Clinical trial results:
Safety and Immunogenicity of Different Dosages of High-Dose Quadrivalent Influenza Vaccine in Children 6 Months to 17 Years of Age

Summary

EudraCT number	2018-005026-39
Trial protocol	Outside EU/EEA
Global end of trial date	16 October 2019

Results information

Result version number	v1 (current)
This version publication date	26 April 2020
First version publication date	26 April 2020

Trial information

Trial identification

Sponsor protocol code	QHD04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03698279
WHO universal trial number (UTN)	U1111-1189-3713

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	Discovery Drive, Swiftwater, United States, PA 18370-0187
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002359-PIP01-18
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes
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	24 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety: To describe the safety of each dosage of high-dose quadrivalent influenza vaccine (QIV-HD) used in the study during the 28 days following each vaccination, and serious adverse events (SAEs) (including adverse events of special interest) throughout the study.
Immunogenicity: To describe the antibody response induced by each dosage of QIV-HD used in the study compared with unadjuvanted standard-dose quadrivalent influenza vaccine (QIV-SD) by haemagglutination inhibition (HAI) measurement method.
To describe the antibody response induced by each dosage of QIV-HD used in the study compared with unadjuvanted QIV-SD by virus seroneutralisation (SN) measurement method.
To describe the antibody response induced by the highest acceptable dosage of QIV-HD compared with adjuvanted trivalent influenza vaccine (TIV) by HAI and virus SN measurement methods.

Protection of trial subjects:

Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 October 2018
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	Canada: 26
Country: Number of subjects enrolled	United States: 639
Worldwide total number of subjects	665
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	118

months)	
Children (2-11 years)	473
Adolescents (12-17 years)	74
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 16 centres in United States (US) and Canada from 09 October 2018 to 16 October 2019.

Pre-assignment

Screening details:

A total of 665 subjects were enrolled in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)

Arm description:

Subjects from US (aged 6 months to 17 years) received 30 microgram (µg) QIV-HD, intramuscularly (IM).

Arm type	Experimental
Investigational medicinal product name	High-Dose Quadrivalent Influenza Vaccine (QIV-HD) (split-virion, inactivated)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 injection at Day 0. Subjects for whom 2 doses of influenza vaccine were recommended, a second dose was administered at Day 28.

Arm title	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)

Arm description:

Subjects from US (aged 6 months to 17 years) received 45 µg QIV-HD, IM.

Arm type	Experimental
Investigational medicinal product name	High-Dose Quadrivalent Influenza Vaccine, (QIV-HD) (split-virion, inactivated)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 injection at Day 0. Subjects for whom 2 doses of influenza vaccine were recommended, a second dose was administered at Day 28.

Arm title	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)

Arm description:

Subjects from US (aged 6 months to 17 years) received 60 µg QIV-HD, IM.

Arm type	Experimental

Investigational medicinal product name	High-Dose Quadrivalent Influenza Vaccine (QIV-HD) (split-virion, purified)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 injection at Day 0. Subjects for whom 2 doses of influenza vaccine were recommended, a second dose was administered at Day 28.

Arm title	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)

Arm description:

Pooled arm consisted of subjects who were from US aged 6 months to 17 years, randomised to Groups 1, 2 and 3 and received 15 µg QIV-SD, IM.

Arm type	Active comparator
Investigational medicinal product name	Fluarix Quadrivalent Influenza vaccine (Unadjuvanted QIV-SD)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 injection at Day 0. Subjects for whom 2 doses of influenza vaccine were recommended, a second dose was administered at Day 28.

Arm title	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)

Arm description:

Subjects from Canada (aged 6 to <24 months) received 60 µg QIV-HD, IM.

Arm type	Experimental
Investigational medicinal product name	High-Dose Quadrivalent Influenza Vaccine (QIV-HD) (split-virion, purified)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 injection at Day 0. Subjects for whom 2 doses of influenza vaccine were recommended, a second dose was administered at Day 28.

Arm title	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)

Arm description:

Subjects from Canada (aged 6 to <24 months) received 7.5 µg adjuvanted TIV, IM.

Arm type	Active comparator
Investigational medicinal product name	FLUAD Pediatric (adjuvanted TIV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 injection at Day 0. Subjects for whom 2 doses of influenza vaccine were recommended, a second dose was administered at Day 28.

Number of subjects in period 1	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)
Started	124	122	159
Safety analysis set population (SafAS)	122	121	158
Completed	119	120	152
Not completed	5	2	7
Consent withdrawn by subject	-	-	1
Lost to follow-up	3	1	4
Withdrawal by parent/guardian	1	1	1
Protocol deviation	1	-	1

Number of subjects in period 1	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)
Started	234	13	13
Safety analysis set population (SafAS)	234	13	13
Completed	228	13	13
Not completed	6	0	0
Consent withdrawn by subject	-	-	-
Lost to follow-up	5	-	-
Withdrawal by parent/guardian	1	-	-
Protocol deviation	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)
Reporting group description:	
Subjects from US (aged 6 months to 17 years) received 30 microgram (µg) QIV-HD, intramuscularly (IM).	
Reporting group title	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)
Reporting group description:	
Subjects from US (aged 6 months to 17 years) received 45 µg QIV-HD, IM.	
Reporting group title	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)
Reporting group description:	
Subjects from US (aged 6 months to 17 years) received 60 µg QIV-HD, IM.	
Reporting group title	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Reporting group description:	
Pooled arm consisted of subjects who were from US aged 6 months to 17 years, randomised to Groups 1, 2 and 3 and received 15 µg QIV-SD, IM.	
Reporting group title	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)
Reporting group description:	
Subjects from Canada (aged 6 to <24 months) received 60 µg QIV-HD, IM.	
Reporting group title	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)
Reporting group description:	
Subjects from Canada (aged 6 to <24 months) received 7.5 µg adjuvanted TIV, IM.	

Reporting group values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)
Number of subjects	124	122	159
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	5.8	6.1	5.2
standard deviation	± 3.91	± 4.30	± 4.22
Gender categorical			
Units: Subjects			
Female	51	61	82
Male	73	61	77
Race			
Units: Subjects			
American Indian or Alaska Native	2	0	0
Asian	1	2	0
Black or African American	22	28	40
Native Hawaiian or Other Pacific Islander	0	3	2
White	92	81	108
Multiple	4	3	8
Not Reported	3	5	1

Reporting group values	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)
Number of subjects	234	13	13
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	5.1	0.8	1.0
standard deviation	± 4.02	± 0.19	± 0.28
Gender categorical			
Units: Subjects			
Female	114	4	6
Male	120	9	7
Race			
Units: Subjects			
American Indian or Alaska Native	2	0	0
Asian	3	0	0
Black or African American	58	2	0
Native Hawaiian or Other Pacific Islander	5	0	1
White	157	9	11
Multiple	7	2	1
Not Reported	2	0	0

Reporting group values	Total		
Number of subjects	665		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	318		
Male	347		
Race			
Units: Subjects			
American Indian or Alaska Native	4		
Asian	6		
Black or African American	150		
Native Hawaiian or Other Pacific Islander	11		
White	458		
Multiple	25		
Not Reported	11		

End points

End points reporting groups

Reporting group title	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)
Reporting group description:	
Subjects from US (aged 6 months to 17 years) received 30 microgram (µg) QIV-HD, intramuscularly (IM).	
Reporting group title	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)
Reporting group description:	
Subjects from US (aged 6 months to 17 years) received 45 µg QIV-HD, IM.	
Reporting group title	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)
Reporting group description:	
Subjects from US (aged 6 months to 17 years) received 60 µg QIV-HD, IM.	
Reporting group title	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Reporting group description:	
Pooled arm consisted of subjects who were from US aged 6 months to 17 years, randomised to Groups 1, 2 and 3 and received 15 µg QIV-SD, IM.	
Reporting group title	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)
Reporting group description:	
Subjects from Canada (aged 6 to <24 months) received 60 µg QIV-HD, IM.	
Reporting group title	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)
Reporting group description:	
Subjects from Canada (aged 6 to <24 months) received 7.5 µg adjuvanted TIV, IM.	
Subject analysis set title	Group 4a: QIV-SD, 15 µg, (US: 6 months to 17 years)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects from US (aged 6 months to 17 years) received 15 µg QIV-SD, IM and were restricted for comparison to relevant experimental study group QIV-HD 30 µg.	
Subject analysis set title	Group 4b: QIV-SD, 15 µg, (US: 6 months to 17 years)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects from US (aged 6 months to 17 years) received 15 µg QIV-SD, IM and were restricted for comparison to relevant experimental study group QIV-HD 45 µg.	
Subject analysis set title	Group 4c: QIV-SD, 15 µg, (US: 6 months to 17 years)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects from US (aged 6 months to 17 years) received 15 µg QIV-SD, IM and were restricted for comparison to relevant experimental study group QIV-HD 60 µg.	

Primary: Number of Subjects With Immediate Unsolicited Adverse Events After any Vaccination

End point title	Number of Subjects With Immediate Unsolicited Adverse Events After any Vaccination[1]
End point description:	
An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the case report book (CRB) in terms of diagnosis and/or onset window post-vaccination. Unsolicited AEs includes both serious (SAEs) and non-serious unsolicited AEs. An SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. All subjects were observed for 30 minutes after vaccination, and any unsolicited systemic AEs occurred during that time were recorded as immediate unsolicited AEs in the CRB. Analysis was performed on SafAS which included subjects who had received at least one dose of the study vaccines.	
End point type	Primary

End point timeframe:

Within 30 minutes after any 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	122	121	158	234
Units: subjects				
number (not applicable)	0	0	1	0

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Unsolicited Adverse Events After any Vaccination

End point title	Number of Subjects With Unsolicited Adverse Events After any Vaccination[2]

End point description:

An unsolicited AE was an observed AE that does not fulfill the conditions prelisted in the CRB in terms of diagnosis and/or onset window post-vaccination. Unsolicited AEs included both serious and non-serious unsolicited AEs. An SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. Adverse reactions (ARs) were AEs related to vaccination. An injection site reaction was an AR at and around the injection site. Systemic AEs were all AEs that were not injection or administration site reactions. Analysis was performed on the SafAS population.

End point type	Primary

End point timeframe:

Within 28 days after any 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	122	121	158	234
Units: subjects				
number (not applicable)				
Unsolicited AE	46	46	53	80
Unsolicited non-serious AR	4	8	8	10
Unsolicited non-serious injection site AR	0	3	0	0
Unsolicited non-serious systemic AE	46	45	52	80
Unsolicited non-serious systemic AR	4	5	8	10

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: subjects				
number (not applicable)				
Unsolicited AE	11	12		
Unsolicited non-serious AR	1	3		
Unsolicited non-serious injection site AR	0	1		
Unsolicited non-serious systemic AE	11	12		
Unsolicited non-serious systemic AR	1	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Serious Adverse Events (SAEs) After any Vaccination

End point title	Number of Subjects With Serious Adverse Events (SAEs) After any Vaccination[3]

End point description:

An SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. An SAE which caused death of the subject was considered as fatal SAE. Adverse events of special interest (AESIs) were captured as SAEs which included new onset of Guillain-Barré syndrome, encephalitis/myelitis (including transverse myelitis), Bell's palsy, convulsions, optic neuritis, and brachial neuritis. Analysis was performed on the SafAS population.

End point type	Primary

End point timeframe:

From Day 0 up to 6 months post-vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	122	121	158	234
Units: subjects				
number (not applicable)				
SAE	0	0	2	0
Fatal SAE	0	0	0	0
AESI	0	0	1	0

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: subjects				
number (not applicable)				
SAE	0	1		
Fatal SAE	0	0		
AESI	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Achieving Seroconversion Against Antigens Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine

End point title	Number of Subjects Achieving Seroconversion Against Antigens Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine[4][5]

End point description:

Anti-influenza antibodies were measured by HAI assay for strains A/H1N1, A/H3N2, B/Victoria lineage and B/Yamagata lineage. Seroconversion was defined as either a HAI titer <10 (1/dilution) at Day 0 and post-vaccination titer greater than or equal to (>=) 40 (1/dilution) at Day 28, or HAI titer >=10 (1/dilution) at Day 0 and >=4-fold increase in HAI titer (1/dilution) at Day 28. Due to complex study design and analysis of dose formulation and age groups, subjects in QIV-HD 30 µg and QIV-HD 45 µg dose formulations groups from age cohort 9 through 17 years old were randomised and shared a matching age group with QIV-SD control group. Hence, those subjects were counted more than once in QIV-SD arms for different dose levels. Analysis was performed on immunogenicity analysis set (IAS) population which included randomised subjects who received 1 dose/2 doses of study vaccine and had a post-vaccination blood sample. Here, 'n'=subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 28 post any vaccination

Notes:

[4] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since the comparison assessment was performed based on the strain and dosages, the inferential statistical analysis and the percentage of comparison against the pooled arm data is not presented.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	115	156	13
Units: subjects				
number (not applicable)				
A/H1N1 (n = 110, 112, 141, 11, 12, 39, 41, 148)	72	71	107	8
A/H3N2 (n = 109, 111, 140, 11, 12, 38, 41, 146)	63	79	102	8
B/Victoria (n= 110, 111, 141, 11, 12, 39, 41, 148)	84	94	117	6
B/Yamagata (n= 110, 109, 141, 11, 12, 38, 41, 147)	79	85	120	8

End point values	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)	Group 4a: QIV-SD, 15 µg, (US: 6 months to 17 years)	Group 4b: QIV-SD, 15 µg, (US: 6 months to 17 years)	Group 4c: QIV-SD, 15 µg, (US: 6 months to 17 years)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	40	41	157
Units: subjects				
number (not applicable)				
A/H1N1 (n = 110, 112, 141, 11, 12, 39, 41, 148)	11	26	24	98
A/H3N2 (n = 109, 111, 140, 11, 12, 38, 41, 146)	12	18	20	71
B/Victoria (n= 110, 111, 141, 11, 12, 39, 41, 148)	12	28	30	111
B/Yamagata (n= 110, 109, 141, 11, 12, 38, 41, 147)	1	26	31	117

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Influenza Antibodies Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-

Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine

End point title	Geometric Mean Titers (GMTs) of Influenza Antibodies Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine[6][7]

End point description:

GMTs of anti-influenza antibodies were measured using an HAI assay for 4 strains: A/H1N1, A/H3N2, B Victoria lineage, and B Yamagata lineage. Due to complex study design and analysis of dose formulation and age groups, subjects in QIV-HD 30 µg & QIV-HD 45 µg dose formulations groups from age cohort 9 through 17 years old were randomised and shared a matching age group with QIV-SD control group. Hence, those subjects were counted more than once in QIV-SD arms for different dose levels.Analysis was performed on IAS population. Here, 'n'= subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 28 post any vaccination

Notes:

[6] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since the comparison assessment was performed based on the strain and dosages, the inferential statistical analysis and the percentage of comparison against the pooled arm data is not presented.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	115	156	13
Units: titers (1/dilution)				
geometric mean (confidence interval 95%)				
A/H1N1 (n = 116, 114, 145, 13, 12, 40, 41, 151)	673 (525 to 863)	676 (524 to 873)	834 (674 to 1033)	59.7 (27.0 to 132)
A/H3N2 (n = 116, 113, 144, 13, 12, 39, 41, 151)	518 (399 to 671)	781 (600 to 1017)	770 (604 to 982)	66.4 (33.0 to 133)
B/Victoria (n= 116, 113, 145, 13, 12, 40, 41, 151)	378 (296 to 483)	432 (334 to 560)	494 (400 to 612)	56.6 (26.2 to 122)
B/Yamagata (n= 116, 112, 144, 13, 12, 39, 41, 151)	723 (582 to 899)	720 (556 to 932)	877 (722 to 1066)	75.8 (38.9 to 148)

End point values	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)	Group 4a: QIV-SD, 15 µg, (US: 6 months to 17 years)	Group 4b: QIV-SD, 15 µg, (US: 6 months to 17 years)	Group 4c: QIV-SD, 15 µg, (US: 6 months to 17 years)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	40	41	157
Units: titers (1/dilution)				
geometric mean (confidence interval 95%)				
A/H1N1 (n = 116, 114, 145, 13, 12, 40, 41, 151)	604 (261 to 1398)	698 (419 to 1161)	791 (480 to 1303)	618 (461 to 830)
A/H3N2 (n = 116, 113, 144, 13, 12, 39, 41, 151)	604 (386 to 946)	314 (184 to 538)	441 (264 to 738)	307 (239 to 395)

B/Victoria (n= 116, 113, 145, 13, 12, 40, 41, 151)	1244 (767 to 2016)	296 (194 to 452)	468 (302 to 726)	310 (246 to 390)
B/Yamagata (n= 116, 112, 144, 13, 12, 39, 41, 151)	21.8 (12.3 to 38.6)	706 (474 to 1050)	727 (501 to 1054)	580 (466 to 721)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titer Ratios (GMTRs) of Influenza Antibodies Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine

End point title	Geometric Mean Titer Ratios (GMTRs) of Influenza Antibodies Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine[8]

End point description:

GMTs of anti-influenza antibodies were measured using an HAI assay for 4 strains: A/H1N1, A/H3N2, B Victoria lineage, and B Yamagata lineage. GMTRs were calculated as the ratio of GMTs post- vaccination and pre-vaccination. Analysis was performed on IAS population. Here, 'n'= subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination), Day 28 (post any vaccination)

Notes:

[8] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	115	156	227
Units: ratio				
geometric mean (confidence interval 95%)				
A/H1N1: Day 28/Day 0 (n = 110,112,141,217,11,12)	8.55 (6.39 to 11.4)	10.0 (7.31 to 13.7)	16.3 (12.1 to 22.0)	10.1 (8.07 to 12.8)
A/H3N2: Day 28/Day 0 (n = 109,111,140,214,11,12)	6.42 (4.95 to 8.34)	9.35 (7.15 to 12.2)	10.3 (8.09 to 13.0)	4.61 (3.90 to 5.45)
B/Victoria: Day 28/Day 0 (n=110,111,141,217,11,12)	10.7 (8.31 to 13.7)	11.7 (9.30 to 14.7)	16.7 (13.2 to 21.0)	11.0 (9.24 to 13.2)
B/Yamagata: Day 28/Day 0 (n=110,109,141,215,11,12)	9.28 (7.10 to 12.1)	11.4 (8.83 to 14.7)	18.1 (13.9 to 23.6)	9.77 (8.15 to 11.7)

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: ratio				
geometric mean (confidence interval 95%)				
A/H1N1: Day 28/Day 0 (n = 110,112,141,217,11,12)	1.41 (0.878 to 2.28)	4.76 (2.72 to 8.32)		
A/H3N2: Day 28/Day 0 (n = 109,111,140,214,11,12)	1.41 (1.00 to 2.00)	15.5 (8.89 to 27.2)		
B/Victoria: Day 28/Day 0 (n=110,111,141,217,11,12)	1.37 (0.949 to 1.98)	11.0 (6.28 to 19.2)		
B/Yamagata: Day 28/Day 0 (n=110,109,141,215,11,12)	1.71 (1.07 to 2.73)	0.944 (0.785 to 1.13)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Neutralisation Antibody Titers >=40 (1/Dilution) Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine

End point title	Number of Subjects With Neutralisation Antibody Titers >=40 (1/Dilution) Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine[9]

End point description:

GMT was measured for each influenza strain using HAI assay method for 4 strains: A/H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage. Analysis was performed on the IAS population. Here, 'n'= subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 28 post any vaccination

Notes:

[9] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	115	156	227
Units: subjects				
number (not applicable)				
A/H1N1: Day 28 (n = 116, 114, 145, 221, 13, 12)	113	110	142	198
A/H3N2: Day 28 (n = 116, 113, 144, 220, 13, 12)	111	110	139	198
B/Victoria: Day 28 (n = 116, 113, 145, 221, 13,12)	112	108	140	202
B/Yamagata: Day 28 (n = 116, 112, 144, 220, 13,12)	115	109	142	215

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: subjects				
number (not applicable)				
A/H1N1: Day 28 (n = 116, 114, 145, 221, 13, 12)	0	7		
A/H3N2: Day 28 (n = 116, 113, 144, 220, 13, 12)	0	9		
B/Victoria: Day 28 (n = 116, 113, 145, 221, 13,12)	0	9		
B/Yamagata: Day 28 (n = 116, 112, 144, 220, 13,12)	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers of Influenza Antibodies (Seroneutralisation Assay Method) Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine

End point title	Geometric Mean Titers of Influenza Antibodies (Seroneutralisation Assay Method) Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine[10]

End point description:

GMT was measured for each influenza strain using SN assay method for 4 strains: A/H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage. Analysis was performed on the IAS population. Here, 'n'= subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 28 post any vaccination

Notes:

[10] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	115	156	227
Units: titers (1/dilution)				
geometric mean (confidence interval				

95%)				
A/H1N1: (n = 112, 112, 147, 216, 12, 11)	6589 (4959 to 8754)	6213 (4672 to 8264)	7045 (5514 to 9001)	4948 (3676 to 6659)
A/H3N2: (n = 113, 111, 142, 215, 11, 11)	641 (515 to 798)	921 (718 to 1181)	884 (717 to 1091)	411 (347 to 487)
B/Victoria: (n=113, 112, 146, 216, 12, 11)	500 (375 to 667)	605 (444 to 825)	628 (484 to 815)	378 (302 to 472)
B/Yamagata: (n=112, 112, 146, 214, 12, 11)	1147 (893 to 1474)	1159 (865 to 1552)	1254 (1015 to 1549)	846 (698 to 1026)

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: titers (1/dilution)				
geometric mean (confidence interval 95%)				
A/H1N1: (n = 112, 112, 147, 216, 12, 11)	33.8 (14.8 to 76.9)	234 (32.0 to 1708)		
A/H3N2: (n = 113, 111, 142, 215, 11, 11)	54.4 (35.3 to 83.9)	188 (119 to 298)		
B/Victoria: (n=113, 112, 146, 216, 12, 11)	6.05 (4.54 to 8.07)	57.9 (39.5 to 84.9)		
B/Yamagata: (n=112, 112, 146, 214, 12, 11)	17.6 (11.1 to 27.8)	17.4 (9.86 to 30.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titer Ratios of Influenza Antibodies (Seroneutralisation Assay Method) Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine

End point title	Geometric Mean Titer Ratios of Influenza Antibodies (Seroneutralisation Assay Method) Following Vaccination With Either a High-Dose Quadrivalent Influenza Vaccine or Standard-Dose Quadrivalent Influenza Vaccine or Adjuvanted Trivalent Influenza Vaccine[11]

End point description:

GMTRs of anti-influenza antibodies were measured using SN assay method for 4 strains: A/H1N1, A/H3N2, B/Victoria lineage and B/Yamagata lineage. GMTRs were calculated as the ratio of GMTs post vaccination and pre-vaccination. Analysis was performed on IAS population. Here, 'n'= subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination), Day 28 (post any vaccination)

Notes:

[11] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	115	156	227
Units: ratio				
geometric mean (confidence interval 95%)				
A/H1N1: Day 28/Day 0 (n = 103,105,138,206,10,11)	11.3 (7.67 to 16.7)	18.8 (12.1 to 29.4)	29.1 (19.6 to 43.2)	14.5 (11.0 to 19.0)
A/H3N2: Day 28/Day 0 (n=101,101,134,206,10,11)	3.60 (2.98 to 4.34)	5.20 (4.11 to 6.59)	5.54 (4.58 to 6.70)	2.66 (2.34 to 3.04)
B/Victoria: Day 28/Day 0 (n=102,105,137,205,10,11)	12.4 (9.51 to 16.2)	15.4 (11.9 to 20.0)	19.9 (15.1 to 26.3)	12.7 (10.4 to 15.4)
B/Yamagata: Day 28/Day 0 (n=101,103,137,204,10,11)	9.75 (7.50 to 12.7)	11.5 (9.06 to 14.7)	14.1 (11.1 to 17.8)	8.49 (7.18 to 10.0)

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: ratio				
geometric mean (confidence interval 95%)				
A/H1N1: Day 28/Day 0 (n = 103,105,138,206,10,11)	2.38 (0.663 to 8.53)	7.12 (3.00 to 16.9)		
A/H3N2: Day 28/Day 0 (n=101,101,134,206,10,11)	1.04 (0.629 to 1.72)	2.81 (1.65 to 4.78)		
B/Victoria: Day 28/Day 0 (n=102,105,137,205,10,11)	1.03 (0.612 to 1.74)	10.5 (6.73 to 16.3)		
B/Yamagata: Day 28/Day 0 (n=101,103,137,204,10,11)	1.16 (0.604 to 2.24)	1.10 (0.760 to 1.61)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Neutralisation Antibody Titers above Pre-Defined Thresholds

End point title	Number of Subjects With Neutralisation Antibody Titers above Pre-Defined Thresholds[12]

End point description:

Neutralising Antibody titer was measured for each influenza strain with SN assay method for 4 strains: A/H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage at pre-defined thresholds of >=20, >=40

and >=80 (1/dilution). Analysis was performed on the IAS population. Here, 'n'= subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 28 post any vaccination

Notes:

[12] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	115	156	227
Units: subjects				
number (not applicable)				
A/H1N1: >=20 (1/dil) (n=112,112,147,216,13,11)	112	112	147	208
A/H1N1: >=40 (1/dil) (n=112,112,147,216,13,11)	112	112	147	202
A/H1N1: >=80 (1/dil) (n=112,112,147,216,13,11)	111	111	146	201
A/H3N2: >=20 (1/dil) (n=113,111,142,215,13,11)	113	111	142	214
A/H3N2: >=40 (1/dil) (n=113,111,142,215,13,11)	111	111	141	208
A/H3N2: >=80 (1/dil) (n=113,111,142,215,13,11)	107	107	138	190
B/Victoria: >=20 (1/dil) (n=113,112,146,216,13,11)	110	108	143	201
B/Victoria: >=40 (1/dil) (n=113,112,146,216,13,11)	108	104	136	195
B/Victoria: >=80 (1/dil) (n=113,112,146,216,13,11)	99	99	128	181
B/Yamagata: >=20 (1/dil) (n=112,112,146,214,13,11)	111	112	146	213
B/Yamagata: >=40 (1/dil) (n=112,112,146,214,13,11)	111	108	145	208
B/Yamagata: >=80 (1/dil) (n=112,112,146,214,13,11)	110	103	140	201

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: subjects				
number (not applicable)				
A/H1N1: >=20 (1/dil) (n=112,112,147,216,13,11)	13	11		
A/H1N1: >=40 (1/dil) (n=112,112,147,216,13,11)	12	11		

A/H1N1: >=80 (1/dil) (n=112,112,147,216,13,11)	11	11		
A/H3N2: >=20 (1/dil) (n=113,111,142,215,13,11)	13	11		
A/H3N2: >=40 (1/dil) (n=113,111,142,215,13,11)	13	11		
A/H3N2: >=80 (1/dil) (n=113,111,142,215,13,11)	11	11		
B/Victoria: >=20 (1/dil) (n=113,112,146,216,13,11)	9	11		
B/Victoria: >=40 (1/dil) (n=113,112,146,216,13,11)	8	11		
B/Victoria: >=80 (1/dil) (n=113,112,146,216,13,11)	6	11		
B/Yamagata: >=20 (1/dil) (n=112,112,146,214,13,11)	13	10		
B/Yamagata: >=40 (1/dil) (n=112,112,146,214,13,11)	9	6		
B/Yamagata: >=80 (1/dil) (n=112,112,146,214,13,11)	7	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Two-Fold and Four-Fold Increase in Neutralisation Antibody Titer at Day 28

End point title	Number of Subjects With Two-Fold and Four-Fold Increase in Neutralisation Antibody Titer at Day 28[13]

End point description:

Neutralising Antibody titer was measured for each influenza strain with SN method for 4 strains: A/H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage. 2-fold and 4-fold rise was defined as the computed value = post-vaccination computed value/pre-vaccination computed value. Analysis was performed on the IAS population. Here, 'n'= subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 28 post any vaccination

Notes:

[13] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	115	156	227
Units: subjects				
number (not applicable)				
2-Fold Rise: A/H1N1 (n=103,105,138,206,10,11)	80	83	118	168
4-Fold Rise: A/H1N1 (n=103,105,138,206,10,11)	65	70	104	141

2-Fold Rise: A/H3N2 (n = 101,101,134, 206,10,11)	69	77	110	111
4-Fold Rise: A/H3N2 (n = 101,101,134, 206,10,11)	44	51	72	61
2-Fold Rise: B/Victoria (n =102,105,137,205,10,11)	95	99	131	185
4-Fold Rise: B/Victoria (n =102,105,137,205,10,11)	80	88	113	158
2-Fold Rise: B/Yamagata (n =101,103,137,204,10,11)	84	95	127	187
4-Fold Rise: B/Yamagata (n =101,103,137,204,10,11)	71	81	109	142

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: subjects				
number (not applicable)				
2-Fold Rise: A/H1N1 (n=103,105,138,206,10,11)	6	10		
4-Fold Rise: A/H1N1 (n=103,105,138,206,10,11)	5	9		
2-Fold Rise: A/H3N2 (n = 101,101,134, 206,10,11)	2	7		
4-Fold Rise: A/H3N2 (n = 101,101,134, 206,10,11)	0	3		
2-Fold Rise: B/Victoria (n =102,105,137,205,10,11)	2	11		
4-Fold Rise: B/Victoria (n =102,105,137,205,10,11)	0	10		
2-Fold Rise: B/Yamagata (n =101,103,137,204,10,11)	4	3		
4-Fold Rise: B/Yamagata (n =101,103,137,204,10,11)	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Solicited Injection Site Reactions After any Vaccination

End point title	Number of Subjects With Solicited Injection Site Reactions After any Vaccination[14]

End point description:

A solicited reaction was an "expected' adverse reaction (sign or symptom) observed and reported under the conditions (nature and onset) prelisted (i.e., solicited) in the CRB and considered as related to the administered vaccination. Solicited injection site reactions included tenderness/pain, erythema, swelling, induration and bruising. Analysis was performed on the SafAS population. Here, 'Number of subjects analysed'= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after any vaccination

Notes:

[14] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	122	119	158	232
Units: subjects				
number (not applicable)				
Injection site tenderness/pain	81	84	100	116
Injection site erythema	31	30	40	48
Injection site swelling	17	15	34	23
Injection site induration	21	18	26	22
Injection site bruising	10	10	13	16

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: subjects				
number (not applicable)				
Injection site tenderness/pain	6	5		
Injection site erythema	5	8		
Injection site swelling	2	2		
Injection site induration	4	5		
Injection site bruising	1	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Solicited Systemic Reactions After any Vaccination: Subjects Aged 6 Months to <36 Months

End point title	Number of Subjects With Solicited Systemic Reactions After any Vaccination: Subjects Aged 6 Months to <36 Months[15]

End point description:

A solicited reaction was an "expected' adverse reaction (sign or symptom) observed and reported under the conditions (nature and onset) prelisted (i.e., solicited) in the CRB and considered as related to the administered vaccination. Solicited systemic reactions included fever, vomiting, crying abnormal, drowsiness, appetite loss and irritability. Analysis was performed on the SafAS population. Here, 'n'= subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Within 7 days after any vaccination

Notes:

[15] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	122	121	158	234
Units: subjects				
number (not applicable)				
Fever (n= 122, 120, 158, 231, 13, 13)	5	6	15	11
Vomiting (n = 29, 30, 54, 74, 13, 13)	1	2	7	11
Crying abnormal (n = 29, 30, 54, 74, 13, 13)	11	9	10	20
Drowsiness (n = 29, 30, 54, 74, 13, 13)	14	11	12	17
Appetite lost (n = 29, 30, 54, 74, 13, 13)	6	10	15	20
Irritability (n = 29, 30, 54, 74, 13, 13)	14	13	18	23

End point values	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: subjects				
number (not applicable)				
Fever (n= 122, 120, 158, 231, 13, 13)	5	6		
Vomiting (n = 29, 30, 54, 74, 13, 13)	5	7		
Crying abnormal (n = 29, 30, 54, 74, 13, 13)	6	9		
Drowsiness (n = 29, 30, 54, 74, 13, 13)	5	5		
Appetite lost (n = 29, 30, 54, 74, 13, 13)	11	11		
Irritability (n = 29, 30, 54, 74, 13, 13)	6	12		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Solicited Systemic Reactions After any Vaccination: Subjects Aged Greater Than (>) 36 Months

End point title	Number of Subjects With Solicited Systemic Reactions After any Vaccination: Subjects Aged Greater Than (>) 36 Months[16][17]

End point description:

A solicited reaction was an "expected' adverse reaction (sign or symptom) observed and reported under the conditions (nature and onset) prelisted (i.e., solicited) in the CRB and considered as related to the administered vaccination. Solicited systemic reactions included: headache, malaise, myalgia and shivering. Analysis was performed on the SafAS population. Here, 'Number of subjects analysed'= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after any vaccination

Notes:

[16] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Systemic reactions data for Subjects Aged >36 months was planned to be collected and analysed for Groups 1-4 only.

End point values	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	89	104	158
Units: subjects				
number (not applicable)				
Headache	18	18	22	21
Malaise	16	28	27	32
Myalgia	29	30	32	42
Shivering	1	8	8	6

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from Day 0 (post-vaccination) up to 28 days after last vaccination. Solicited Reaction (SR) data were collected up to Day 7 after any vaccination. SAE data were collected throughout the study (up to 180 days after last vaccination).

Adverse event reporting additional description:

A SR was an AE that was prelisted (i.e., solicited) in the CRB and considered to be related to vaccination (adverse drug reaction). An unsolicited AE was an observed AE that did not fulfill the conditions prelisted (i.e., solicited) in the CRB in terms of diagnosis and/or onset window post-vaccination. Analysis was performed on SafAS population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)

Reporting group description:

Subjects from US (aged 6 months to 17 years) received 30 µg QIV-HD, IM.

Reporting group title	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)

Reporting group description:

Subjects from US (aged 6 months to 17 years) received 45 µg QIV-HD, IM.

Reporting group title	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)

Reporting group description:

Subjects from US (aged 6 months to 17 years) received 60 µg QIV-HD, IM.

Reporting group title	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)

Reporting group description:

Pooled arm consisted of subjects who were from US aged 6 months to 17 years, randomised to Group 1, 2 and 3 and received 15 µg QIV-SD, IM.

Reporting group title	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)

Reporting group description:

Subjects form Canada (aged 6 to <24 months) received 60 µg QIV-HD, IM.

Reporting group title	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)

Reporting group description:

Subjects from Canada (aged 6 to <24 months) received 7.5 µg adjuvanted TIV, IM.

Serious adverse events	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	2 / 158 (1.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile Convulsion			

subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	1 / 158 (0.63%)
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			
Ear Infection			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Syncytial Virus Infection			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Ear Infection			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
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 Syncytial Virus Infection			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	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	Group 1: QIV-HD 30 µg (US: 6 months to 17 years)	Group 2: QIV-HD 45 µg (US: 6 months to 17 years)	Group 3: QIV-HD, 60 µg (US: 6 months to 17 years)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	101 / 122 (82.79%)	100 / 121 (82.64%)	118 / 158 (74.68%)
Injury, poisoning and procedural complications			
Tongue Injury			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	18 / 122 (14.75%)	19 / 121 (15.70%)	22 / 158 (13.92%)
occurrences (all)	19	19	22
Somnolence			
subjects affected / exposed	14 / 122 (11.48%)	11 / 121 (9.09%)	12 / 158 (7.59%)
occurrences (all)	15	12	17
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 122 (0.82%)	8 / 121 (6.61%)	8 / 158 (5.06%)
occurrences (all)	1	8	8
Crying			
subjects affected / exposed	11 / 122 (9.02%)	9 / 121 (7.44%)	10 / 158 (6.33%)
occurrences (all)	12	10	12
Influenza Like Illness			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Injection Site Bruising			

subjects affected / exposed	10 / 122 (8.20%)	11 / 121 (9.09%)	13 / 158 (8.23%)
occurrences (all)	10	11	14
Injection Site Erythema			
subjects affected / exposed	31 / 122 (25.41%)	30 / 121 (24.79%)	40 / 158 (25.32%)
occurrences (all)	32	32	44
Injection Site Induration			
subjects affected / exposed	21 / 122 (17.21%)	19 / 121 (15.70%)	26 / 158 (16.46%)
occurrences (all)	22	20	27
Injection Site Pain			
subjects affected / exposed	81 / 122 (66.39%)	84 / 121 (69.42%)	100 / 158 (63.29%)
occurrences (all)	89	96	111
Injection Site Swelling			
subjects affected / exposed	17 / 122 (13.93%)	15 / 121 (12.40%)	34 / 158 (21.52%)
occurrences (all)	17	17	35
Injection Site Warmth			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	16 / 122 (13.11%)	28 / 121 (23.14%)	27 / 158 (17.09%)
occurrences (all)	16	29	27
Pyrexia			
subjects affected / exposed	11 / 122 (9.02%)	10 / 121 (8.26%)	19 / 158 (12.03%)
occurrences (all)	12	11	22
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 122 (0.00%)	2 / 121 (1.65%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Diarrhoea			
subjects affected / exposed	5 / 122 (4.10%)	5 / 121 (4.13%)	9 / 158 (5.70%)
occurrences (all)	5	6	10
Oral Mucosal Eruption			

subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Teething			
subjects affected / exposed	2 / 122 (1.64%)	1 / 121 (0.83%)	1 / 158 (0.63%)
occurrences (all)	2	1	1
Vomiting			
subjects affected / exposed	10 / 122 (8.20%)	10 / 121 (8.26%)	12 / 158 (7.59%)
occurrences (all)	12	10	13
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	17 / 122 (13.93%)	19 / 121 (15.70%)	15 / 158 (9.49%)
occurrences (all)	17	22	17
Nasal Congestion			
subjects affected / exposed	2 / 122 (1.64%)	8 / 121 (6.61%)	3 / 158 (1.90%)
occurrences (all)	2	8	3
Rhinorrhoea			
subjects affected / exposed	7 / 122 (5.74%)	6 / 121 (4.96%)	4 / 158 (2.53%)
occurrences (all)	7	6	7
Skin and subcutaneous tissue disorders			
Dermatitis Diaper			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	2 / 158 (1.27%)
occurrences (all)	1	0	3
Erythema			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 122 (0.00%)	2 / 121 (1.65%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Irritability			

subjects affected / exposed	14 / 122 (11.48%)	13 / 121 (10.74%)	18 / 158 (11.39%)
occurrences (all)	16	15	24
Sleep Terror			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	29 / 122 (23.77%)	30 / 121 (24.79%)	33 / 158 (20.89%)
occurrences (all)	33	31	34
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Conjunctivitis			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	2 / 158 (1.27%)
occurrences (all)	1	1	2
Ear Infection			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	1 / 158 (0.63%)
occurrences (all)	2	0	1
Gastroenteritis			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	0 / 158 (0.00%)
occurrences (all)	1	1	0
Nasopharyngitis			
subjects affected / exposed	4 / 122 (3.28%)	4 / 121 (3.31%)	8 / 158 (5.06%)
occurrences (all)	4	4	8
Otitis Media			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	2 / 158 (1.27%)
occurrences (all)	0	1	2
Pharyngitis			
subjects affected / exposed	0 / 122 (0.00%)	0 / 121 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Sinusitis			

subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 122 (4.10%)	0 / 121 (0.00%)	6 / 158 (3.80%)
occurrences (all)	5	0	6
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	6 / 122 (4.92%)	10 / 121 (8.26%)	15 / 158 (9.49%)
occurrences (all)	6	11	18

Non-serious adverse events	Group 4: Pooled QIV-SD, 15 µg (US: 6 months to 17 years)	Group 5: QIV-HD, 60 µg (Canada: 6 to <24 months)	Group 6: Adjuvanted TIV (Canada: 6 to <24 months)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	165 / 234 (70.51%)	13 / 13 (100.00%)	13 / 13 (100.00%)
Injury, poisoning and procedural complications			
Tongue Injury			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 234 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	22 / 234 (9.40%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	22	0	0
Somnolence			
subjects affected / exposed	18 / 234 (7.69%)	5 / 13 (38.46%)	5 / 13 (38.46%)
occurrences (all)	21	6	7
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Chills			
subjects affected / exposed	6 / 234 (2.56%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	6	0	0
Crying			

subjects affected / exposed	20 / 234 (8.55%)	6 / 13 (46.15%)	9 / 13 (69.23%)
occurrences (all)	24	9	10
Influenza Like Illness			
subjects affected / exposed	0 / 234 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Injection Site Bruising			
subjects affected / exposed	16 / 234 (6.84%)	1 / 13 (7.69%)	2 / 13 (15.38%)
occurrences (all)	16	1	2
Injection Site Erythema			
subjects affected / exposed	48 / 234 (20.51%)	5 / 13 (38.46%)	8 / 13 (61.54%)
occurrences (all)	52	7	9
Injection Site Induration			
subjects affected / exposed	22 / 234 (9.40%)	4 / 13 (30.77%)	5 / 13 (38.46%)
occurrences (all)	24	5	6
Injection Site Pain			
subjects affected / exposed	116 / 234 (49.57%)	6 / 13 (46.15%)	5 / 13 (38.46%)
occurrences (all)	126	8	6
Injection Site Swelling			
subjects affected / exposed	23 / 234 (9.83%)	2 / 13 (15.38%)	2 / 13 (15.38%)
occurrences (all)	25	2	2
Injection Site Warmth			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	32 / 234 (13.68%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	33	0	0
Pyrexia			
subjects affected / exposed	24 / 234 (10.26%)	9 / 13 (69.23%)	9 / 13 (69.23%)
occurrences (all)	25	15	17
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	1 / 234 (0.43%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Abdominal Pain			

subjects affected / exposed	1 / 234 (0.43%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	1	2	0
Diarrhoea			
subjects affected / exposed	12 / 234 (5.13%)	1 / 13 (7.69%)	4 / 13 (30.77%)
occurrences (all)	13	1	8
Oral Mucosal Eruption			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Teething			
subjects affected / exposed	1 / 234 (0.43%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	1
Vomiting			
subjects affected / exposed	15 / 234 (6.41%)	5 / 13 (38.46%)	7 / 13 (53.85%)
occurrences (all)	16	9	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	30 / 234 (12.82%)	2 / 13 (15.38%)	1 / 13 (7.69%)
occurrences (all)	30	4	1
Nasal Congestion			
subjects affected / exposed	6 / 234 (2.56%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	6	1	0
Rhinorrhoea			
subjects affected / exposed	13 / 234 (5.56%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	13	0	1
Skin and subcutaneous tissue disorders			
Dermatitis Diaper			
subjects affected / exposed	3 / 234 (1.28%)	1 / 13 (7.69%)	1 / 13 (7.69%)
occurrences (all)	3	1	1
Erythema			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Rash			

subjects affected / exposed	1 / 234 (0.43%)	2 / 13 (15.38%)	1 / 13 (7.69%)
occurrences (all)	1	2	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 234 (0.00%)	1 / 13 (7.69%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Irritability			
subjects affected / exposed	23 / 234 (9.83%)	7 / 13 (53.85%)	12 / 13 (92.31%)
occurrences (all)	27	11	19
Sleep Terror			
subjects affected / exposed	0 / 234 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	43 / 234 (18.38%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	45	0	0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 234 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 234 (0.00%)	3 / 13 (23.08%)	0 / 13 (0.00%)
occurrences (all)	0	3	0
Conjunctivitis			
subjects affected / exposed	2 / 234 (0.85%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	2	1	0
Ear Infection			
subjects affected / exposed	3 / 234 (1.28%)	3 / 13 (23.08%)	3 / 13 (23.08%)
occurrences (all)	3	4	4
Gastroenteritis			
subjects affected / exposed	1 / 234 (0.43%)	3 / 13 (23.08%)	1 / 13 (7.69%)
occurrences (all)	1	3	1
Nasopharyngitis			
subjects affected / exposed	5 / 234 (2.14%)	7 / 13 (53.85%)	7 / 13 (53.85%)
occurrences (all)	5	9	13
Otitis Media			

subjects affected / exposed	2 / 234 (0.85%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	2	1	0
Pharyngitis			
subjects affected / exposed	0 / 234 (0.00%)	2 / 13 (15.38%)	2 / 13 (15.38%)
occurrences (all)	0	2	2
Sinusitis			
subjects affected / exposed	1 / 234 (0.43%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Upper Respiratory Tract Infection			
subjects affected / exposed	8 / 234 (3.42%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	8	0	1
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	20 / 234 (8.55%)	11 / 13 (84.62%)	11 / 13 (84.62%)
occurrences (all)	24	14	14

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2019	Following changes were made: - Clarified exclusion criteria to describe how subjects 6 months to 8 years of age were considered as "previously influenza vaccinated" or "previously influenza unvaccinated" based on the Advisory Committee on Immunization Practices and National Advisory Committee on Immunization Guidelines. - Clarified the collection of vaccinations and medications in case of reporting a SAE. - Explained how blinding was maintained for the subject/parent/guardian. - Clarified that SRs were to be considered as being related to the product administered. Therefore, the assessment of causality by the Investigator was not required. - Described an additional data protection measures as per requirement from the European data privacy regulations; the purpose of the collection of race and ethnicity was to be defined in the study protocol and justified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported