

**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	v3 (current)
This version publication date	19 December 2020
First version publication date	06 January 2018
Version creation reason	<ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Results have been amended to account for consistency with other registries.

**Trial information****Trial identification**

Sponsor protocol code	110058
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**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 <sup>[1]</sup>
Roles blinded	Carer, Assessor, Subject, Monitor, Data analyst

Blinding implementation details:

Data was collected in an observer-blinded manner.

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Refrigerator-stored Priorix-Tetra Group
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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)

<b>Arm title</b>	Freezer-stored Priorix-Tetra Group
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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)

<b>Arm title</b>	ProQuad Group
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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 Prevenar 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.

<b>Number of subjects in period 1</b> <sup>[2]</sup>	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
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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
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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
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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
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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
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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
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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) <sup>[1]</sup>
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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
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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) <sup>[2]</sup>
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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<sup>[3]</sup>

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 <sup>[4]</sup>
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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
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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 <sup>[5]</sup>
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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
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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)<sup>[6]</sup>

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<sup>[7]</sup>

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.

<b>End point values</b>	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

<b>End point values</b>	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
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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
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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
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End point description:

Cut-off value assessed include 0.05 micrograms per milliliter ( $\mu\text{g/mL}$ ).

End point type	Secondary
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End point timeframe:

At Day 42 after vaccination

<b>End point values</b>	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 ( $\mu\text{g/mL}$ ).
End point type	Secondary
End point timeframe:	At Day 42 after vaccination

<b>End point values</b>	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

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**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**

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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
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End point description:

Cut-off value assessed include 0.5 micrograms per milliliter ( $\mu\text{g/mL}$ ).

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End point type	Secondary
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End point timeframe:

At Day 42 after vaccination

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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	

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**Statistical analyses**

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No statistical analyses for this end point

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**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**

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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
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End point description:

Cut-off value assessed include 1.0 micrograms per milliliter ( $\mu\text{g/mL}$ ).

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End point type	Secondary
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End point timeframe:

At Day 42 after vaccination

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<b>End point values</b>	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

<b>End point values</b>	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 $\geq 38.0^{\circ}\text{C}/100.4^{\circ}\text{F}$ and $> 39.5^{\circ}\text{C}/103.1^{\circ}\text{F}$ during the 15-day follow up period after vaccination

End point title	Number of subjects reporting fever $\geq 38.0^{\circ}\text{C}/100.4^{\circ}\text{F}$ and $> 39.5^{\circ}\text{C}/103.1^{\circ}\text{F}$ during the 15-day follow up period after vaccination
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End point description:

Fever was measured rectally.

End point type Secondary

End point timeframe:

During the 15-day follow-up period following vaccination

<b>End point values</b>	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

<b>End point values</b>	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
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End point description:

End point type	Secondary
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End point timeframe:

During the 43-day follow-up period after vaccination

<b>End point values</b>	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
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End point description:

End point type	Secondary
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End point timeframe:

During the 43-day follow-up period after vaccination

<b>End point values</b>	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
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End point description:

End point type	Secondary
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End point timeframe:

During the 43-day follow-up period after vaccination

<b>End point values</b>	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)
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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
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End point timeframe:

During the 43-day follow-up period after vaccination

<b>End point values</b>	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
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End point description:

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

End point type	Secondary
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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
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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
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End point timeframe:

For approximately 6 months (Day 0-180)

<b>End point values</b>	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**

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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).

Adverse event reporting additional description:

Events collected by systematic assessment are reported for subjects with a symptom diary card available.

Events collected by non-systematic method are reported for the Total Vaccinated Cohort.

For the systematically assessed non-serious AEs, the occurrence of reported AEs was not available and encoded as equal to the number of subjects affected.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

### Reporting groups

Reporting group title	Refrigerator-stored Priorix-Tetra Group
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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	Proquad Group
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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 title	Freezer-stored Priorix-Tetra Group
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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.

Serious adverse events	Refrigerator-stored Priorix-Tetra Group	Proquad Group	Freezer-stored Priorix-Tetra Group
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 705 (1.99%)	7 / 389 (1.80%)	20 / 689 (2.90%)
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%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 / 389 (0.00%)	0 / 689 (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 / 389 (0.00%)	0 / 689 (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%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body trauma subjects affected / exposed	0 / 705 (0.00%)	1 / 389 (0.26%)	0 / 689 (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
Thermal burn subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	2 / 689 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion subjects affected / exposed	1 / 705 (0.14%)	0 / 389 (0.00%)	0 / 689 (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%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 705 (0.14%)	0 / 389 (0.00%)	0 / 689 (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 / 389 (0.00%)	0 / 689 (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%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 389 (0.00%)	0 / 689 (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%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			

subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	2 / 689 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Hypoxia</b>			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Respiratory distress</b>			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Psychiatric disorders</b>			
<b>Autism spectrum disorder</b>			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Infections and infestations</b>			
<b>Abscess</b>			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Acute sinusitis</b>			
subjects affected / exposed	0 / 705 (0.00%)	1 / 389 (0.26%)	0 / 689 (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
<b>Bronchiolitis</b>			
subjects affected / exposed	0 / 705 (0.00%)	1 / 389 (0.26%)	0 / 689 (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
<b>Cellulitis</b>			
subjects affected / exposed	2 / 705 (0.28%)	0 / 389 (0.00%)	0 / 689 (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
<b>Croup infectious</b>			

subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Ear infection</b>			
subjects affected / exposed	1 / 705 (0.14%)	0 / 389 (0.00%)	0 / 689 (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
<b>Gastroenteritis</b>			
subjects affected / exposed	1 / 705 (0.14%)	0 / 389 (0.00%)	2 / 689 (0.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Gastroenteritis rotavirus</b>			
subjects affected / exposed	0 / 705 (0.00%)	1 / 389 (0.26%)	0 / 689 (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
<b>Groin abscess</b>			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	2 / 689 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Otitis media</b>			
subjects affected / exposed	1 / 705 (0.14%)	0 / 389 (0.00%)	0 / 689 (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
<b>Periorbital cellulitis</b>			
subjects affected / exposed	0 / 705 (0.00%)	1 / 389 (0.26%)	0 / 689 (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
<b>Perirectal abscess</b>			
subjects affected / exposed	0 / 705 (0.00%)	1 / 389 (0.26%)	0 / 689 (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
<b>Pneumonia</b>			

subjects affected / exposed	0 / 705 (0.00%)	2 / 389 (0.51%)	0 / 689 (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
Pneumonia viral			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 389 (0.00%)	0 / 689 (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 / 389 (0.00%)	0 / 689 (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%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 705 (0.14%)	0 / 389 (0.00%)	0 / 689 (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%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			

subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 705 (0.00%)	0 / 389 (0.00%)	1 / 689 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Refrigerator-stored Priorix-Tetra Group	Proquad Group	Freezer-stored Priorix-Tetra Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	547 / 705 (77.59%)	297 / 389 (76.35%)	541 / 689 (78.52%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed <sup>[1]</sup>	136 / 673 (20.21%)	65 / 378 (17.20%)	114 / 666 (17.12%)
occurrences (all)	136	65	114
Redness			
subjects affected / exposed <sup>[2]</sup>	111 / 673 (16.49%)	54 / 378 (14.29%)	120 / 666 (18.02%)
occurrences (all)	111	54	120
Swelling			
subjects affected / exposed <sup>[3]</sup>	50 / 673 (7.43%)	21 / 378 (5.56%)	49 / 666 (7.36%)
occurrences (all)	50	21	49
Fever			
subjects affected / exposed <sup>[4]</sup>	312 / 676 (46.15%)	163 / 379 (43.01%)	302 / 668 (45.21%)
occurrences (all)	312	163	302
Rash			
subjects affected / exposed <sup>[5]</sup>	221 / 676 (32.69%)	128 / 379 (33.77%)	219 / 668 (32.78%)
occurrences (all)	221	128	219
Irritability			

alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	25 / 705 (3.55%) 30	20 / 389 (5.14%) 22	35 / 689 (5.08%) 39
Gastrointestinal disorders Teething alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)  Diarrhoea alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	42 / 705 (5.96%) 54  37 / 705 (5.25%) 45	28 / 389 (7.20%) 37  29 / 389 (7.46%) 29	53 / 689 (7.69%) 69  46 / 689 (6.68%) 55
Respiratory, thoracic and mediastinal disorders Rhinorrhoea alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	29 / 705 (4.11%) 31	24 / 389 (6.17%) 26	21 / 689 (3.05%) 24
Infections and infestations Otitis media alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)  Upper respiratory tract infection alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	71 / 705 (10.07%) 77  49 / 705 (6.95%) 52	34 / 389 (8.74%) 36  42 / 389 (10.80%) 43	62 / 689 (9.00%) 67  58 / 689 (8.42%) 61

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom diary cards completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom diary cards completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom diary cards completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom dairy cards completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom dairy cards completed.

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported