



Clinical trial results: Immunogenicity and Safety of a Multi-Dose Quadrivalent Influenza Vaccine in Children Aged 6 months to 17 Years

Summary

EudraCT number	2017-001044-35
Trial protocol	Outside EU/EEA
Global end of trial date	25 August 2018

Results information

Result version number	v1 (current)
This version publication date	13 March 2019
First version publication date	13 March 2019

Trial information

Trial identification

Sponsor protocol code	GQM00016
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03391193
WHO universal trial number (UTN)	U1111-1183-5881

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur
Sponsor organisation address	14 Espace Henry Vallée, Lyon, France, 69007
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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 October 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the hemagglutination inhibition (HAI) antibody response induced by quadrivalent influenza vaccine (QIV) in multi-dose vial (MDV) presentation compared with QIV in single dose syringe presentation for the four strains.

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	19 December 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Mexico: 302
Worldwide total number of subjects	302
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)	80
Children (2-11 years)	147
Adolescents (12-17 years)	75
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled in 3 centers in Mexico from 19 December 2017 to 19 January 2018.

Pre-assignment

Screening details:

A total of 302 subjects who met all inclusion and none of the exclusion criteria were enrolled and randomized in the study.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	QIV thio-containing: 6 to 35 Months

Arm description:

Subjects aged 6 to 35 months received 1 dose of QIV (in a MDV presentation) at Day 0 and 1 dose at Day 28.

Arm type	Experimental
Investigational medicinal product name	QIV (split-virion, inactivated) in a MDV presentation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use, Subcutaneous use

Dosage and administration details:

0.5 mL, Intramuscular (IM) or deep subcutaneous (SC) injection, 1 dose each at Day 0 and at Day 28.

Arm title	QIV thio-free: 6 to 35 Months
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Arm description:

Subjects aged 6 to 35 months received 1 dose of QIV (in a syringe presentation) at Day 0 and 1 dose at Day 28.

Arm type	Active comparator
Investigational medicinal product name	QIV (split-virion, inactivated) in a syringe presentation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use, Subcutaneous use

Dosage and administration details:

0.5 mL, IM or deep SC injection, 1 dose each at Day 0 and at Day 28.

Arm title	QIV thio-containing: 3 to 8 Years
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Arm description:

Subjects aged 3 to 8 years received 1 dose of QIV (in a MDV presentation) at Day 0 and 1 dose at Day 28.

Arm type	Experimental
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Investigational medicinal product name	QIV (split-virion, inactivated) in a MDV presentation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use, Subcutaneous use
Dosage and administration details:	
0.5 mL, IM or deep SC injection, 1 dose each at Day 0 and at Day 28.	
Arm title	QIV thio-free: 3 to 8 Years

Arm description:

Subjects aged 3 to 8 years received 1 dose of QIV (in a syringe presentation) at Day 0 and 1 dose at Day 28.

Arm type	Active comparator
Investigational medicinal product name	QIV (split-virion, inactivated) in a syringe presentation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use, Subcutaneous use
Dosage and administration details:	
0.5 mL, IM or deep SC injection, 1 dose each at Day 0 and at Day 28.	
Arm title	QIV thio-containing: 9 to 17 Years

Arm description:

Subjects aged 9 to 17 years received 1 dose of QIV in a MDV presentation at Day 0.

Arm type	Experimental
Investigational medicinal product name	QIV (split-virion, inactivated) in a MDV presentation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use, Subcutaneous use
Dosage and administration details:	
0.5 mL, IM or deep SC injection, single dose at Day 0.	
Arm title	QIV thio-free: 9 to 17 Years

Arm description:

Subjects aged 9 to 17 years received 1 dose of QIV in a syringe presentation at Day 0.

Arm type	Active comparator
Investigational medicinal product name	QIV (split-virion, inactivated) in a syringe presentation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use, Subcutaneous use

Dosage and administration details:

0.5 mL, IM or deep SC injection, single dose at Day 0.

Number of subjects in period 1	QIV thio-containing: 6 to 35 Months	QIV thio-free: 6 to 35 Months	QIV thio-containing: 3 to 8 Years
Started	61	60	31
Completed	50	54	28
Not completed	11	6	3
Lost to follow-up	3	1	2
Withdrawal by parent/guardian	8	5	1
Protocol deviation	-	-	-

Number of subjects in period 1	QIV thio-free: 3 to 8 Years	QIV thio-containing: 9 to 17 Years	QIV thio-free: 9 to 17 Years
Started	28	61	61
Completed	25	61	61
Not completed	3	0	0
Lost to follow-up	-	-	-
Withdrawal by parent/guardian	1	-	-
Protocol deviation	2	-	-

Baseline characteristics

Reporting groups

Reporting group title	QIV thio-containing: 6 to 35 Months
Reporting group description: Subjects aged 6 to 35 months received 1 dose of QIV (in a MDV presentation) at Day 0 and 1 dose at Day 28.	
Reporting group title	QIV thio-free: 6 to 35 Months
Reporting group description: Subjects aged 6 to 35 months received 1 dose of QIV (in a syringe presentation) at Day 0 and 1 dose at Day 28.	
Reporting group title	QIV thio-containing: 3 to 8 Years
Reporting group description: Subjects aged 3 to 8 years received 1 dose of QIV (in a MDV presentation) at Day 0 and 1 dose at Day 28.	
Reporting group title	QIV thio-free: 3 to 8 Years
Reporting group description: Subjects aged 3 to 8 years received 1 dose of QIV (in a syringe presentation) at Day 0 and 1 dose at Day 28.	
Reporting group title	QIV thio-containing: 9 to 17 Years
Reporting group description: Subjects aged 9 to 17 years received 1 dose of QIV in a MDV presentation at Day 0.	
Reporting group title	QIV thio-free: 9 to 17 Years
Reporting group description: Subjects aged 9 to 17 years received 1 dose of QIV in a syringe presentation at Day 0.	

Reporting group values	QIV thio-containing: 6 to 35 Months	QIV thio-free: 6 to 35 Months	QIV thio-containing: 3 to 8 Years
Number of subjects	61	60	31
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	37	43	0
Children (2-11 years)	24	17	31
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	0.984	0.850	4.77
standard deviation	± 0.904	± 0.840	± 1.73
Gender categorical Units: Subjects			
Female	29	27	15
Male	32	33	16

Reporting group values	QIV thio-free: 3 to 8 Years	QIV thio-containing: 9 to 17 Years	QIV thio-free: 9 to 17 Years
Number of subjects	28	61	61
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	28	21	26
Adolescents (12-17 years)	0	40	35
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	4.46	12.8	12.4
standard deviation	± 1.69	± 2.46	± 2.62
Gender categorical Units: Subjects			
Female	10	32	27
Male	18	29	34

Reporting group values	Total		
Number of subjects	302		
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)	80		
Children (2-11 years)	147		
Adolescents (12-17 years)	75		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	140		
Male	162		

End points

End points reporting groups

Reporting group title	QIV thio-containing: 6 to 35 Months
Reporting group description: Subjects aged 6 to 35 months received 1 dose of QIV (in a MDV presentation) at Day 0 and 1 dose at Day 28.	
Reporting group title	QIV thio-free: 6 to 35 Months
Reporting group description: Subjects aged 6 to 35 months received 1 dose of QIV (in a syringe presentation) at Day 0 and 1 dose at Day 28.	
Reporting group title	QIV thio-containing: 3 to 8 Years
Reporting group description: Subjects aged 3 to 8 years received 1 dose of QIV (in a MDV presentation) at Day 0 and 1 dose at Day 28.	
Reporting group title	QIV thio-free: 3 to 8 Years
Reporting group description: Subjects aged 3 to 8 years received 1 dose of QIV (in a syringe presentation) at Day 0 and 1 dose at Day 28.	
Reporting group title	QIV thio-containing: 9 to 17 Years
Reporting group description: Subjects aged 9 to 17 years received 1 dose of QIV in a MDV presentation at Day 0.	
Reporting group title	QIV thio-free: 9 to 17 Years
Reporting group description: Subjects aged 9 to 17 years received 1 dose of QIV in a syringe presentation at Day 0.	

Primary: Antibody Titers After Vaccination With Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine

End point title	Antibody Titers After Vaccination With Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine ^[1]
End point description: Serum antibody titers for the Influenza vaccine serogroups A/H1N1, A/H3N2, B/Victoria and B/Yamagata were assessed by HAI assay. Antibody titers were expressed as geometric mean titers (GMTs). Analysis was performed on Immunogenicity Analysis Set which included all randomized subjects who received at least 1 dose of the study vaccine and had a post-vaccination blood sample. Here "n" signifies subjects with available data for specified category.	
End point type	Primary
End point timeframe: Day 0 (pre-vaccination) and Day 28 (post-last vaccination)	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only descriptive statistical analyses has been reported for this end point.	

End point values	QIV thio-containing: 6 to 35 Months	QIV thio-free: 6 to 35 Months	QIV thio-containing: 3 to 8 Years	QIV thio-free: 3 to 8 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	54	28	25
Units: Titer (1/dilution)				
geometric mean (confidence interval 95%)				

A/H1N1: Pre vaccination (n=49,54,28,25,61,60)	8.32 (5.71 to 12.1)	10.3 (6.56 to 16.2)	80.0 (38.4 to 167)	46.6 (21.2 to 103)
A/H1N1: Post vaccination (n=49,52,28,25,61,59)	286 (182 to 450)	243 (157 to 377)	987 (694 to 1403)	658 (438 to 988)
A/H3N2: Pre vaccination (n=48,52,28,25,61,61)	11.6 (7.54 to 18.0)	10.0 (6.86 to 14.6)	84.1 (40.0 to 177)	88.2 (38.5 to 202)
A/H3N2: Post vaccination (n=49,51,27,25,61,61)	560 (356 to 879)	281 (186 to 425)	1676 (1244 to 2257)	1084 (710 to 1655)
B/Victoria: Pre vaccination (n=48,52,28,25,61,61)	8.47 (6.03 to 11.9)	7.12 (5.30 to 9.57)	20.0 (9.50 to 42.1)	20.8 (9.53 to 45.6)
B/Victoria: Post vaccination (n=49,52,28,25,61,61)	261 (167 to 406)	190 (137 to 264)	664 (424 to 1040)	513 (282 to 931)
B/Yamagata: Pre vaccination (n=48,53,28,25,61,61)	11.0 (7.45 to 16.2)	7.40 (6.03 to 9.08)	51.2 (26.6 to 98.8)	55.8 (24.9 to 125)
B/Yamagata: Post vaccination (n=49,52,28,25,61,61)	390 (271 to 562)	245 (188 to 320)	1233 (880 to 1729)	1099 (753 to 1605)

End point values	QIV thio-containing: 9 to 17 Years	QIV thio-free: 9 to 17 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	61		
Units: Titer (1/dilution)				
geometric mean (confidence interval 95%)				
A/H1N1: Pre vaccination (n=49,54,28,25,61,60)	229 (167 to 315)	244 (170 to 349)		
A/H1N1: Post vaccination (n=49,52,28,25,61,59)	1475 (1180 to 1845)	1318 (1041 to 1668)		
A/H3N2: Pre vaccination (n=48,52,28,25,61,61)	329 (231 to 470)	254 (182 to 353)		
A/H3N2: Post vaccination (n=49,51,27,25,61,61)	1598 (1326 to 1924)	1258 (1004 to 1577)		
B/Victoria: Pre vaccination (n=48,52,28,25,61,61)	156 (111 to 221)	156 (105 to 233)		
B/Victoria: Post vaccination (n=49,52,28,25,61,61)	1884 (1474 to 2407)	1780 (1375 to 2303)		
B/Yamagata: Pre vaccination (n=48,53,28,25,61,61)	216 (151 to 309)	201 (143 to 282)		
B/Yamagata: Post vaccination (n=49,52,28,25,61,61)	1434 (1153 to 1784)	1450 (1167 to 1803)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs Ratio after Vaccination with Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine

End point title	GMTs Ratio after Vaccination with Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine ^[2]
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End point description:

Serum antibody titer ratio for the Influenza vaccine serogroups A/H1N1, A/H3N2, B/Victoria and B/Yamagata were assessed by HAI assay. Analysis was performed on Immunogenicity Analysis Set.

Here 'n' signifies subjects with available data for specified category.

End point type	Primary
End point timeframe:	
Day 0 and Day 28 (post-last vaccination)	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistical analyses has been reported for this end point.

End point values	QIV thio-containing: 6 to 35 Months	QIV thio-free: 6 to 35 Months	QIV thio-containing: 3 to 8 Years	QIV thio-free: 3 to 8 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	54	28	25
Units: Ratio				
geometric mean (confidence interval 95%)				
A/H1N1 serogroup (n=48,52,28,25,61,59)	34.6 (20.6 to 58.2)	23.6 (15.4 to 36.0)	12.3 (7.13 to 21.3)	14.1 (7.83 to 25.5)
A/H3N2 serogroup (n=47,50,27,25,61,61)	47.3 (28.8 to 77.6)	26.2 (17.2 to 39.9)	21.0 (10.7 to 40.9)	12.3 (6.03 to 25.1)
B/Victoria serogroup (n=47,50,28,25,61,61)	31.8 (20.3 to 49.6)	26.0 (17.7 to 38.3)	33.2 (19.5 to 56.5)	24.6 (15.1 to 40.0)
B/Yamagata serogroup (n=47,51,28,25,61,61)	35.0 (22.0 to 55.6)	32.7 (22.7 to 46.9)	24.1 (14.2 to 40.7)	19.7 (10.7 to 36.3)

End point values	QIV thio-containing: 9 to 17 Years	QIV thio-free: 9 to 17 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	61		
Units: Ratio				
geometric mean (confidence interval 95%)				
A/H1N1 serogroup (n=48,52,28,25,61,59)	6.45 (4.51 to 9.22)	5.33 (3.63 to 7.84)		
A/H3N2 serogroup (n=47,50,27,25,61,61)	4.85 (3.31 to 7.11)	4.96 (3.41 to 7.22)		
B/Victoria serogroup (n=47,50,28,25,61,61)	12.0 (8.29 to 17.5)	11.4 (7.78 to 16.6)		
B/Yamagata serogroup (n=47,51,28,25,61,61)	6.63 (4.57 to 9.63)	7.22 (4.93 to 10.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Seroconversion Rates After Vaccination With Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine

End point title	Seroconversion Rates After Vaccination With Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine ^[3]
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End point description:

The seroconversion rates for each serogroups were defined as the percentages of subjects with a pre-vaccination titer (Day 0) < 10 (1/dilution) and a post-vaccination titer (Day 28 or Day 56) >= 40 (1/dilution), or with a pre-vaccination titer (Day 0) >=10 (1/dilution) and >= 4-fold increase of the titer. Analysis was performed on Immunogenicity Analysis Set.

End point type Primary

End point timeframe:

Day 0 and Day 28 (post-last 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: Only descriptive statistical analyses has been reported for this end point.

End point values	QIV thio-containing: 6 to 35 Months	QIV thio-free: 6 to 35 Months	QIV thio-containing: 3 to 8 Years	QIV thio-free: 3 to 8 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	54	28	25
Units: percentage of subjects				
number (not applicable)				
A/H1N1 serogroup	85.4	78.8	78.6	92.0
A/H3N2 serogroup	93.6	88.0	92.6	72.0
B/Victoria serogroup	89.4	88.0	96.4	92.0
B/Yamagata serogroup	93.6	90.2	89.3	84.0

End point values	QIV thio-containing: 9 to 17 Years	QIV thio-free: 9 to 17 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	61		
Units: percentage of subjects				
number (not applicable)				
A/H1N1 serogroup	63.9	54.2		
A/H3N2 serogroup	47.5	49.2		
B/Victoria serogroup	72.1	73.8		
B/Yamagata serogroup	65.6	60.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting Solicited Injection (Inj.) Site or Systemic Reaction After Vaccination With Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine: 6 to 35 Months

End point title Percentage of Subjects Reporting Solicited Injection (Inj.) Site or Systemic Reaction After Vaccination With Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine: 6 to 35 Months^[4]

End point description:

Percentage of subjects experiencing at least 1 solicited injection site reaction (tenderness/pain,

erythema, swelling, induration and ecchymosis) and at least 1 systemic reaction (fever, headache, malaise, myalgia, shivering, vomiting, crying abnormal, drowsiness, appetite lost and irritability) were reported. Analysis was performed on safety analysis set which included all subjects who had received at least 1 dose of the study vaccines. Here 'n' signifies subjects with available data for specified category.

End point type	Secondary
End point timeframe:	
Day 0 (pre-vaccination) to Day 7 (after any vaccination)	

Notes:

[4] - 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: Data for rest of the arms is provided in separate endpoint.

End point values	QIV thio-containing: 6 to 35 Months	QIV thio-free: 6 to 35 Months		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	58		
Units: percentage of subjects				
number (not applicable)				
Inj. site tenderness/pain (n=50,54)	44.0	44.4		
Inj. site erythema (n=50,54)	26.0	13.0		
Inj. site swelling (n=50,54)	12.0	11.1		
Inj. site induration (n=50,54)	10.0	7.4		
Inj. site ecchymosis (n=50,54)	10.0	7.4		
Fever (n=49,54)	34.7	16.7		
Headache (n=23,17)	17.4	5.9		
Malaise (n=23,17)	43.5	29.4		
Myalgia (n=23,17)	34.8	11.8		
Shivering (n=23,17)	17.4	0		
Vomiting (n=27,37)	11.1	8.1		
Crying abnormal (n=27,37)	63.0	32.4		
Drowsiness (n=27,37)	37.0	21.6		
Appetite lost (n=27,37)	29.6	27.0		
Irritability (n=27,37)	44.4	37.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting Solicited Inj. Site or Systemic Reaction After Vaccination With Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine: 3 to 17 Years

End point title	Percentage of Subjects Reporting Solicited Inj. Site or Systemic Reaction After Vaccination With Multi-Dose Quadrivalent Influenza Vaccine or Single-Dose Quadrivalent Influenza Vaccine: 3 to 17 Years ^[5]
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End point description:

Percentage of subjects experiencing at least 1 solicited injection site reaction (tenderness/pain, erythema, swelling, induration and ecchymosis) and at least 1 systemic reaction (fever, headache, malaise, myalgia and shivering) were reported. Analysis was performed on safety analysis set. Here 'n' signifies subjects with available data for specified category.

End point type	Secondary
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End point timeframe:

Day 0 (pre-vaccination) to Day 7 (after any vaccination)

Notes:

[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: Data for rest of the arms is provided in separate endpoint.

End point values	QIV thio-containing: 3 to 8 Years	QIV thio-free: 3 to 8 Years	QIV thio-containing: 9 to 17 Years	QIV thio-free: 9 to 17 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	28	61	61
Units: percentage of subjects				
number (not applicable)				
Inj. site tenderness/pain (n=28,27,61,61)	53.6	51.9	42.6	63.9
Inj. site erythema (n=28,27,61,61)	14.3	14.8	3.3	9.8
Inj. site swelling (n=28,27,61,61)	14.3	29.6	4.9	9.8
Inj. site induration (n=28,27,61,61)	17.9	18.5	3.3	6.6
Inj. site ecchymosis (n=28,27,61,61)	14.3	7.4	0	1.6
Fever (n=27,25,61,61)	11.1	4.0	4.9	4.9
Headache (n=28,27,61,61)	17.9	22.2	21.3	36.1
Malaise (n=28,27,61,61)	42.9	40.7	24.6	21.3
Myalgia (n=28,27,61,61)	32.1	37.0	27.9	32.8
Shivering (n=28,27,61,61)	10.7	18.5	3.3	11.5

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) data collected from Day 0 up to 28 days post-vaccination. Serious AE data was collected throughout the study (up to Day 208 for subjects aged 6 months to 8 years and up to Day 180 for subjects aged 9 to 17 years).

Adverse event reporting additional description:

Solicited reaction (SR): An AE, i.e. prelisted in electronic case report form (eCRF) and considered related to vaccination. SR is an adverse drug reaction observed, reported under the conditions (nature and onset) prelisted (i.e. solicited) in eCRF. An unsolicited AE is an observed AE that does not fulfill the conditions prelisted in eCRF. Safety set.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	QIV thio-containing: 6 to 35 months
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Reporting group description:

Subjects aged 6 to 35 months received 1 dose of QIV (in a MDV presentation) at Day 0 and 1 dose at Day 28.

Reporting group title	QIV thio-free: 6 to 35 months
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Reporting group description:

Subjects aged 6 to 35 months received 1 dose of QIV (in a syringe presentation) at Day 0 and 1 dose at Day 28.

Reporting group title	QIV thio-containing: 3 to 8 years
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Reporting group description:

Subjects aged 3 to 8 years received 1 dose of QIV (in a MDV presentation) at Day 0 and 1 dose at Day 28.

Reporting group title	QIV thio-free: 3 to 8 years
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Reporting group description:

Subjects aged 3 to 8 years received 1 dose of QIV (in a syringe presentation) at Day 0 and 1 dose at Day 28.

Reporting group title	QIV thio-containing: 9 to 17 years
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Reporting group description:

Subjects aged 9 to 17 years received 1 dose of QIV in a MDV presentation at Day 0.

Reporting group title	QIV thio-free: 9 to 17 years
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Reporting group description:

Subjects aged 9 to 17 years received 1 dose of QIV in a syringe presentation at Day 0.

Serious adverse events	QIV thio-containing: 6 to 35 months	QIV thio-free: 6 to 35 months	QIV thio-containing: 3 to 8 years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 59 (0.00%)	1 / 58 (1.72%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Haemolytic Anaemia			

subjects affected / exposed	0 / 59 (0.00%)	1 / 58 (1.72%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	QIV thio-free: 3 to 8 years	QIV thio-containing: 9 to 17 years	QIV thio-free: 9 to 17 years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 61 (0.00%)	0 / 61 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Haemolytic Anaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 61 (0.00%)	0 / 61 (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	QIV thio-containing: 6 to 35 months	QIV thio-free: 6 to 35 months	QIV thio-containing: 3 to 8 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 59 (66.10%)	36 / 58 (62.07%)	19 / 30 (63.33%)
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 59 (6.78%)	1 / 58 (1.72%)	5 / 30 (16.67%)
occurrences (all)	4	1	5
Somnolence			
subjects affected / exposed	10 / 59 (16.95%)	8 / 58 (13.79%)	0 / 30 (0.00%)
occurrences (all)	13	11	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	4 / 59 (6.78%)	0 / 58 (0.00%)	3 / 30 (10.00%)
occurrences (all)	4	0	3
Crying			
subjects affected / exposed	17 / 59 (28.81%)	12 / 58 (20.69%)	0 / 30 (0.00%)
occurrences (all)	20	17	0
Injection Site Erythema			

subjects affected / exposed occurrences (all)	13 / 59 (22.03%) 17	7 / 58 (12.07%) 11	4 / 30 (13.33%) 6
Injection Site Haemorrhage subjects affected / exposed occurrences (all)	5 / 59 (8.47%) 5	4 / 58 (6.90%) 5	4 / 30 (13.33%) 4
Injection Site Induration subjects affected / exposed occurrences (all)	5 / 59 (8.47%) 5	4 / 58 (6.90%) 7	5 / 30 (16.67%) 5
Injection Site Pain subjects affected / exposed occurrences (all)	22 / 59 (37.29%) 34	24 / 58 (41.38%) 36	15 / 30 (50.00%) 21
Injection Site Swelling subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 8	6 / 58 (10.34%) 9	4 / 30 (13.33%) 5
Malaise subjects affected / exposed occurrences (all)	10 / 59 (16.95%) 14	5 / 58 (8.62%) 6	12 / 30 (40.00%) 16
Pyrexia subjects affected / exposed occurrences (all)	18 / 59 (30.51%) 18	10 / 58 (17.24%) 10	5 / 30 (16.67%) 5
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	1 / 58 (1.72%) 1	1 / 30 (3.33%) 1
Vomiting subjects affected / exposed occurrences (all)	4 / 59 (6.78%) 4	3 / 58 (5.17%) 4	1 / 30 (3.33%) 1
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	8 / 59 (13.56%) 8	3 / 58 (5.17%) 3	3 / 30 (10.00%) 4
Psychiatric disorders			
Irritability subjects affected / exposed occurrences (all)	12 / 59 (20.34%) 15	14 / 58 (24.14%) 20	0 / 30 (0.00%) 0
Musculoskeletal and connective tissue disorders			

Myalgia subjects affected / exposed occurrences (all)	8 / 59 (13.56%) 9	2 / 58 (3.45%) 3	9 / 30 (30.00%) 12
Infections and infestations			
Gastroenteritis subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	1 / 58 (1.72%) 1	2 / 30 (6.67%) 2
Nasopharyngitis subjects affected / exposed occurrences (all)	14 / 59 (23.73%) 17	14 / 58 (24.14%) 15	1 / 30 (3.33%) 1
Pharyngitis subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 6	8 / 58 (13.79%) 8	2 / 30 (6.67%) 2
Metabolism and nutrition disorders			
Decreased Appetite subjects affected / exposed occurrences (all)	8 / 59 (13.56%) 9	10 / 58 (17.24%) 13	0 / 30 (0.00%) 0

Non-serious adverse events	QIV thio-free: 3 to 8 years	QIV thio-containing: 9 to 17 years	QIV thio-free: 9 to 17 years
Total subjects affected by non-serious adverse events subjects affected / exposed	20 / 28 (71.43%)	39 / 61 (63.93%)	50 / 61 (81.97%)
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	6 / 28 (21.43%) 6	13 / 61 (21.31%) 13	22 / 61 (36.07%) 22
Somnolence subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 61 (0.00%) 0	0 / 61 (0.00%) 0
General disorders and administration site conditions			
Chills subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 5	2 / 61 (3.28%) 2	7 / 61 (11.48%) 7
Crying subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 61 (0.00%) 0	0 / 61 (0.00%) 0
Injection Site Erythema			

subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 5	2 / 61 (3.28%) 2	6 / 61 (9.84%) 6
Injection Site Haemorrhage subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 3	0 / 61 (0.00%) 0	1 / 61 (1.64%) 1
Injection Site Induration subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 6	2 / 61 (3.28%) 2	4 / 61 (6.56%) 4
Injection Site Pain subjects affected / exposed occurrences (all)	14 / 28 (50.00%) 20	26 / 61 (42.62%) 26	39 / 61 (63.93%) 39
Injection Site Swelling subjects affected / exposed occurrences (all)	8 / 28 (28.57%) 10	3 / 61 (4.92%) 3	6 / 61 (9.84%) 6
Malaise subjects affected / exposed occurrences (all)	11 / 28 (39.29%) 13	15 / 61 (24.59%) 15	13 / 61 (21.31%) 13
Pyrexia subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 4	3 / 61 (4.92%) 3	3 / 61 (4.92%) 3
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 61 (0.00%) 0	0 / 61 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 61 (0.00%) 0	0 / 61 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 4	2 / 61 (3.28%) 2	2 / 61 (3.28%) 2
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 61 (0.00%) 0	0 / 61 (0.00%) 0
Musculoskeletal and connective tissue disorders			

Myalgia subjects affected / exposed occurrences (all)	10 / 28 (35.71%) 11	17 / 61 (27.87%) 17	20 / 61 (32.79%) 20
Infections and infestations			
Gastroenteritis subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 61 (0.00%) 0	0 / 61 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	1 / 61 (1.64%) 1	2 / 61 (3.28%) 2
Pharyngitis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 61 (0.00%) 0	0 / 61 (0.00%) 0
Metabolism and nutrition disorders			
Decreased Appetite subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 61 (0.00%) 0	0 / 61 (0.00%) 0

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