Clinical trial results:
A Phase 3, Randomized, Multicenter, Observer-blinded, Noninferiority Study to Evaluate the Immunogenicity and Safety of a Quadrivalent Inactivated Influenza Virus Vaccine (Seqirus QIV) with a US-licensed Quadrivalent Inactivated Comparator Influenza Virus Vaccine (Comparator QIV) in a Pediatric Population 6 Months Through 59 Months of Age

Summary

EudraCT number	2016-004753-33
Trial protocol	Outside EU/EEA
Global end of trial date	11 August 2017

Results information

Result version number	v1 (current)
This version publication date	04 October 2018
First version publication date	04 October 2018

Trial information

Trial identification

Sponsor protocol code	CSLCT-QIV-15-03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02914275
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Seqirus
Sponsor organisation address	The Point, 29 Market Street, Maidenhead, United Kingdom, SL6 8AA
Public contact	Clinical Study Disclosure Manager, Seqirus, Seqirus.ClinicalTrials@Seqirus.com
Scientific contact	Clinical Study Disclosure Manager, 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	05 October 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 August 2017
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 the US-licensed comparator QIV (Comparator QIV) containing the same virus strains as Seqirus QIV among a pediatric population 6 months through 59 months of age

Protection of trial subjects:

This study was conducted under a Food and Drug Administration (FDA) Investigational New Drug (IND) application, and documented in accordance with the applicable regulatory guidelines and requirements. The procedures set out in this study protocol were designed to ensure that the Sponsor and the Investigators abide by the principles of the current International Conference on Harmonisation Good Clinical Practice (ICH GCP) guideline on the conduct, evaluation and of this study, as described in ICH Topic E6 (Guideline for GCP). The study was carried out according to all applicable international and national regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 2016
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: 2247
Worldwide total number of subjects	2247
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)	505
Children (2-11 years)	1742
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:

Subjects were enrolled from 27 September 2016 to 11 August 2017 from 39 study sites in the United States of America.

Pre-assignment

Screening details:

A total of 2339 subjects were screened. Of these, 2247 subjects gave informed consent and were randomized to treatment.

Period 1

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

Arms

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

Arm description:

Subjects 6 months through 59 months of age who received Seqirus Quadrivalent Inactivated Influenza Vaccine.

Arm type	Experimental
Investigational medicinal product name	Seqirus Quadrivalent 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 either a 0.25mL or 0.5 mL intramuscular dose depending on the age of subjects. The vaccine is presented in a prefilled needleless syringe for the different formulations.

Arm title	Comparator Quadrivalent Influenza Vaccine

Arm description:

Subjects 6 months through 59 months of age who received Comparator Quadrivalent Inactivated Influenza Vaccine.

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 Comparator QIV, inactivated, split-virion, thimerosal-free, quadrivalent influenza vaccine, administered as either a 0.25mL or 0.5 mL intramuscular dose depending on the age of subjects. The vaccine is presented in a prefilled needleless syringe for the different formulations.

Number of subjects in period 1	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine
Started	1684	563
Completed	1566	521
Not completed	118	42
Consent withdrawn by subject	26	10
Physician decision	3	1
Other	4	1
Lost to follow-up	84	29
Protocol deviation	1	1

Baseline characteristics

Reporting groups

Reporting group title	Seqirus Quadrivalent Influenza Vaccine

Reporting group description:

Subjects 6 months through 59 months of age who received Seqirus Quadrivalent Inactivated Influenza Vaccine.

Reporting group title	Comparator Quadrivalent Influenza Vaccine

Reporting group description:

Subjects 6 months through 59 months of age who received Comparator Quadrivalent Inactivated Influenza Vaccine.

Reporting group values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine	Total
Number of subjects	1684	563	2247
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	36.6	36.5	
standard deviation	± 14.70	± 14.68	-
Gender categorical Units: Subjects			
Female	820	268	1088
Male	864	295	1159
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	434	160	594
Not Hispanic or Latino	1243	400	1643
Unknown or Not Reported	7	3	10
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	5	2	7
Asian	15	10	25
Native Hawaiian or Other Pacific Islander	13	3	16
Black or African American	361	123	484
White	1205	391	1596
More than one race	0	0	0

Unknown or Not Reported	85	34	119
Vaccination against influenza 2015/2016 season Units: Subjects			
Yes	845	294	1139
No	838	269	1107
Missing	1	0	1
Region of Enrollment Units: Subjects			
United States	1684	563	2247
Weight Units: kilograms			
arithmetic mean	15.36	15.40	
standard deviation	± 4.224	± 4.149	-
Prevaccination Axillary Temperature Units: Temp (°F)			
arithmetic mean	97.17	97.25	
standard deviation	± 0.963	± 0.935	-

End points

End points reporting groups

Reporting group title	Seqirus Quadrivalent Influenza Vaccine
Reporting group description:	
Subjects 6 months through 59 months of age who received Seqirus Quadrivalent Inactivated Influenza Vaccine.	

Reporting group title	Comparator Quadrivalent Influenza Vaccine
Reporting group description:	
Subjects 6 months through 59 months of age who received Comparator Quadrivalent Inactivated Influenza Vaccine.	
Subject analysis set title	Seqirus QIV Cohort A
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects 6 months through 35 months of age who received Seqirus Quadrivalent Inactivated Influenza Vaccine.	
Subject analysis set title	Seqirus QIV Cohort B
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects 36 months through 59 months of age who received Seqirus Quadrivalent Inactivated Influenza Vaccine.	
Subject analysis set title	Comparator QIV Cohort A
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects 6 months through 35 months of age who received Comparator Quadrivalent Inactivated Influenza Vaccine.	
Subject analysis set title	Comparator QIV Cohort B
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects 36 months through 59 months of age who received Comparator Quadrivalent Inactivated Influenza Vaccine.	

Primary: Immunogenicity Endpoint: The Geometric Mean Titer (GMT) Ratio of Each Virus Strain.

End point title	Immunogenicity Endpoint: The Geometric Mean Titer (GMT) Ratio of Each Virus Strain.
End point description:	
Noninferiority of Seqirus QIV compared to Comparator QIV will be assessed by hemagglutination inhibition (HI) antibody geometric mean titer (GMT) for each viral strain included in the vaccines. The GMT ratio is defined as the geometric mean of the postvaccination HI titer for the Comparator QIV over the geometric mean of the postvaccination HI titer for Seqirus QIV.	
End point type	Primary
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	1456[1]	484[2]		
Units: Geometric Mean Titer				
number (not applicable)				
A/H1N1	353.5	281.0		
A/H3N2	393.0	500.5		
B/Yamagata	23.7	26.5		
B/Victoria	54.6	52.9		

Notes:

[1] - Strain specific N:
A/H1N1, B/Yamagata and B/Victoria=1455; A/H3N2=1454
[2] - Strain specific N:
A/H1N1, A/H3N2 and B/Yamagata=484; B/Victoria=483

Statistical analyses

Statistical analysis title	Non-inferiority, A/H1N1, GMT ratio, Day 28

Statistical analysis description:

Non-inferiority of immune responses to A/H1N1 vaccine strain measured in terms of Geometric Mean Titer ratios 28 days after the last vaccination.

Comparison groups	Seqirus Quadrivalent Influenza Vaccine v Comparator Quadrivalent Influenza Vaccine
Number of subjects included in analysis	1940
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Geometric Mean Titer Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.88

Notes:

[3] - The non-inferiority 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 Seqirus QIV GMT, should not exceed 1.5

Statistical analysis title	Non-inferiority, A/H3N2, GMT ratio, Day 28

Statistical analysis description:

Non-inferiority of immune responses to A/H3N2 vaccine strain measured in terms of Geometric Mean Titer ratios 28 days after the last vaccination.

Comparison groups	Seqirus Quadrivalent Influenza Vaccine v Comparator Quadrivalent Influenza Vaccine
Number of subjects included in analysis	1940
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Geometric Mean Titer Ratio
Point estimate	1.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	1.42

Notes:

[4] - The non-inferiority 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 Seqirus QIV GMT, should not exceed 1.5

Statistical analysis title	Non-inferiority, B/Yamagata, GMT ratio, Day 28

Statistical analysis description:

Non-inferiority of immune responses to B/Yamagata vaccine strain measured in terms of Geometric Mean Titer ratios 28 days after the last vaccination.

Comparison groups	Seqirus Quadrivalent Influenza Vaccine v Comparator Quadrivalent Influenza Vaccine
Number of subjects included in analysis	1940
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Geometric Mean Titer Ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.24

Notes:

[5] - The non-inferiority 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 Seqirus QIV GMT, should not exceed 1.5

Statistical analysis title	Non-inferiority, B/Victoria, GMT ratio, Day 28

Statistical analysis description:

Non-inferiority of immune responses to B/Victoria vaccine strain measured in terms of Geometric Mean Titer ratios 28 days after the last vaccination.

Comparison groups	Seqirus Quadrivalent Influenza Vaccine v Comparator Quadrivalent Influenza Vaccine
Number of subjects included in analysis	1940
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Geometric Mean Titer Ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.09

Notes:

[6] - The non-inferiority 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 Seqirus QIV GMT, should not exceed 1.5

Primary: Immunogenicity Endpoint: Difference in Seroconversion Rate (SCR) for Each Virus Strain

End point title	Immunogenicity Endpoint: Difference in Seroconversion Rate (SCR) for Each Virus Strain

End point description:

Noninferiority of Seqirus QIV compared to comparator QIV will be assessed by seroconversion rate (SCR) for each viral strain. 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 vaccine (for each strain) will be determined.

End point type	Primary

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	1456[7]	484[8]		
Units: Percentage of Participants				
number (confidence interval 95%)				
A/H1N1	79.1 (76.9 to 81.1)	68.8 (64.5 to 72.9)		
A/H3N2	82.3 (80.2 to 84.2)	84.9 (81.4 to 88.0)		
B/Yamagata	38.9 (36.4 to 41.4)	41.9 (37.5 to 46.5)		
B/Victoria	60.2 (57.6 to 62.7)	61.1 (56.6 to 65.4)		

Notes:

[7] - Strain specific N:
A/H1N1, B/Yamagata and B/Victoria=1456; A/H3N2=1455
[8] - Strain specific N: A/H1N1, A/H3N2 and B/Yamagata=484; B/Victoria=483

Statistical analyses

Statistical analysis title	Non-inferiority:A/H1N1, SCR difference, Day 28

Statistical analysis description:

Non-inferiority of immune responses to A/H1N1 vaccine strain measured in terms of Seroconversion Rate Difference 28 days after the last vaccination

Comparison groups	Seqirus Quadrivalent Influenza Vaccine v Comparator Quadrivalent Influenza Vaccine
Number of subjects included in analysis	1940
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	Seroconversion Rate Difference
Point estimate	-10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.4
upper limit	-5.1

Notes:

[9] - 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%.

Statistical analysis title	Non-inferiority:A/H3N2, SCR difference, Day 28

Statistical analysis description:

Non-inferiority of immune responses to A/H3N2 vaccine strain measured in terms of Seroconversion Rate Difference 28 days after the last vaccination

Comparison groups	Seqirus Quadrivalent Influenza Vaccine v Comparator Quadrivalent Influenza Vaccine
Number of subjects included in analysis	1940
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	Seroconversion Rate Difference
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.54
upper limit	7.8

Notes:

[10] - 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%.

Statistical analysis title	Non-inferiority:B/Yamagata, SCR difference, Day 28

Statistical analysis description:

Non-inferiority of immune responses to B/Yamagata vaccine strain measured in terms of Seroconversion Rate Difference 28 days after the last vaccination

Comparison groups	Seqirus Quadrivalent Influenza Vaccine v Comparator Quadrivalent Influenza Vaccine
Number of subjects included in analysis	1940
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	Seroconversion Rate Difference
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	8.2

Notes:

[11] - 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%.

Statistical analysis title	Non-inferiority:B/Victoria, SCR difference, Day 28

Statistical analysis description:

Non-inferiority of immune responses to B/Victoria vaccine strain measured in terms of Seroconversion Rate Difference 28 days after the last vaccination

Comparison groups	Seqirus Quadrivalent Influenza Vaccine v Comparator Quadrivalent Influenza Vaccine
Number of subjects included in analysis	1940
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	Seroconversion Rate Difference
Point estimate	0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	6.1

Notes:

[12] - 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%.

Secondary: Safety Endpoint: Frequency and Severity of Solicited Local Adverse Reactions and Solicited Systemic Adverse Events

End point title	Safety Endpoint: Frequency and Severity of Solicited Local Adverse Reactions and Solicited Systemic Adverse Events

End point description:

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	1618[13]	545[14]		
Units: Count of participants				
Solicited AEs, Any	940	312		
Solicited AEs, Grade 1	592	189		
Solicited AEs, Grade 2	277	83		
Solicited AEs, Grade 3	71	39		
Solicited AEs, Local	645	208		
Solicited AEs, Systemic	633	215		

Notes:

[13] - Solicited Safety Population N=1618

[14] - Solicited Safety Population N=545

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: Frequency of Cellulitis-like Reactions

End point title	Safety Endpoint: Frequency of Cellulitis-like Reactions

End point description:

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	1618[15]	545[16]		
Units: Count of participants	0	1		

Notes:

[15] - Solicited Safety Population N=1618

[16] - Solicited Safety Population N=545

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: Frequency and Severity of Unsolicited AEs

End point title	Safety Endpoint: Frequency and Severity of Unsolicited AEs

End point description:

End point type	Secondary

End point timeframe:

28 days after each vaccination dose `

End point values	Seqirus Quadrivalent Influenza Vaccine	Comparator Quadrivalent Influenza Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1673[17]	559[18]		
Units: Count of participants				
Unsolicited AEs, Any	536	171		
Unsolicited AEs, Grade 1	285	92		
Unsolicited AEs, Grade 2	206	65		
Unsolicited AEs, Grade 3	45	14		

Notes:

[17] - Overall Safety Population=1673

[18] - Overall Safety Population=559

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: Frequency of Serious Adverse Events (SAE)

End point title	Safety Endpoint: Frequency of Serious Adverse Events (SAE)

End point description:

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	1673[19]	559[20]		
Units: Count of participants				
SAE (Day 1 to Day 28)	4	0		
SAE (Day 29 to Day 180)	7	3		
Related SAE	0	0		
Death	0	0		
AESI (Day 1 to Day 28)	0	0		
AESI (Day 29 to Day 180)	2	0		

Notes:

[19] - Overall Safety Population = 1673

[20] - Overall Safety Population = 559

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Geometric Mean Titers, HI Assay Prevaccination and Postvaccination, by Age Subgroup

End point title	Immunogenicity Endpoint: Geometric Mean Titers, HI Assay Prevaccination and Postvaccination, by Age Subgroup

End point description:

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

End point type	Secondary

End point timeframe:

28 days after last vaccination

End point values	Seqirus QIV Cohort A	Seqirus QIV Cohort B	Comparator QIV Cohort A	Comparator QIV Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	586[21]	870	193	291[22]
Units: Geometric Mean Titer				
number (confidence interval 95%)				
A/H1N1, Prevaccination	13.8 (12.30 to 15.57)	60.7 (53.97 to 68.20)	14.9 (12.25 to 18.22)	68.7 (55.84 to 84.62)
A/H1N1, Postvaccination	184.9 (165.15 to 207.05)	590.2 (548.62 to 634.93)	168.3 (137.69 to 205.62)	469.2 (413.72 to 532.05)
A/H3N2, Prevaccination	14.3 (12.48 to 16.39)	62.4 (55.50 to 70.19)	16.4 (12.86 to 20.91)	65.5 (53.76 to 79.88)
A/H3N2, Postvaccination	184.9 (164.57 to 207.65)	778.6 (710.83 to 852.82)	247.5 (202.14 to 302.95)	1047 (911.69 to 1202.48)

B/Yamagata, Prevaccination	5.9 (5.66 to 6.13)	7.9 (7.55 to 8.33)	5.8 (5.47 to 6.22)	8.3 (7.58 to 9.17)
B/Yamagata, Postvaccination	15.6 (14.33 to 17.00)	35.4 (32.73 to 38.26)	16.3 (14.03 to 18.95)	44.1 (38.30 to 50.87)
B/Victoria, Prevaccination	7.1 (6.75 to 7.55)	9.6 (9.04 to 10.19)	6.9 (6.26 to 7.53)	10.4 (9.35 to 11.64)
B/Victoria, Postvaccination	39.8 (36.02 to 44.04)	72.1 (65.62 to 79.25)	31.9 (26.88 to 37.81)	85.9 (73.16 to 100.96)

Notes:

[21] - Strain specific N for postvaccination GMT results: A/H1N1, B/Yamagata and B/Victoria=586; A/H3N2=585

[22] - Strain specific N for prevaccination GMT results: A/H1N1, A/H3N2 and B/Yamagata=291; B/Victoria=290

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Seroconversion Rates (SCR), HI Assay, by Age Subgroup

End point title	Immunogenicity Endpoint: Seroconversion Rates (SCR), HI Assay, by Age Subgroup

End point description:

The humoral immune response will be assessed for Seqirus QIV & comparator QIV. Serum HI titers against the 4 influenza vaccine strains will be used to calculate SCRs defined as the % 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.

End point type	Secondary

End point timeframe:

28 days after last vaccination

End point values	Seqirus QIV Cohort A	Seqirus QIV Cohort B	Comparator QIV Cohort A	Comparator QIV Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	586[23]	870	193	291[24]
Units: Percent of Participants				
number (confidence interval 95%)				
A/H1N1	81.9 (78.6 to 84.9)	77.1 (74.2 to 79.9)	80.3 (74.0 to 85.7)	61.2 (55.3 to 66.8)
A/H3N2	82.4 (79.1 to 85.4)	82.2 (79.5 to 84.7)	85.0 (79.1 to 89.7)	84.9 (80.2 to 88.8)
B/Yamagata	22.5 (19.2 to 26.1)	49.9 (46.5 to 53.3)	26.9 (20.8 to 33.8)	51.9 (46.0 to 57.8)
B/Victoria	52.9 (48.8 to 57.0)	65.1 (61.8 to 68.2)	49.7 (42.5 to 57.0)	68.6 (62.9 to 73.9)

Notes:

[23] - Strain specific N: A/H1N1, B/Yamagata and B/Victoria=586; A/H3N2=585

[24] - Strain specific N: A/H1N1, A/H3N2 and B/Yamagata=291; B/Victoria=290

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Seroprotection Rates, HI Assay by Age Subgroup

End point title	Immunogenicity Endpoint: Seroprotection Rates, HI Assay by Age Subgroup

End point description:

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

End point type	Secondary

End point timeframe:

28 days after last vaccination

End point values	Seqirus QIV Cohort A	Seqirus QIV Cohort B	Comparator QIV Cohort A	Comparator QIV Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	586[25]	870	193	291
Units: Percentage of participants				
number (confidence interval 95%)				
A/H1N1	90.1 (87.4 to 92.4)	99.1 (98.2 to 99.6)	88.6 (83.3 to 92.7)	98.3 (96.0 to 99.4)
A/H3N2	92.5 (90.0 to 94.5)	98.4 (97.3 to 99.1)	95.3 (91.3 to 97.8)	98.6 (96.5 to 99.6)
B/Yamagata	24.7 (21.3 to 28.4)	57.1 (53.8 to 60.4)	29.0 (22.7 to 36.0)	61.5 (55.7 to 67.1)
B/Victoria	55.6 (51.5 to 59.7)	71.0 (67.9 to 74.0)	52.8 (45.6 to 60.1)	75.3 (69.9 to 80.1)

Notes:

[25] - Strain specific N: A/H1N1, B/Yamagata and B/Victoria=586; A/H3N2=585

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Geometric Mean Fold Increase (GMFI) by Age Subgroup

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

End point description:

The humoral immune response will be assessed for Seqirus QIV & comparator QIV. Serum HI titers against the 4 influenza vaccine strains will be used to calculate GMFIs, defined as the geometric mean fold titer rise from Day 1 to Study Exit Visit.

End point type	Secondary

End point timeframe:

28 days after last vaccination

End point values	Seqirus QIV Cohort A	Seqirus QIV Cohort B	Comparator QIV Cohort A	Comparator QIV Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	586[26]	870	193	291[27]
Units: Geometric Mean Folder Titer Increase				
number (confidence interval 95%)				
A/H1N1	13.4 (11.98 to 14.90)	9.7 (8.90 to 10.64)	11.3 (9.40 to 13.49)	6.8 (5.83 to 7.99)
A/H3N2	13.0 (11.62 to 14.50)	12.5 (11.42 to 13.62)	15.1 (12.60 to 18.08)	16.0 (13.62 to 18.74)
B/Yamagata	2.6 (2.45 to 2.86)	4.5 (4.17 to 4.77)	2.8 (2.45 to 3.19)	5.3 (4.67 to 6.00)
B/Victoria	5.6 (5.11 to 6.09)	7.5 (6.93 to 8.15)	4.6 (3.97 to 5.42)	8.2 (7.18 to 9.42)

Notes:

[26] - Strain specific N: A/H1N1, B/Yamagata and B/Victoria=586; A/H3N2=585

[27] - Strain specific N: A/H1N1, A/H3N2 and B/Yamagata=291; B/Victoria=290

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Non-serious unsolicited AEs and serious AEs were collected from Day 1 through Day 180	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Seqirus QIV
Reporting group description:	
Subjects 6 months through 59 months of age who received Seqirus Quadrivalent Inactivated Influenza Vaccine.	
Reporting group title	Comparator QIV
Reporting group description:	
Subjects 6 months through 59 months of age who received Comparator Quadrivalent Inactivated Influenza Vaccine.	

Serious adverse events	Seqirus QIV	Comparator QIV	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 1673 (0.66%)	3 / 559 (0.54%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 1673 (0.06%)	0 / 559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body aspiration			
subjects affected / exposed	1 / 1673 (0.06%)	0 / 559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 1673 (0.00%)	1 / 559 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Febrile convulsion			
subjects affected / exposed	2 / 1673 (0.12%)	0 / 559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 1673 (0.06%)	0 / 559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 1673 (0.00%)	1 / 559 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 1673 (0.06%)	0 / 559 (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			
Croup infectious			
subjects affected / exposed	2 / 1673 (0.12%)	0 / 559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 1673 (0.00%)	1 / 559 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 1673 (0.06%)	0 / 559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			

subjects affected / exposed	1 / 1673 (0.06%)	0 / 559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 1673 (0.06%)	0 / 559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 1673 (0.06%)	0 / 559 (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: 4 %

Non-serious adverse events	Seqirus QIV	Comparator QIV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	320 / 1673 (19.13%)	80 / 559 (14.31%)	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	153 / 1673 (9.15%)	41 / 559 (7.33%)	
occurrences (all)	167	52	
Rhinorrhoea			
subjects affected / exposed	134 / 1673 (8.01%)	53 / 559 (9.48%)	
occurrences (all)	155	63	
Infections and infestations			
Pyrexia			
subjects affected / exposed	91 / 1673 (5.44%)	25 / 559 (4.47%)	
occurrences (all)	100	29	
Upper respiratory tract infection			
subjects affected / exposed	67 / 1673 (4.00%)	17 / 559 (3.04%)	
occurrences (all)	72	17	

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