).

End point description:

Frequency and severity of solicited systemic adverse events (AEs) for 7 days (ie, day of vaccination and 6 subsequent days) after each vaccination dose

Analysis Population Description: The Solicited Safety Population comprised all subjects in the FAS who received at least one dose or partial dose of Study Vaccine and provided any evaluable data on solicited events.

End point type	Secondary

End point timeframe:

7 days after each vaccination

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1621	535		
Units: participants				
number (not applicable)				
Frequency of Solicited Systemic AEs	499	147		
Severe (Grade 3) Solicited Systemic AEs	24	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: The Frequency of Cellulitis-like Reaction

End point title	Safety Endpoint: The Frequency of Cellulitis-like Reaction

End point description:

Frequency of cellulitis-like reaction for at least 28 days after each vaccination dose

Analysis Population Description: The Solicited Safety Population comprises all subjects in the FAS who received at least one dose or partial dose of Study Vaccine and provided any evaluable data on solicited events.

End point type	Secondary

End point timeframe:

28 days after each vaccination.

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1621	535		
Units: participants				
number (not applicable)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: The Frequency and Severity of Unsolicited Adverse Events (AEs).

End point title	Safety Endpoint: The Frequency and Severity of Unsolicited Adverse Events (AEs).

End point description:

Frequency and severity of unsolicited AEs for at least 28 days (ie, day of vaccination and 27 subsequent days) after each vaccination dose

Analysis Population Description: The Overall Safety Population comprises all subjects in the FAS who received at least one dose or partial dose of Study Vaccine and provided any evaluable follow-up safety data.

End point type	Secondary

End point timeframe:

28 days after each vaccination

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1692	560		
Units: participants				
number (not applicable)				
At least one Unsolicited AE	269	70		
Severe (Grade 3) Unsolicited AE	11	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: The Frequency of Serious Adverse Events (SAEs).

End point title	Safety Endpoint: The Frequency of Serious Adverse Events (SAEs).

End point description:

Frequency of serious adverse events (SAEs) for 180 days after the last vaccination dose

Analysis Population Description: The Overall Safety Population comprises all subjects in the FAS who received at least one dose or partial dose of Study Vaccine and provided any evaluable follow-up safety data

End point type	Secondary

End point timeframe:

180 days after the last vaccination dose.

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1692	560		
Units: participants				
number (not applicable)	8	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: GMTs - Geometric Mean of HI Titers Prevaccination (Day 1) and Postvaccination (Study Exit Visit)

End point title	Immunogenicity Endpoint: GMTs - Geometric Mean of HI Titers Prevaccination (Day 1) and Postvaccination (Study Exit Visit)

End point description:

The humoral immune response was assessed for Seqirus QIV & comparator QIV. Serum HI titers against the 4 influenza vaccine strains was used to calculate Geometric mean of HI titers prevaccination & postvaccination

Analysis Population Description: The Per-Protocol Population comprised all subjects in the Evaluable Population who did not have any protocol deviations that were medically assessed as potentially impacting on immunogenicity results

End point type	Secondary

End point timeframe:

28 days after last vaccination

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1605	528		
Units: Titer				
geometric mean (confidence interval 95%)				
A/H1N1 (pre-vaccination)	114.8 (106.79 to 123.33)	119.5 (105.48 to 135.38)		
A/H3N2 (pre-vaccination)	75.2 (70.8 to 79.88)	72.1 (64.61 to 80.4)		
B/Yamagata (pre-vaccination)	10.5 (10.12 to 10.99)	10.4 (9.69 to 11.22)		
B/Victoria (pre-vaccination)	17 (16.1 to 17.85)	16.9 (15.42 to 18.46)		
A/H1N1 (post-vaccination)	858.7 (821.46 to 897.65)	875.1 (814.14 to 940.59)		
A/H3N2 (post-vaccination)	803.6 (763.01 to 846.26)	825.6 (756.12 to 901.55)		
B/Yamagata (post-vaccination)	60.7 (57 to 64.01)	54.3 (49.65 to 59.28)		
B/Victoria (post-vaccination)	140.9 (132.97 to 149.26)	130.3 (117.07 to 145.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Seroconversion Rate (SCR)

End point title	Immunogenicity Endpoint: Seroconversion Rate (SCR)

End point description:

The humoral immune response was assessed for Seqirus QIV & comparator QIV. Serum HI titers against the 4 influenza vaccine strains was used to calculate SCRs: % of subjects with either a prevaccination HI titer < 1:10 and a postvaccination HI titer ≥ 1:40 or a prevaccination titer ≥ 1:10 and a ≥ 4-fold increase in postvaccination titer

Analysis Population Description: The Per-Protocol Population comprised all subjects in the Evaluable Population who did not have any protocol deviations that were medically assessed as potentially impacting on immunogenicity results

End point type	Secondary

End point timeframe:

28 days after last vaccination

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1605	528		
Units: percentage of participants				
number (confidence interval 95%)				
A/H1N1	66.4 (64 to 68.7)	63.3 (59 to 67.4)		
A/H3N2	82.9 (81 to 84.7)	83.3 (79.9 to 86.4)		
B/Yamagata	58.5 (56 to 60.9)	55.1 (50.8 to 59.4)		
B/Victoria	72.1 (69.8 to 74.3)	70.1 (66 to 74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Seroprotection Rate

End point title	Immunogenicity Endpoint: Seroprotection Rate

End point description:

The humoral immune response was assessed for Seqirus QIV & comparator QIV. Serum HI titers against the 4 influenza vaccine strains was used to calculate the % of subjects with a titer ≥40 (seroprotection rates) at Day 1 and at Exit Visit

Analysis Population Description: The Per-Protocol Population comprised all subjects in the Evaluable Population who did not have any protocol deviations that were medically assessed as potentially impacting on immunogenicity results

End point type	Secondary

End point timeframe:

28 days after last vaccination

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1605	528		
Units: percentage of participants				
number (confidence interval 95%)				
A/H1N1 (pre-vaccination)	81.2 (79.2 to 83.1)	82 (78.5 to 85.2)		
A/H3N2 (pre-vaccination)	76.7 (74.6 to 78.7)	74.2 (70.3 to 77.9)		
B/Yamagata (pre-vaccination)	13 (11.4 to 14.7)	14.2 (11.3 to 17.5)		
B/Victoria (pre-vaccination)	27.9 (25.7 to 30.2)	27.8 (24.1 to 31.9)		
A/H1N1 (post-vaccination)	99.7 (99.3 to 99.9)	99.6 (98.6 to 100)		
A/H3N2 (post-vaccination)	99.4 (98.9 to 99.7)	99.4 (98.3 to 99.9)		
B/Yamagata (post-vaccination)	75 (72.8 to 77.1)	74.2 (70.3 to 77.9)		
B/Victoria (post-vaccination)	90.3 (88.7 to 91.7)	88.6 (85.6 to 91.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Geometric Mean Fold Increase (GMFI)

End point title	Immunogenicity Endpoint: Geometric Mean Fold Increase (GMFI)

End point description:

The humoral immune response was assessed for Seqirus QIV & comparator QIV. Serum HI titers against the 4 influenza vaccine strains was used to calculate Geometric mean fold increase (GMFI): geometric mean fold titer rise from Day 1 to Exit Visit

Analysis Population Description: The Per-Protocol Population comprised all subjects in the Evaluable Population who did not have any protocol deviations that were medically assessed as potentially impacting on immunogenicity results.

End point type	Secondary

End point timeframe:

28 days after last vaccination

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1605	528		
Units: Fold Change Titer				
geometric mean (confidence interval 95%)				

A/H1N1	7.5 (6.99 to 8.01)	7.3 (6.46 to 8.3)		
A/H3N2	10.7 (10.09 to 11.31)	11.5 (10.32 to 12.71)		
B/Yamagata	5.8 (5.44 to 6.08)	5.2 (4.75 to 5.71)		
B/Victoria	8.3 (7.81 to 8.84)	7.7 (6.92 to 8.62)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local and systemic solicited AEs collected from Day 1 to Day 7. Unsolicited AEs collected for 28 days after each vaccination dose. SAEs collected for 180 days after last vaccination.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	Seqirus Quadrivalent Influenza Vaccine

Reporting group description:

The Seqirus study vaccine is a sterile, thiomersal-free suspension containing 60 mcg total hemagglutinin antigen per 0.5 mL dose (15 mcg each of the four recommended influenza strains for the Northern Hemisphere 2015/2016 influenza season).

Reporting group title	Comparator Quadrivalent Influenza Vaccine

Reporting group description:

The Comparator Quadrivalent Inactivated Influenza vaccine is a US-licensed product containing four recommended influenza strains for the Northern Hemisphere 2015/2016 influenza season.

Serious adverse events	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 1692 (0.47%)	2 / 560 (0.36%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic injury			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	0 / 1692 (0.00%)	1 / 560 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder relapse prophylaxis			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 1692 (0.00%)	1 / 560 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Gastritis viral			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 1692 (0.06%)	0 / 560 (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: 3 %

Non-serious adverse events	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1094 / 1692 (64.66%)	337 / 560 (60.18%)	
Nervous system disorders			
Headache			
subjects affected / exposed	251 / 1692 (14.83%)	67 / 560 (11.96%)	
occurrences (all)	293	79	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	833 / 1692 (49.23%)	254 / 560 (45.36%)	
occurrences (all)	905	280	
Swelling			
subjects affected / exposed	224 / 1692 (13.24%)	62 / 560 (11.07%)	
occurrences (all)	241	68	
Redness			
subjects affected / exposed	278 / 1692 (16.43%)	93 / 560 (16.61%)	
occurrences (all)	302	104	
Fever			
subjects affected / exposed	54 / 1692 (3.19%)	12 / 560 (2.14%)	
occurrences (all)	57	12	
Malaise and Fatigue			

subjects affected / exposed	152 / 1692 (8.98%)	36 / 560 (6.43%)	
occurrences (all)	167	39	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	120 / 1692 (7.09%)	44 / 560 (7.86%)	
occurrences (all)	132	44	
Vomiting			
subjects affected / exposed	34 / 1692 (2.01%)	18 / 560 (3.21%)	
occurrences (all)	38	18	
Diarrhoea			
subjects affected / exposed	86 / 1692 (5.08%)	21 / 560 (3.75%)	
occurrences (all)	97	23	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	213 / 1692 (12.59%)	60 / 560 (10.71%)	
occurrences (all)	229	62	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 August 2015	Protocol amendment 1 (dated 05 Aug 2015), made the following revisions: 1) To clarify definitions of secondary safety endpoints; 2) To clarify when screening evaluations can be performed; 3) To adjust inclusion criterion to require ability of parent/guardian to use a Smartphone or computer to complete the eDiaries; 4) To clarify exclusion criterion concerning active infection or fever on day of vaccination; 5) To clarify exclusion criterion concerning current or recent medical conditions; 6) To add administration of second vaccination in procedures list for Visit 2, 2-dose group; 7) To clarify composition of the Safety Population; 8) To add instructions on postponing vaccination in the event of a febrile illness (oral temperature 100.0°F [37.8°C] or higher) or prophylactic antipyretic use on the day of vaccination; 9) To add instructions on retention of samples as requested by the IRB; 10) To remove reference to oral temperature and body weight as clinical signs; 11) To correct minor grammatical and typographic errors

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported