Clinical trial results:
A Phase II randomized, observer blind, multicenter study of GlaxoSmithKline (GSK) Biologicals' combined measles-mumps-rubella-varicella vaccine (MMRV) versus ProQuad, according to a one dose schedule, both administered subcutaneously at 12-14 months of age, concomitantly with hepatitis A vaccine (HAV) and pneumococcal conjugate vaccine (PCV) but at separate sites

Summary

EudraCT number	2017-000454-18
Trial protocol	Outside EU/EEA
Global end of trial date	17 March 2009

Results information

Result version number	v2
This version publication date	23 September 2018
First version publication date	06 January 2018
Version creation reason	• Correction of full data set Non-serious adverse events section: Value corrected for the row - Total subjects affected by non serious adverse events, subjects affected / exposed

Trial information

Trial identification

Sponsor protocol code	110058

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00578175
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)	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	17 March 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 February 2009
Global end of trial reached?	Yes
Global end of trial date	17 March 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To demonstrate non-inferiority of GSK Biologicals' Refrigerator-stored Priorix-Tetra co-administered with HAV and PCV compared to ProQuad co-administered with HAV and PCV at Day 42 with respect to
a. the seroresponse rate for antibodies to varicella virus, measles virus and rubella virus and mumps virus.
b. the geometric mean concentration (GMC) for anti-bodies to varicella virus, hepatitis A virus in a subset of subjects and S. pneumoniae serotypes (anti-PS) 4, 6B, 9V, 14, 18C, 19F and 23F in a subset of subjects.
2. To demonstrate non-inferiority of GSK Biologicals' Freezer-stored Priorix-Tetra co-administered with HAV and PCV compared to ProQuad co-administered with HAV and PCV at Day 42 with respect to
a. the seroresponse rate for antibodies to varicella virus, measles virus and rubella virus and mumps virus.
b. GMC for antibodies to varicella virus, hepatitis A virus in a subset of subjects and anti-PS serotypes 4, 6B, 9V, 14, 18C, 19F and 23F in a subset of subjects.

Protection of trial subjects:

The vaccinees were observed closely for at least 30 minutes following the administration of vaccines, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 November 2007
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	United States: 1851
Worldwide total number of subjects	1851
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	1851
Children (2-11 years)	0
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:

While the total numbers of subjects enrolled in the study was of 1851, the total number of subjects that entered the study was 1783. The remaining 67 subjects received a subject number but no vaccine dose and were therefore excluded from the analysis and group assignment.

Period 1

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

Blinding implementation details:

Data was collected in an observer-blinded manner.

Arms

Are arms mutually exclusive?	Yes
Arm title	Refrigerator-stored Priorix-Tetra Group

Arm description:

Subjects received at Day 0 a single dose of refrigerator-stored Priorix-Tetra subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly in the left thigh.

Arm type	Experimental
Investigational medicinal product name	Priorix-Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose of Priorix-Tetra was administered at Visit 1 (Day 0)

Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of Prevenar was administered at Visit 1 (Day 0)

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

Dosage and administration details:

First dose of Havrix was administered at Visit 1 (Day 0) and second dose at Visit 3 (Day 180)

Arm title	Freezer-stored Priorix-Tetra Group

Arm description:

Subjects received at Day 0 a single dose of freezer-stored Priorix-Tetra subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right

thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly in the left thigh.

Arm type	Experimental
Investigational medicinal product name	Priorix-Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose of Priorix-Tetra was administered at Visit 1 (Day 0)

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

Dosage and administration details:

First dose of Havrix was administered at Visit 1 (Day 0) and second dose at Visit 3 (Day 180)

Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of Prevenar was administered at Visit 1 (Day 0)

Arm title	ProQuad Group

Arm description:

Subjects received at Day 0 a single dose of ProQuad subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly.

Arm type	Active comparator
Investigational medicinal product name	ProQuad
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose of ProQuad was administered at Visit 1 (Day 0)

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

Dosage and administration details:

First dose of Havrix was administered at Visit 1 (Day 0) and second dose at Visit 3 (Day 180)

Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of Prevenar was administered at Visit 1 (Day 0)

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: Data was collected in an observer-blinded manner.

Number of subjects in period 1[2]	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group
Started	705	689	389
Completed	635	646	365
Not completed	70	43	24
Adverse event, non-fatal	-	1	1
Other reasons	70	42	23

Notes:

[2] - 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: While the total numbers of subjects enrolled in the study was of 1851, the total number of subjects that entered the study was 1783. The remaining 67 subjects received a subject number but no vaccine dose and were therefore excluded from the analysis and group assignment.

Baseline characteristics

Reporting groups	
Reporting group title	Refrigerator-stored Priorix-Tetra Group
Reporting group description:	
Subjects received at Day 0 a single dose of refrigerator-stored Priorix-Tetra subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly in the left thigh.	
Reporting group title	Freezer-stored Priorix-Tetra Group
Reporting group description:	
Subjects received at Day 0 a single dose of freezer-stored Priorix-Tetra subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly in the left thigh.	
Reporting group title	ProQuad Group
Reporting group description:	
Subjects received at Day 0 a single dose of ProQuad subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly.	

Reporting group values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group
Number of subjects	705	689	389
Age categorical Units: Subjects			
Age continuous Units: months arithmetic mean standard deviation	 12.3 ± 0.58	 12.3 ± 0.59	 12.3 ± 0.61
Gender categorical Units: Subjects			
Female	356	346	186
Male	349	343	203

Reporting group values	Total		
Number of subjects	1783		
Age categorical Units: Subjects			
Age continuous Units: months arithmetic mean standard deviation	 -		
Gender categorical Units: Subjects			
Female	888		
Male	895		

End points

End points reporting groups

Reporting group title	Refrigerator-stored Priorix-Tetra Group

Reporting group description:

Subjects received at Day 0 a single dose of refrigerator-stored Priorix-Tetra subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly in the left thigh.

Reporting group title	Freezer-stored Priorix-Tetra Group

Reporting group description:

Subjects received at Day 0 a single dose of freezer-stored Priorix-Tetra subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly in the left thigh.

Reporting group title	ProQuad Group

Reporting group description:

Subjects received at Day 0 a single dose of ProQuad subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly.

Primary: Number of subjects with seroresponse for antibodies to varicella virus (VZV)

End point title	Number of subjects with seroresponse for antibodies to varicella virus (VZV)[1]

End point description:

Seroresponse for antibodies to VZV is defined as the appearance post-vaccination of anti-VZV antibodies [concentration greater than or equal to the threshold of 75 milli-international units per milliliter (mIU/mL)] in the serum of subjects below the assay cut-off value of 25 mIU/mL before vaccination.

End point type	Primary

End point timeframe:

At Day 42 after 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	622	630	347	
Units: Subjects				
Subjects	355	440	301	

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of antibodies to varicella virus (VZV)

End point title	Concentration of antibodies to varicella virus (VZV)[2]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Day 42 after 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	629	636	352	
Units: Milli-international units per milliliter				
geometric mean (confidence interval 95%)				
Milli-international units per milliliter	83.6 (77.0 to 90.8)	109.9 (102.1 to 118.3)	164.3 (152.3 to 177.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with seroresponse for antibodies to mumps virus

End point title	Number of subjects with seroresponse for antibodies to mumps virus[3]

End point description:

Seroresponse for antibodies to mumps virus is defined as the appearance post-vaccination of anti-mumps virus antibodies [titer greater than or equal to the threshold of 51 Effective Doses (ED50)] in the serum of subjects below the assay cut-off value of 24 ED50 before vaccination.

End point type	Primary

End point timeframe:

At Day 42 after 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	532	531	276	
Units: Subjects				
Subjects	491	498	256	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with seroresponse for antibodies to measles virus

End point title	Number of subjects with seroresponse for antibodies to measles virus[4]

End point description:

Seroresponse for antibodies to measles virus is defined as the appearance post-vaccination of anti-measles virus antibodies [concentration greater than or equal to the threshold of 200 milli-international units per milliliter (mIU/mL)] in the serum of subjects below the assay cut-off value of 150 mIU/mL before vaccination.

End point type	Primary

End point timeframe:

At Day 42 after vaccination

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	626	636	350	
Units: Subjects				
Subjects	616	633	342	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with seroresponse for antibodies to rubella virus

End point title	Number of subjects with seroresponse for antibodies to rubella virus[5]

End point description:

Seroresponse for antibodies to rubella virus is defined as the appearance post-vaccination of anti-rubella virus antibodies [concentration greater than or equal to the threshold of 10 international units per milliliter (IU/mL)] in the serum of subjects below the assay cut-off value of 4 IU/mL before vaccination.

End point type	Primary

End point timeframe:

At Day 42 after vaccination

Notes:

[5] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	628	636	351	
Units: Subjects				
Subjects	616	622	349	

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of antibodies to hepatitis A virus (HAV)

End point title	Concentration of antibodies to hepatitis A virus (HAV)[6]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Day 42 after vaccination

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	404	409	227	
Units: Milli-international units per milliliter				
geometric mean (confidence interval 95%)				
Milli-international units per milliliter	40.5 (37.1 to 44.2)	40.3 (37.0 to 44.0)	40.0 (35.7 to 44.9)	

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F

End point title	Concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F[7]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Day 42 after vaccination

Notes:

[7] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	461	468	266	
Units: Micrograms per milliliter (µg/mL)				
geometric mean (confidence interval 95%)				
S.Pneu.4 (n= 461, 463, 266)	3.35 (3.10 to 3.63)	3.31 (3.04 to 3.59)	3.02 (2.72 to 3.34)	
S.Pneu.6B (n= 460, 464, 265)	5.65 (5.16 to 6.19)	5.91 (5.40 to 6.45)	5.43 (4.90 to 6.02)	
S.Pneu.9V (n=461, 468, 266)	5.81 (5.37 to 6.29)	5.66 (5.23 to 6.13)	5.54 (5.02 to 6.12)	
S.Pneu.14 (n= 460, 465, 266)	9.71 (8.99 to 10.50)	9.54 (8.81 to 10.34)	8.96 (8.07 to 9.95)	
S.Pneu.18C (n= 458, 465, 263)	5.50 (5.04 to 6.01)	5.80 (5.30 to 6.34)	5.51 (4.95 to 6.12)	
S.Pneu.19F (n= 454, 460, 261)	2.52 (2.32 to 2.74)	2.52 (2.32 to 2.73)	2.31 (2.06 to 2.59)	
S.Pneu.23F (n= 459, 464, 266)	10.10 (9.22 to 11.06)	10.85 (9.87 to 11.91)	9.79 (8.65 to 11.07)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers to mumps virus

End point title	Antibody titers to mumps virus

End point description:

Data are expressed as Geometric Mean Titers (GMTs). The titer is the serum dilution giving a 50 percent reduction of the signal compared to a control without serum.

End point type	Secondary

End point timeframe:

At Day 42 after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	591	601	327	
Units: Titer				
geometric mean (confidence interval 95%)				
Titer	222.4 (202.5 to 244.3)	224.6 (206.9 to 243.9)	253.1 (222.7 to 287.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies to measles virus

End point title	Concentration of antibodies to measles virus

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Secondary

End point timeframe:

At Day 42 after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	626	636	350	
Units: Milli-international units per milliliter				
geometric mean (confidence interval 95%)				
Milli-international units per milliliter	4723.1 (4436.4 to 5028.4)	4650.3 (4430.9 to 4880.5)	4207.1 (3823.3 to 4629.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies to rubella virus

End point title	Concentration of antibodies to rubella virus

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Secondary

End point timeframe:

At Day 42 after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	629	636	352	
Units: International units per milliliter				
geometric mean (confidence interval 95%)				
International units per milliliter	59.9 (55.9 to 64.1)	57.9 (54.4 to 61.7)	71.4 (65.5 to 77.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with vaccine response to Havrix

End point title	Number of subjects with vaccine response to Havrix

End point description:

Vaccine response to Havrix is defined as the appearance post-vaccination of anti-hepatitis A virus (anti-HAV) antibodies [concentration greater than or equal to 15 milli-international units per milliliter (mIU/mL)] in the serum of subjects seronegative before vaccination (concentration below the assay cut-off value of 15 mIU/mL) or having a 2-fold increase above the pre-vaccination concentration in subjects who were seropositive before vaccination.

End point type	Secondary

End point timeframe:

At Day 42 after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	404	409	227	
Units: Subjects				
Subjects	344	345	195	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F equal or above the cut-off value

End point title	Number of subjects with concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F equal or above the cut-off value

End point description:

Cut-off value assessed include 0.05 micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Day 42 after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	461	468	266	
Units: Subjects				
Anti-S.Pneu-4 (n= 461, 463, 266)	461	463	266	
Anti-S.Pneu-6B (n= 460, 464, 265)	459	463	265	
Anti-S.Pneu-9V (n= 461, 468, 266)	461	468	266	
Anti-S.Pneu-14 (n= 460, 465, 266)	460	465	266	
Anti-S.Pneu-18C (n= 458, 465, 263)	458	465	263	
Anti-S.Pneu-19F (n= 454, 460, 261)	454	460	261	
Anti-S.Pneu-23F (n= 459, 464, 266)	459	464	266	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F equal or above the cut-off value

End point title	Number of subjects with concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F equal or above the cut-off value

End point description:

Cut-off value assessed include 0.2 micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Day 42 after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	461	468	266	
Units: Subjects				
Anti-S.Pneu-4 (n= 461, 463, 266)	461	463	266	
Anti-S.Pneu-6B (n= 460, 464, 265)	458	460	265	
Anti-S.Pneu-9V (n= 461, 468, 266)	461	468	266	
Anti-S.Pneu-14 (n= 460, 465, 266)	460	465	266	
Anti-S.Pneu-18C (n= 458, 465, 263)	458	464	263	
Anti-S.Pneu-19F (n= 454, 460, 261)	451	459	259	
Anti-S.Pneu-23F (n= 459, 464, 266)	459	464	266	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F equal or above the cut-off value

End point title	Number of subjects with concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F equal or above the cut-off value

End point description:

Cut-off value assessed include 0.5 micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Day 42 after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	461	468	266	
Units: Subjects				
Anti-S.Pneu-4 (n= 461, 463, 266)	456	459	265	
Anti-S.Pneu-6B (n= 460, 464, 265)	453	459	264	
Anti-S.Pneu-9V (n= 461, 468, 266)	459	466	266	
Anti-S.Pneu-14 (n= 460, 465, 266)	459	464	266	
Anti-S.Pneu-18C (n= 458, 465, 263)	458	463	263	
Anti-S.Pneu-19F (n= 454, 460, 261)	431	448	249	
Anti-S.Pneu-23F (n= 459, 464, 266)	458	462	266	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F equal or above the cut-off value

End point title	Number of subjects with concentration of antibodies to S. pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F and 23F equal or above the cut-off value

End point description:

Cut-off value assessed include 1.0 micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Day 42 after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	461	468	266	
Units: Subjects				
Anti-S.Pneu-4 (n= 461, 463, 266)	437	423	249	
Anti-S.Pneu-6B (n= 460, 464, 265)	442	453	259	
Anti-S.Pneu-9V (n= 461, 468, 266)	450	459	265	
Anti-S.Pneu-14 (n= 460, 465, 266)	458	463	266	
Anti-S.Pneu-18C (n= 458, 465, 263)	446	455	259	
Anti-S.Pneu-19F (n= 454, 460, 261)	390	390	214	
Anti-S.Pneu-23F (n= 459, 464, 266)	446	458	265	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms

End point title	Number of subjects reporting solicited local symptoms

End point description:

Solicited local symptoms assessed include pain, redness and swelling.

End point type	Secondary

End point timeframe:

During the 4 day follow up period following vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	673	666	378	
Units: Subjects				
Pain	136	114	65	
Redness	111	120	54	
Swelling	50	49	21	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting fever ≥ 38.0°C/100.4°F and > 39.5°C/103.1°F during the 15-day follow up period after vaccination

End point title	Number of subjects reporting fever ≥ 38.0°C/100.4°F and > 39.5°C/103.1°F during the 15-day follow up period after vaccination

End point description:

Fever was measured rectally.

End point type	Secondary

End point timeframe:

During the 15-day follow-up period following vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	676	668	379	
Units: Subjects				
≥ 38.0°C/100.4°F	248	241	120	
> 39.5°C/103.1°F	33	48	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting fever ≥ 38.0°C/100.4°F and > 39.5°C/103.1°F during the 43-day follow-up period after vaccination

End point title	Number of subjects reporting fever ≥ 38.0°C/100.4°F and > 39.5°C/103.1°F during the 43-day follow-up period after vaccination

End point description:

Fever was measured rectally.

End point type	Secondary

End point timeframe:

During the 43-day follow-up period following vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	676	668	379	
Units: subjects				
≥ 38.0°C/100.4°F	312	301	162	
> 39.5°C/103.1°F	52	71	24	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting investigator-confirmed measles/rubella-like rash

End point title	Number of subjects reporting investigator-confirmed measles/rubella-like rash

End point description:

End point type	Secondary

End point timeframe:

During the 43-day follow-up period after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	676	668	379	
Units: Subjects				
Subjects	37	25	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting investigator-confirmed varicella-like rash

End point title	Number of subjects reporting investigator-confirmed varicella-like rash

End point description:

End point type	Secondary

End point timeframe:

During the 43-day follow-up period after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	676	668	379	
Units: Subjects				
Subjects	10	9	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting investigator-confirmed parotid/salivary gland swelling

End point title	Number of subjects reporting investigator-confirmed parotid/salivary gland swelling

End point description:

End point type	Secondary

End point timeframe:

During the 43-day follow-up period after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	676	668	379	
Units: Subjects				
Subjects	14	7	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events and medically-attended adverse events (excluding rash and parotid/salivary gland swelling)

End point title	Number of subjects reporting unsolicited adverse events and medically-attended adverse events (excluding rash and parotid/salivary gland swelling)

End point description:

Unsolicited adverse event covers any adverse event 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. Medically-attended adverse event covers any adverse event which received medical attention. Medical attention is defined as hospitalization, an emergency room visit or a visit to or from medical personnel.

End point type	Secondary

End point timeframe:

During the 43-day follow-up period after vaccination

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	705	689	389	
Units: Subjects				
Unsolicited adverse events	338	332	191	
Medically-attended adverse events	217	213	124	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting new onset chronic illnesses and conditions prompting emergency room visits

End point title	Number of subjects reporting new onset chronic illnesses and conditions prompting emergency room visits

End point description:

New onset chronic illnesses include autoimmune disorders, asthma, type I diabetes and allergies.

End point type	Secondary

End point timeframe:

For approximately 6 months (Day 0-180)

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	705	689	389	
Units: Subjects				
New onsets of chronic diseases	11	11	7	
Emergency room visits	63	63	44	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events

End point title	Number of subjects reporting serious adverse events

End point description:

Serious adverse events assessed include medical occurrences that result in death, is life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

For approximately 6 months (Day 0-180)

End point values	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	ProQuad Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	705	689	389	
Units: Subjects				
Subjects	14	20	7	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local AEs: during 4-day follow-up period after vaccination. Solicited general & Unsolicited AEs: during 43-day follow-up period after vaccination. SAEs: during the entire study period (approximately 6 months; Day 0 to Day 180).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Refrigerator-stored Priorix-Tetra Group

Reporting group description:

Subjects received at Day 0 a single dose of refrigerator-stored Priorix-Tetra subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly in the left thigh.

Reporting group title	Freezer-stored Priorix-Tetra Group

Reporting group description:

Subjects received at Day 0 a single dose of freezer-stored Priorix-Tetra subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly in the left thigh.

Reporting group title	Proquad Group

Reporting group description:

Subjects received at Day 0 a single dose of ProQuad subcutaneously in the right upper arm co-administered with a single dose of Havrix and Prevnar intramuscularly in the left and right thigh respectively. At Day 180 they received a second dose of Havrix intramuscularly.

Serious adverse events	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	Proquad Group
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 705 (1.99%)	20 / 689 (2.90%)	7 / 389 (1.80%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Primitive neuroectodermal tumour			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Injury, poisoning and procedural complications			
Accidental drug intake by child			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Accidental exposure			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burns second degree			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Foreign body trauma			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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

Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Atelectasis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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

Respiratory distress			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Psychiatric disorders			
Autism spectrum disorder			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Acute sinusitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 705 (0.28%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Ear infection			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis			
subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess			
subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	2 / 389 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Respiratory syncytial virus bronchiolitis			

subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Viral infection			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Dehydration			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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
Type 1 diabetes mellitus			

subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (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

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

Non-serious adverse events	Refrigerator-stored Priorix-Tetra Group	Freezer-stored Priorix-Tetra Group	Proquad Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	547 / 705 (77.59%)	541 / 689 (78.52%)	297 / 389 (76.35%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Essential thrombocythaemia			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Inguinal hernia repair			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Myringotomy			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Sinus operation			
subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	2 / 389 (0.51%)
occurrences (all)	1	3	3
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Discomfort			

subjects affected / exposed	2 / 705 (0.28%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	2	2	2
Fatigue			
subjects affected / exposed	2 / 705 (0.28%)	2 / 689 (0.29%)	2 / 389 (0.51%)
occurrences (all)	2	2	2
Foreign body reaction			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Gait disturbance			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	1	1	1
Induration			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	2 / 705 (0.28%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	2	1	0
Injection site haematoma			
subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences (all)	1	2	0
Injection site erythema			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Injection site induration			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	25 / 705 (3.55%)	35 / 689 (5.08%)	20 / 389 (5.14%)
occurrences (all)	30	39	22
Local swelling			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	2 / 705 (0.28%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences (all)	2	2	0
Pain			

subjects affected / exposed	136 / 705 (19.29%)	116 / 689 (16.84%)	65 / 389 (16.71%)
occurrences (all)	137	117	65
Pyrexia			
subjects affected / exposed	2 / 705 (0.28%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	2	1	0
Swelling			
subjects affected / exposed	50 / 705 (7.09%)	51 / 689 (7.40%)	21 / 389 (5.40%)
occurrences (all)	50	51	21
Thirst			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Food allergy			
subjects affected / exposed	2 / 705 (0.28%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	2	1	0
Hypersensitivity			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Milk allergy			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Multiple allergies			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	3 / 389 (0.77%)
occurrences (all)	1	0	3
Seasonal allergy			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Balanitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Posthitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Testicular swelling			

subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal adhesion			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Asthma			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Bronchial hyperreactivity			
subjects affected / exposed	6 / 705 (0.85%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	6	2	1
Bronchospasm			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	2 / 389 (0.51%)
occurrences (all)	0	0	2
Choking			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	30 / 705 (4.26%)	23 / 689 (3.34%)	17 / 389 (4.37%)
occurrences (all)	31	24	19
Epistaxis			
subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences (all)	2	2	0
Nasal congestion			
subjects affected / exposed	11 / 705 (1.56%)	11 / 689 (1.60%)	4 / 389 (1.03%)
occurrences (all)	11	11	4
Oropharyngeal blistering			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Pharyngeal erythema			

subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Respiratory disorder			
subjects affected / exposed	2 / 705 (0.28%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	2	1	1
Respiratory tract congestion			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	29 / 705 (4.11%)	21 / 689 (3.05%)	24 / 389 (6.17%)
occurrences (all)	31	24	26
Sinus disorder			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Sneezing			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Tachypnoea			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	6 / 705 (0.85%)	4 / 689 (0.58%)	3 / 389 (0.77%)
occurrences (all)	6	4	3
Psychiatric disorders			
Breath holding			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0

Decreased activity			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	1	2	1
Listless			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Reactive attachment disorder of infancy or early childhood			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Investigations			
Haematocrit decreased			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Thyroid function test abnormal			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Arthropod bite			
subjects affected / exposed	5 / 705 (0.71%)	7 / 689 (1.02%)	1 / 389 (0.26%)
occurrences (all)	5	7	1
Burns second degree			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	1	1	0
Contusion			
subjects affected / exposed	2 / 705 (0.28%)	1 / 689 (0.15%)	2 / 389 (0.51%)
occurrences (all)	2	1	2
Ear canal abrasion			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Excoriation			

subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Eye injury			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Eye penetration			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Face injury			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Foreign body trauma			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	0	2	1
Joint sprain			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Joint dislocation			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	1	1	0
Limb crushing injury			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	1	1	0
Limb injury			
subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences (all)	0	2	0
Road traffic accident			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Skin laceration			

subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	0	2	1
Sunburn			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Tibia fracture			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Traumatic brain injury			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	1	1	0
Upper limb fracture			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
Talipes			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	0	1	1
Tibial torsion			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Nervous system disorders			
Crying			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	1	1	0
Encephalopathy			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Febrile convulsion			
subjects affected / exposed	2 / 705 (0.28%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	2	0	1
Hypersomnia			

subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	1	1	0
Poor quality sleep			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	0	1	1
Somnolence			
subjects affected / exposed	2 / 705 (0.28%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	2	2	1
Tremor			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 705 (0.43%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	3	1	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences (all)	0	2	0
Lymphadenopathy			
subjects affected / exposed	2 / 705 (0.28%)	3 / 689 (0.44%)	0 / 389 (0.00%)
occurrences (all)	2	3	0
Neutropenia			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Ear pain			
subjects affected / exposed	3 / 705 (0.43%)	1 / 689 (0.15%)	4 / 389 (1.03%)
occurrences (all)	3	1	4
Ear haemorrhage			

subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Eustachian tube dysfunction			
subjects affected / exposed	2 / 705 (0.28%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	2	1	0
Middle ear effusion			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Otorrhoea			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	1	0	1
Tympanic membrane perforation			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Chalazion			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	17 / 705 (2.41%)	20 / 689 (2.90%)	7 / 389 (1.80%)
occurrences (all)	20	20	7
Eye discharge			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Eye disorder			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	2	0
Eye irritation			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Eye swelling			
subjects affected / exposed	2 / 705 (0.28%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	2	1	0
Lacrimation increased			
subjects affected / exposed	0 / 705 (0.00%)	3 / 689 (0.44%)	1 / 389 (0.26%)
occurrences (all)	0	3	1

Ocular hyperaemia			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Abdominal hernia			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Anal fissure			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Aphthous stomatitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	5 / 705 (0.71%)	5 / 689 (0.73%)	3 / 389 (0.77%)
occurrences (all)	5	6	3
Diarrhoea			
subjects affected / exposed	37 / 705 (5.25%)	46 / 689 (6.68%)	29 / 389 (7.46%)
occurrences (all)	45	55	29
Faecaloma			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	2 / 705 (0.28%)	4 / 689 (0.58%)	1 / 389 (0.26%)
occurrences (all)	2	4	1
Gastrointestinal pain			

subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Haematemesis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Gingival pain			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Gingival swelling			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	1 / 705 (0.14%)	3 / 689 (0.44%)	0 / 389 (0.00%)
occurrences (all)	1	3	0
Teething			
subjects affected / exposed	42 / 705 (5.96%)	53 / 689 (7.69%)	28 / 389 (7.20%)
occurrences (all)	54	69	37
Tooth discolouration			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	35 / 705 (4.96%)	25 / 689 (3.63%)	15 / 389 (3.86%)
occurrences (all)	42	30	15
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1

Dermatitis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Dermatitis diaper			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	1	1	0
Eczema			
subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	1	2	1
Erythema			
subjects affected / exposed	114 / 705 (16.17%)	123 / 689 (17.85%)	55 / 389 (14.14%)
occurrences (all)	114	126	55
Ingrowing nail			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Keratosis pilaris			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Petechiae			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Skin discolouration			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	0	1	1
Skin irritation			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	1	0	1
Skin reaction			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	1	0	1
Skin lesion			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0

Urticaria			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Bone swelling			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Limb discomfort			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	3 / 705 (0.43%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	3	1	1
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Adenovirus infection			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
African trypanosomiasis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	8 / 705 (1.13%)	7 / 689 (1.02%)	1 / 389 (0.26%)
occurrences (all)	8	7	1
Bronchiolitis			
subjects affected / exposed	2 / 705 (0.28%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences (all)	2	2	0
Candidiasis			
subjects affected / exposed	2 / 705 (0.28%)	2 / 689 (0.29%)	2 / 389 (0.51%)
occurrences (all)	2	2	2
Cellulitis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	2 / 389 (0.51%)
occurrences (all)	0	1	2
Conjunctivitis bacterial			

subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Conjunctivitis viral			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Conjunctivitis infective			
subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences (all)	0	2	0
Coxsackie viral infection			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Croup infectious			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	2 / 389 (0.51%)
occurrences (all)	1	1	2
Diarrhoea infectious			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	6 / 705 (0.85%)	1 / 689 (0.15%)	2 / 389 (0.51%)
occurrences (all)	6	1	2
Erysipelas			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Eye infection viral			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Fungal infection			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Fungal skin infection			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Furuncle			

subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences (all)	1	2	0
Gastroenteritis			
subjects affected / exposed	10 / 705 (1.42%)	12 / 689 (1.74%)	2 / 389 (0.51%)
occurrences (all)	11	12	2
Gastroenteritis viral			
subjects affected / exposed	4 / 705 (0.57%)	0 / 689 (0.00%)	4 / 389 (1.03%)
occurrences (all)	4	0	4
Gingival infection			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	0 / 389 (0.00%)
occurrences (all)	1	2	0
Herpangina			
subjects affected / exposed	2 / 705 (0.28%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	2	2	1
Hordeolum			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Impetigo			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	1	2	1
Infected bites			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	9 / 705 (1.28%)	10 / 689 (1.45%)	9 / 389 (2.31%)
occurrences (all)	9	11	10
Neonatal candida infection			

subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	2 / 389 (0.51%)
occurrences (all)	0	2	2
Oral herpes			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	0	1	1
Otitis media			
subjects affected / exposed	71 / 705 (10.07%)	62 / 689 (9.00%)	34 / 389 (8.74%)
occurrences (all)	77	67	36
Otitis externa			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	0	1	1
Otitis media acute			
subjects affected / exposed	13 / 705 (1.84%)	11 / 689 (1.60%)	4 / 389 (1.03%)
occurrences (all)	14	12	4
Paronychia			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	0	1	1
Pharyngitis			
subjects affected / exposed	20 / 705 (2.84%)	16 / 689 (2.32%)	7 / 389 (1.80%)
occurrences (all)	20	17	7
Pharyngitis streptococcal			
subjects affected / exposed	0 / 705 (0.00%)	4 / 689 (0.58%)	1 / 389 (0.26%)
occurrences (all)	0	4	1
Pharyngotonsillitis			
subjects affected / exposed	1 / 705 (0.14%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	1	1	0
Pneumonia			
subjects affected / exposed	5 / 705 (0.71%)	3 / 689 (0.44%)	1 / 389 (0.26%)
occurrences (all)	5	3	1
Pneumonia viral			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	1 / 389 (0.26%)
occurrences (all)	0	0	1
Rhinitis			

subjects affected / exposed	10 / 705 (1.42%)	6 / 689 (0.87%)	5 / 389 (1.29%)
occurrences (all)	10	6	5
Roseola			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	0	1	1
Sinusitis			
subjects affected / exposed	8 / 705 (1.13%)	8 / 689 (1.16%)	5 / 389 (1.29%)
occurrences (all)	8	8	5
Streptococcal infection			
subjects affected / exposed	0 / 705 (0.00%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	0	2	1
Subcutaneous abscess			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	1 / 389 (0.26%)
occurrences (all)	0	1	1
Tinea pedis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Tinea infection			
subjects affected / exposed	2 / 705 (0.28%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	2	0	0
Urethritis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	49 / 705 (6.95%)	57 / 689 (8.27%)	42 / 389 (10.80%)
occurrences (all)	52	61	43
Urinary tract infection			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Viraemia			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Viral infection			

subjects affected / exposed	22 / 705 (3.12%)	20 / 689 (2.90%)	12 / 389 (3.08%)
occurrences (all)	22	20	12
Viral pharyngitis			
subjects affected / exposed	3 / 705 (0.43%)	3 / 689 (0.44%)	1 / 389 (0.26%)
occurrences (all)	3	3	1
Viral tonsillitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	0
Viral rash			
subjects affected / exposed	0 / 705 (0.00%)	0 / 689 (0.00%)	2 / 389 (0.51%)
occurrences (all)	0	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 705 (0.28%)	3 / 689 (0.44%)	2 / 389 (0.51%)
occurrences (all)	2	4	2
Wound infection			
subjects affected / exposed	0 / 705 (0.00%)	1 / 689 (0.15%)	0 / 389 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 705 (0.14%)	2 / 689 (0.29%)	1 / 389 (0.26%)
occurrences (all)	1	2	1
Decreased appetite			
subjects affected / exposed	3 / 705 (0.43%)	4 / 689 (0.58%)	3 / 389 (0.77%)
occurrences (all)	3	4	3
Hyperglycaemia			
subjects affected / exposed	1 / 705 (0.14%)	0 / 689 (0.00%)	0 / 389 (0.00%)
occurrences (all)	1	0	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