Clinical trial results:
A phase III, observer-blind, randomized, multi-country, non-influenza vaccine comparator-controlled study to demonstrate the efficacy of GlaxoSmithKline Biologicals' quadrivalent seasonal influenza candidate vaccine GSK2321138A (FLU D-QIV), administered intramuscularly in children 6 to 35 months of age.

Summary

EudraCT number	2011-000758-41
Trial protocol	CZ ES BE GB PL Outside EU/EEA
Global end of trial date	31 December 2014

Results information

Result version number	v1
This version publication date	07 January 2017
First version publication date	07 January 2017

Trial information

Trial identification

Sponsor protocol code	115345

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01439360
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89,, Rixensart,, Belgium,
Public contact	Clinical Trials Call Center,, GlaxoSmithKline Biologicals, 44 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center,, GlaxoSmithKline Biologicals, 44 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000817-PIP02-11
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	13 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To evaluate the efficacy of FLU D-QIV in the prevention of RT-PCR confirmed moderate to severe influenza A and/or B disease due to any seasonal influenza strain, when compared to non-influenza vaccine controls in children aged 6 to 35 months.
• To evaluate the efficacy of FLU D-QIV in the prevention of RT-PCR confirmed influenza A and/or B disease due to any seasonal influenza strain, when compared to non-influenza vaccine controls in children aged 6 to 35 months.

Protection of trial subjects:

All subjects were observed closely for at least 30 minutes following the administration of the vaccine(s)/placebo, with appropriate medical treatment readily available in case of anaphylaxis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2011
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	Bangladesh: 2911
Country: Number of subjects enrolled	Belgium: 147
Country: Number of subjects enrolled	Czech Republic: 416
Country: Number of subjects enrolled	Dominican Republic: 1962
Country: Number of subjects enrolled	Honduras: 1314
Country: Number of subjects enrolled	India: 465
Country: Number of subjects enrolled	Lebanon: 250
Country: Number of subjects enrolled	Philippines: 1448
Country: Number of subjects enrolled	Poland: 1266
Country: Number of subjects enrolled	Spain: 858
Country: Number of subjects enrolled	Thailand: 602
Country: Number of subjects enrolled	Turkey: 37
Country: Number of subjects enrolled	United Kingdom: 370
Worldwide total number of subjects	12046
EEA total number of subjects	3057

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)	6445
Children (2-11 years)	5601
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	12046
Number of subjects completed	12018

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Invalid ICF: 21
Reason: Number of subjects	Vaccine not administered subject number allocated: 7

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, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Data will be collected in an observer-blind manner. The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

Arms

Are arms mutually exclusive?	Yes
Arm title	D-QIV

Arm description:

Subjects received 1 or 2 doses of candidate influenza Influsplit™ Tetra vaccine (GSK2321138A).

Arm type	Experimental
Investigational medicinal product name	Influsplit™ Tetra (D-QIV)
Investigational medicinal product code	
Other name	Fluarix™ Tetra, GSK2321138A
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 or 2 doses adminstered intramuscurlarly at Day 0 (primed subjects) and Days 0 and 28 (unprimed subjects)

Arm title	Control

Arm description:

In function of their age and D-QIV-vaccine status, subjects received Prevenar 13® or Havrix® Junior and possibly a varicella vaccine (Varilrix® or Varivax/ProVarivax ®).

Arm type	Active comparator
Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	Pfizer’s pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) (PCV-13)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

-2 doses administered at Days 0 and 28 and 1 booster dose at study completion (Day 180 approximately), according to the prescribing information for subjects < 12 months of age.

Investigational medicinal product name	Varivax®
Investigational medicinal product code	SUB25312
Other name	ProVarivax®
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered (depending on the licensed vaccine in the participating country) at Day 0 in unprimed subjects ≥12 months of age.

Investigational medicinal product name	Varilrix®
Investigational medicinal product code	SUB20954
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose administered subcutaneously (depending on the licensed vaccine in the participating country) at Day 0 in unprimed subjects ≥12 months of age.

Investigational medicinal product name	Havrix®
Investigational medicinal product code	SUB25294
Other name	Havrix® Junior
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly at Day 0 and booster dose at study completion (Day 180 approximately)

Number of subjects in period 1[1]	D-QIV	Control
Started	6006	6012
Completed	5808	5804
Not completed	198	208
Consent withdrawn by subject	140	129
Others	10	5
Adverse event, non-fatal	4	16
Lost to follow-up	43	58
Protocol deviation	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of the 12046 enrolled subjects, 21 subjects were excluded from all statistical analyses due to an invalid informed consent form (IC F), 7 subjects did not receive any study vaccine despite being allocated a subject number.

Baseline characteristics

Reporting groups	
Reporting group title	D-QIV
Reporting group description:	
Subjects received 1 or 2 doses of candidate influenza Influsplit™ Tetra vaccine (GSK2321138A).	
Reporting group title	Control
Reporting group description:	
In function of their age and D-QIV-vaccine status, subjects received Prevenar 13® or Havrix® Junior and possibly a varicella vaccine (Varilrix® or Varivax/ProVarivax ®).	

Reporting group values	D-QIV	Control	Total
Number of subjects	6006	6012	12018
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean	21.9	21.8	
standard deviation	± 8	± 8	-
Gender categorical			
Units: Subjects			
Female	2933	2925	5858
Male	3073	3087	6160
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage / African American	24	20	44
Asian - Central/South Asian Heritage	1062	1053	2115
Asian - East Asian Heritage	2	0	2
Asian - Japanese Heritage	2	0	2
Asian - South East Asian Heritage	1661	1666	3327
Native Hawaiian or Other Pacific Islander	3	0	3
Other	1639	1642	3281
White - Arabic / North African Heritage	142	149	291
White - Caucasian / European Heritage	1471	1482	2953

End points

End points reporting groups	
Reporting group title	D-QIV
Reporting group description:	
Subjects received 1 or 2 doses of candidate influenza Influsplit™ Tetra vaccine (GSK2321138A).	
Reporting group title	Control
Reporting group description:	
In function of their age and D-QIV-vaccine status, subjects received Prevenar 13® or Havrix® Junior and possibly a varicella vaccine (Varilrix® or Varivax/ProVarivax ®).	

Primary: Number of subjects with moderate to severe RT-PCR confirmed influenza.	
End point title	Number of subjects with moderate to severe RT-PCR confirmed influenza.
End point description:	
Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.	
End point type	Primary
End point timeframe:	
During the surveillance period (approximately 6 to 8 months)	

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5707	5697		
Units: Subjects	90	242		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
The efficacy of the D-QIV vaccine would be demonstrated if the LL of the two-sided 97.5% CI for vaccine efficacy (VE) is above (>) 25%.	
Comparison groups	D-QIV v Control
Number of subjects included in analysis	11404
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Cox
Parameter estimate	Vaccine efficacy (VE)
Point estimate	63.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	51.8
upper limit	72.3

Primary: Number of subjects with RT-PCR confirmed influenza of any severity.	
End point title	Number of subjects with RT-PCR confirmed influenza of any severity.
End point description:	
Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.	
End point type	Primary
End point timeframe:	
During the surveillance period (approximately 6 to 8 months)	

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5707	5697		
Units: Subjects	344	662		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
The efficacy of the D-QIV vaccine would be demonstrated if the LL of the two-sided 97.5% CI for VE is above 15%.	
Comparison groups	D-QIV v Control
Number of subjects included in analysis	11404
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Cox
Parameter estimate	Vaccine efficacy (VE)
Point estimate	49.8
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	41.8
upper limit	56.8

Secondary: Number of subjects with first occurrence of lower respiratory illness (LRI) with RT-PCR confirmed influenza.	
End point title	Number of subjects with first occurrence of lower respiratory illness (LRI) with RT-PCR confirmed influenza.
End point description:	
Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.	
End point type	Secondary

End point timeframe:

At any time starting 7 days before the onset of LRI and ending 7 days after end of LRI during the surveillance period (approximately 6 to 8 months)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5707	5697		
Units: Subjects	28	61		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of culture-confirmed moderate to severe influenza A and/or B disease due to antigenically-matching influenza strains.

End point title	Number of subjects with first occurrence of culture-confirmed moderate to severe influenza A and/or B disease due to antigenically-matching influenza strains.

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

End point type	Secondary

End point timeframe:

During the surveillance period (approximately 6 to 8 months)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5707	5697		
Units: Subjects	20	88		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of culture-confirmed influenza A and/or B disease of any severity due to antigenically-matching influenza strains

End point title	Number of subjects with first occurrence of culture-confirmed influenza A and/or B disease of any severity due to antigenically-matching influenza strains

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

End point type	Secondary

End point timeframe:

During the surveillance period (approximately 6 to 8 months)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5707	5697		
Units: Subjects	88	216		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of culture-confirmed moderate to severe influenza A and/or B disease due to any seasonal influenza strain.

End point title	Number of subjects with first occurrence of culture-confirmed moderate to severe influenza A and/or B disease due to any seasonal influenza strain.

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

End point type	Secondary

End point timeframe:

During the surveillance period (approximately 6 to 8 months)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5707	5697		
Units: Subjects	79	216		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of culture-confirmed influenza A and/or B disease of any severity due to any seasonal influenza strain.

End point title	Number of subjects with first occurrence of culture-confirmed influenza A and/or B disease of any severity due to any seasonal influenza strain.

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

End point type	Secondary

End point timeframe:

During the surveillance period (approximately 6 to 8 months)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5707	5697		
Units: Subjects	303	602		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of acute otitis media (AOM) with RT-PCR confirmed influenza A and/or B infection due to any seasonal influenza strain.

End point title	Number of subjects with first occurrence of acute otitis media (AOM) with RT-PCR confirmed influenza A and/or B infection due to any seasonal influenza strain.

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

End point type	Secondary

End point timeframe:

At any time starting 7 days before the onset of LRI and ending 7 days after end of LRI during the surveillance period (approximately 6 to 8 months)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5707	5697		
Units: Subjects	12	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of RT-PCR confirmed severe influenza A and/or B due to any seasonal influenza strain.

End point title	Number of subjects with first occurrence of RT-PCR confirmed severe influenza A and/or B due to any seasonal influenza strain.

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed

influenza event.

End point type	Secondary

End point timeframe:

During the surveillance period (approximately 6 to 8 months)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5707	5697		
Units: Subjects	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Humoral immune response in terms of haemagglutination-inhibition (HI) antibody titres against each of four vaccine strains contained in the D-QIV (in immuno subcohort of subjects only)

End point title	Humoral immune response in terms of haemagglutination-inhibition (HI) antibody titres against each of four vaccine strains contained in the D-QIV (in immuno subcohort of subjects only)

End point description:

Titers were expressed as geometric mean antibody titers (GMTs). The vaccine strains assessed were A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria) and B/Brisbane/3/2007 (Yamagata). PRE= Pre-vaccination at Day 0; POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects

End point type	Secondary

End point timeframe:

At Days 0 and 28/56

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	753	579		
Units: Titers				
geometric mean (confidence interval 95%)				
H1N1, PRE [N=744, 567]	11.9 (10.6 to 13.2)	11.9 (10.5 to 13.5)		
H1N1, POST [N=752, 578]	165.3 (148.6 to 183.8)	12.6 (11.1 to 14.3)		
H3N2, PRE [N=746,568]	14.8 (13.2 to 16.5)	13.4 (11.8 to 15.2)		
H3N2, POST [N=753,578]	132.1 (119.1 to 146.5)	14.7 (12.9 to 16.7)		
Victoria, PRE [N=745,567]	10 (9.1 to 11)	9.2 (8.3 to 10.1)		

Victoria, POST [N=750,579]	92.6 (82.3 to 104.1)	9.2 (8.4 to 10.1)		
Yamagata, PRE [N=745,568]	7.3 (6.8 to 7.8)	7.3 (6.8 to 7.9)		
Yamagata, POST [N=753,579]	121.4 (110.1 to 133.8)	7.6 (7 to 8.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

End point title	Number of seropositive subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

End point description:

A seropositive subject was a subject whose HI antibody titer was greater than or equal to the assay cut-off value of 1:10. The vaccine strains assessed were A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria) and B/Brisbane/3/2007 (Yamagata). PRE= Pre-vaccination at Day 0; POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects.

End point type	Secondary

End point timeframe:

At Day 0 and Day 28/56

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	753	579		
Units: Subjects				
H1N1, PRE	200	152		
H1N1, POST	728	170		
H3N2, PRE	266	187		
H3N2, POST	740	210		
Victoria, PRE	205	138		
Victoria, POST	701	147		
Yamagata, PRE	134	93		
Yamagata, POST	719	108		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

End point title	Number of seroconverted subjects for HI antibodies against

	each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

End point description:

Seroconversion rate (SCR) was defined as the number of subjects who have either a pre-vaccination reciprocal HI titer < 1:10 and a post-vaccination reciprocal titer ≥ 1:40, or a pre-vaccination reciprocal HI titer ≥ 10 and at least a 4 fold increase in post vaccination reciprocal titer against the vaccine virus. PRE= Pre-vaccination at Day 0; POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects

End point type	Secondary

End point timeframe:

At Day 28/56 (POST)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	746	568		
Units: Subjects				
H1N1	596	20		
H3N2	513	24		
Victoria	514	5		
Yamagata	605	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean geometric increase (MGI) for HI antibody titer against each of the 4 vaccine influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only).

End point title	Mean geometric increase (MGI) for HI antibody titer against each of the 4 vaccine influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only).

End point description:

MGI also known as the seroconversion factor [SCF] was defined as the fold increase in serum HI GMTs post vaccination compared to pre-vaccination (Day 0). The vaccine strains assessed were A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria) and B/Brisbane/3/2007 (Yamagata). POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects.

End point type	Secondary

End point timeframe:

At Day 28/56 (POST)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	746	568		
Units: Fold increase				
geometric mean (confidence interval 95%)				
H1N1	14 (12.8 to 15.3)	1.1 (1 to 1.1)		
H3N2	9 (8.2 to 9.8)	1.1 (1 to 1.2)		
Victoria	9.3 (8.6 to 10.2)	1 (1 to 1.1)		
Yamagata	16.7 (15.2 to 18.3)	1.1 (1 to 1.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

End point title	Number of seroprotected subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

End point description:

Seroprotection rate (SPR) was defined as the number of subjects with H1N1 reciprocal HI titers ≥ 1:40 against the tested vaccine virus.The vaccine strains assessed were A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria) and B/Brisbane/3/2007 (Yamagata). PRE= Pre-vaccination at Day 0; POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects

End point type	Secondary

End point timeframe:

At Day 0 and Day 28/56

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	753	579		
Units: Subjects				
H1N1, PRE	182	134		
H1N1, POST	640	146		
H3N2, PRE	238	159		
H3N2, POST	612	175		
Victoria, PRE	143	103		
Victoria, POST	539	101		
Yamagata, PRE	73	59		
Yamagata, POST	638	64		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms.

End point title	Number of subjects reporting any and grade 3 solicited local symptoms.

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any was defined as any solicited local symptom reported irrespective of intensity. Grade 3 pain was defined as pain that resulted crying when limb was moved/ spontaneously painful. Grade 3 redness and swelling was greater than 50 millimeters (mm) i.e. >50mm.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5907	5901		
Units: Subjects				
Any Pain, Dose 1 [N=5899, 5896]	1015	1047		
Grade 3 Pain, Dose 1 [N=5899, 5896]	23	30		
Any Redness, Dose 1 [N=5899, 5896]	775	831		
Grade 3 Redness, Pain, Dose 1 [N=5899, 5896]	1	0		
Any Swelling, Dose 1 [N=5899, 5896]	467	518		
Grade 3 Swelling, Dose 1 [N=5899, 5896]	0	0		
Any Pain, Dose 2 [N=5757, 5766]	808	820		
Grade 3 Pain, Dose 2 [N=5757, 5766]	21	21		
Any Redness, Dose 2 [N=5757, 5766]	587	631		
Grade 3 Redness, Dose 2 [N=5757, 5766]	2	0		
Any Swelling, Dose 2 [N=5757, 5766]	375	409		
Grade 3 Swelling, Dose 2 [N=5757, 5766]	2	3		
Any Pain, Across doses [N=5907,5901]	1350	1375		
Grade 3 Pain, Across doses [N=5907,5901]	42	48		
Any Redness, Across doses [N=5907,5901]	980	1091		
Grade 3 Redness, Across doses [N=5907,5901]	3	0		
Any Swelling, Across doses [N=5907,5901]	665	742		

Grade 3 Swelling, Across doses [N=5907,5901]	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms.

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms.

End point description:

Solicited general symptoms assessed were Drowsiness, Irritability/fussiness, Loss of appetite and Temperature (Axillary). Any was defined as any general symptom reported irrespective of intensity or relationship to vaccination. Grade 3 was defined as symptoms that prevented normal activity. Related was defined as general symptom assessed by the investigator to have a causal relationship to vaccination.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5908	5901		
Units: Subjects				
Any Drowsiness, Dose 1 [N=5898, 5896]	739	829		
Grade 3 Drowsiness, Dose 1 [N=5898, 5896]	39	52		
Related Drowsiness, Dose 1 [N=5898, 5896]	490	535		
Any Irritability, Dose 1 [N=5898, 5896]	955	1029		
Grade 3 Irritability, Dose 1 [N=5898, 5896]	42	62		
Related Irritability, Dose 1 [N=5898, 5896]	617	669		
Any Loss of appetite, Dose 1 [N=5898, 5896]	847	872		
Grade 3 Loss of appetite, Dose 1 [N=5898, 5896]	68	60		
Related Loss of appetite, Dose 1 [N=5898, 5896]	541	523		
Any Fever, Dose 1 [N=5898, 5896]	372	425		
Grade 3 Fever, Dose 1 [N=5898, 5896]	78	76		
Related Fever, Dose 1 [N=5898, 5896]	243	287		
Any Drowsiness, Dose 2 [N=5755, 5762]	519	558		
Grade 3 Drowsiness, Dose 2 [N=5755, 5762]	25	24		

Related Drowsiness, Dose 2 [N=5755, 5762]	324	361		
Any Irritability, Dose 2 [N=5755, 5762]	777	777		
Grade 3 Irritability, Dose 2 [N=5755, 5762]	36	52		
Related Irritability, Dose 2 [N=5755, 5762]	488	495		
Any Loss of appetite, Dose 2 [N=5755, 5762]	652	681		
Grade 3 Loss of appetite, Dose 2 [N=5755, 5762]	47	44		
Related Loss of appetite, Dose 2 [N=5755, 5762]	378	413		
Any Fever, Dose 2 [N=5755, 5762]	336	363		
Grade 3 Fever, Dose 2 [N=5755, 5762]	65	70		
Related Fever, Dose 2 [N=5755, 5762]	195	215		
Any Drowsiness, Across Doses [N=5908, 5901]	1024	1129		
Grade 3 Drowsiness, Across Doses [N=5908, 5901]	61	73		
Related Drowsiness, Across Doses [N=5908, 5901]	673	738		
Any Irritability, Across Doses [N=5908, 5901]	1383	1427		
Grade 3 Irritability, Across Doses [N=5908, 5901]	77	107		
Related Irritability, Across Doses [N=5908, 5901]	905	940		
Any Loss of appetite, Across Doses [N=5908, 5901]	1227	1288		
Grade3 Loss of appetite,Across Doses[N=5908, 5901]	111	97		
Related Loss of appetite,AcrossDoses[N=5908, 5901]	774	809		
Any Fever, Across Doses [N=5908, 5901]	659	732		
Grade 3 Fever, Across Doses [N=5908, 5901]	137	141		
Related Fever, Across Doses [N=5908, 5901]	413	476		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of solicited local symptoms

End point title	Duration of solicited local symptoms

End point description:

Duration was defined as number of days with any grade of local symptoms.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1015	1047		
Units: Days				
median (full range (min-max))				
Pain, Dose 1 [N=1015,1047]	1 (1 to 2)	1 (1 to 2)		
Pain, Dose 2 [N=808,820]	1 (1 to 2)	1 (1 to 2)		
Redness, Dose 1 [N=775,831]	2 (1 to 3)	2 (1 to 3)		
Redness, Dose 2 [N=587,631]	2 (1 to 3)	2 (1 to 3)		
Swelling, Dose 1 [N=467,518]	2 (1 to 3)	2 (1 to 3)		
Swelling, Dose 2 [N=375,409]	1 (1 to 2)	2 (1 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of solicited general symptoms

End point title	Duration of solicited general symptoms

End point description:

Duration was defined as number of days with any grade of general symptoms.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	955	1029		
Units: Days				
median (full range (min-max))				
Drowsiness, Dose 1 [N=739,829]	2 (1 to 3)	2 (1 to 3)		
Drowsiness, Dose 2 [N=519,558]	2 (1 to 3)	2 (1 to 3)		
Irritability, Dose 1 [N=955,1029]	2 (1 to 3)	2 (1 to 3)		
Irritability, Dose 2 [N=777,777]	2 (1 to 3)	2 (1 to 3)		
Loss of appetite, Dose 1 [N=847,872]	2 (1 to 4)	2 (1 to 4)		
Loss of appetite, Dose 2 [N=652,681]	3 (2 to 4)	2 (1 to 4)		
Fever, Dose 1 [N=390,438]	1 (1 to 2)	1 (1 to 2)		
Fever, Dose 2 [N=347,372]	2 (1 to 3)	1 (1 to 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related unsolicited adverse events (AEs)

End point title	Number of subjects reporting any, grade 3 and related unsolicited adverse events (AEs)

End point description:

Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination. Grade 3 was an event that prevented normal activities and related was defined as an unsolicited AE assessed by the investigator to be causally related to the study vaccination.

End point type	Secondary

End point timeframe:

During the 28-day (Days 0-27) post-vaccination period

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6006	6012		
Units: Subjects				
Any unsolicited AEs	2640	2679		
Grade 3 unsolicited AEs	160	149		
Related unsolicited AEs	106	116		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related AEs with medically attended visits (MAVs)

End point title	Number of subjects reporting any, grade 3 and related AEs with medically attended visits (MAVs)

End point description:

MAVs were defined as AEs with a medically-attended visit i.e. prompting emergency room (ER) visits, hospitalizations or physician visits and that were not routine visits for physical examination or vaccination. Any MAV was defined as at least one MAV experienced. Grade 3 was defined as MAVs that prevented normal activities and related was defined as MAVs assessed by the investigator to be causally related to the study vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (approximately 6- 8 months per subject)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6006	6012		
Units: Subjects				
Any MAVs	3885	3988		
Grade 3 MAVs	200	211		
Related MAVs	57	58		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related potential immune-mediated diseases (pIMDs).

End point title	Number of subjects reporting any, grade 3 and related potential immune-mediated diseases (pIMDs).

End point description:

pIMDs are a subset of adverse events (AEs) that include both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which may or may not have an autoimmune etiology. Grade 3 = pIMDs that prevented normal activities. Related = symptom assed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (approximately 6- 8 months per subject)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6006	6012		
Units: Subjects				
Any pIMDs	5	0		
Grade 3 pIMDs	3	0		
Related pIMDs	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and related serious adverse events (SAEs).

End point title	Number of subjects reporting any and related serious adverse events (SAEs).

End point description:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects. Related = symptom assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (approximately 6- 8 months per subject)

End point values	D-QIV	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6006	6012		
Units: Subjects				
Any SAEs	217	201		
Related SAEs	6	2		
Fatal SAEs	1	3		
Related fatal SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Serious Adverse events: During the entire study period (approximately 6- 8 months per subject)

Adverse event reporting additional description:

The frequent adverse event data is currently being re-analyzed and the record will be updated once it becomes available.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Control

Reporting group description:

In function of their age and D-QIV-vaccine status, subjects received Prevenar 13® or Havrix® Junior and possibly a varicella vaccine (Varilrix® or Varivax/ProVarivax ®).

Reporting group title	D-QIV

Reporting group description:

Subjects received 1 or 2 doses of candidate influenza Influsplit™ Tetra vaccine (GSK2321138A).

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The frequent adverse event data is currently being re-analyzed and the record will be updated once it becomes available.

Serious adverse events	Control	D-QIV	
Total subjects affected by serious adverse events			
subjects affected / exposed	201 / 6012 (3.34%)	217 / 6006 (3.61%)	
number of deaths (all causes)	3	1	
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Drowning			

subjects affected / exposed	2 / 6012 (0.03%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Oedema peripheral			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	4 / 6012 (0.07%)	4 / 6006 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 6012 (0.00%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular pain			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			

subjects affected / exposed	1 / 6012 (0.02%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnoea			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	8 / 6012 (0.13%)	6 / 6006 (0.10%)	
occurrences causally related to treatment / all	0 / 8	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthmatic crisis			
subjects affected / exposed	2 / 6012 (0.03%)	5 / 6006 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity			
subjects affected / exposed	2 / 6012 (0.03%)	3 / 6006 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial obstruction			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	10 / 6012 (0.17%)	4 / 6006 (0.07%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			

subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 6012 (0.02%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	1 / 6012 (0.02%)	3 / 6006 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood electrolytes abnormal			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental poisoning			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Animal bite			
subjects affected / exposed	0 / 6012 (0.00%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			
subjects affected / exposed	2 / 6012 (0.03%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemical poisoning			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 6012 (0.02%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			
subjects affected / exposed	2 / 6012 (0.03%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body aspiration			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	2 / 6012 (0.03%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Near drowning			

subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	1 / 6012 (0.02%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	16 / 6012 (0.27%)	13 / 6006 (0.22%)	
occurrences causally related to treatment / all	1 / 16	2 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 6012 (0.03%)	3 / 6006 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure anoxic			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 6012 (0.05%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoplastic anaemia			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Aphthous ulcer			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	9 / 6012 (0.15%)	8 / 6006 (0.13%)	
occurrences causally related to treatment / all	0 / 9	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	2 / 6012 (0.03%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 6012 (0.00%)	3 / 6006 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 6012 (0.00%)	3 / 6006 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 6012 (0.03%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 6012 (0.00%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abscess limb			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acarodermatitis			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebiasis			
subjects affected / exposed	3 / 6012 (0.05%)	3 / 6006 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebic dysentery			
subjects affected / exposed	3 / 6012 (0.05%)	8 / 6006 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascariasis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	1 / 6012 (0.02%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			

subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	6 / 6012 (0.10%)	7 / 6006 (0.12%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchitis			
subjects affected / exposed	9 / 6012 (0.15%)	11 / 6006 (0.18%)	
occurrences causally related to treatment / all	0 / 9	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest wall abscess			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chikungunya virus infection			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholera			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	1 / 6012 (0.02%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			

subjects affected / exposed	10 / 6012 (0.17%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 10	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysentery			
subjects affected / exposed	2 / 6012 (0.03%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovirus infection			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia pyelonephritis			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	19 / 6012 (0.32%)	27 / 6006 (0.45%)	
occurrences causally related to treatment / all	0 / 20	0 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			

subjects affected / exposed	0 / 6012 (0.00%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	8 / 6012 (0.13%)	5 / 6006 (0.08%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis shigella			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	2 / 6012 (0.03%)	4 / 6006 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 6012 (0.02%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis a			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious mononucleosis			
subjects affected / exposed	0 / 6012 (0.00%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	2 / 6012 (0.03%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 6012 (0.02%)	4 / 6006 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 6012 (0.05%)	6 / 6006 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycoplasma infection			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 6012 (0.02%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 6012 (0.02%)	4 / 6006 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			

subjects affected / exposed	2 / 6012 (0.03%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 6012 (0.02%)	3 / 6006 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parasitic gastroenteritis			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	5 / 6012 (0.08%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	66 / 6012 (1.10%)	56 / 6006 (0.93%)	
occurrences causally related to treatment / all	0 / 71	0 / 60	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia measles			

subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 6012 (0.02%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 6012 (0.00%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	2 / 6012 (0.03%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	2 / 6012 (0.03%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhoid fever			
subjects affected / exposed	3 / 6012 (0.05%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 6012 (0.05%)	4 / 6006 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	4 / 6012 (0.07%)	4 / 6006 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			

subjects affected / exposed	1 / 6012 (0.02%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rash			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rhinitis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral sepsis			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 6012 (0.02%)	0 / 6006 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	7 / 6012 (0.12%)	8 / 6006 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			

subjects affected / exposed	0 / 6012 (0.00%)	2 / 6006 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polydipsia			
subjects affected / exposed	0 / 6012 (0.00%)	1 / 6006 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Control	D-QIV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 6012 (0.00%)	0 / 6006 (0.00%)	

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