Clinical trial results:
A phase IIIb, open, randomised, multicentre, primary study in healthy children, to establish the non-inferiority of GlaxoSmithKline (GSK) Biologicals' MeMuRu-OKA vaccine (administered at 9 and 15 months of age) versus Priorix™ (9 months of age) and Priorix™ co-administered with Varilrix™ at 15 months of age (comparator) and also to evaluate the non-inferiority of Priorix™ (9 months of age) and MeMuRu-OKA vaccine (15 months of age) versus the comparator, all administered subcutaneously as two-dose primary vaccination course

Summary

EudraCT number	2011-005882-19
Trial protocol	Outside EU/EEA
Global end of trial date	21 February 2011

Results information

Result version number	v2 (current)
This version publication date	24 May 2023
First version publication date	29 July 2015
Version creation reason	• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	109995

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00969436
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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	Yes

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 October 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2011
Global end of trial reached?	Yes
Global end of trial date	21 February 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the non-inferiority of two doses of GSK Biologicals' measles-mumps-rubella-varicella vaccine (MeMuRu-OKA) compared to Priorix followed by Priorix co-administered with Varilrix (the current standard of care in India) in terms of measles, mumps, rubella and varicella seroconversion rates, 42 – 56 days after the second dose.
- To demonstrate the non-inferiority of GSK Biologicals' Priorix followed by MeMuRu-OKA vaccine compared to Priorix followed by Priorix co-administered with Varilrix (the current standard of care in India) in terms of measles, mumps, rubella and varicella seroconversion rates, 42 – 56 days after the second dose.

Protection of trial subjects:

All subjects were supervised for at least 30 min after vaccination/product administration with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines. Vaccines/products were administered by qualified and trained personnel.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 2009
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	India: 450
Worldwide total number of subjects	450
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	450
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:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

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

Arm description:

Subjects received 2 doses of Priorix-Tetra vaccine, 1 at Day 0 and 1 at Month 6, administered subcutaneously in the left anterolateral thigh.

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

Dosage and administration details:

Priorix-Tetra vaccine was administered subcutaneously in the left anterolateral thigh.

Arm title	Priorix/Priorix-Tetra Group

Arm description:

Subjects received 1 dose of Priorix vaccine at Day 0 and 1 dose of Priorix-Tetra vaccine at Month 6, both administered subcutaneously in the left anterolateral thigh.

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

Dosage and administration details:

Priorix vaccine was administered subcutaneously in the left anterolateral thigh.

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

Dosage and administration details:

Priorix-Tetra vaccine was administered subcutaneously in the left anterolateral thigh.

Arm title	Control Group

Arm description:

Subjects received 1 dose of Priorix vaccine at Day 0 and 1 dose of Priorix vaccine co-administered with

Varilrix vaccine at Month 6, administered subcutaneously in the left and right anterolateral thigh.

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

Dosage and administration details:

Priorix vaccine was administered subcutaneously in the left anterolateral thigh.

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

Dosage and administration details:

Varilrix vaccine was administered subcutaneously in the right anterolateral thigh.

Number of subjects in period 1	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group
Started	180	180	90
Completed	155	159	79
Not completed	25	21	11
Consent withdrawn by subject	3	-	2
Parents personal problem	-	-	1
Migrated/moved from study area	12	10	2
Subject took other vaccine hence eliminated	1	-	-
Lost to follow-up	8	8	5
Father was admitted in serious health problem	-	-	1
Protocol deviation	1	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Priorix-Tetra Group
Reporting group description:	
Subjects received 2 doses of Priorix-Tetra vaccine, 1 at Day 0 and 1 at Month 6, administered subcutaneously in the left anterolateral thigh.	
Reporting group title	Priorix/Priorix-Tetra Group
Reporting group description:	
Subjects received 1 dose of Priorix vaccine at Day 0 and 1 dose of Priorix-Tetra vaccine at Month 6, both administered subcutaneously in the left anterolateral thigh.	
Reporting group title	Control Group
Reporting group description:	
Subjects received 1 dose of Priorix vaccine at Day 0 and 1 dose of Priorix vaccine co-administered with Varilrix vaccine at Month 6, administered subcutaneously in the left and right anterolateral thigh.	

Reporting group values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group
Number of subjects	180	180	90
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	180	180	90
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	9	9	9
standard deviation	± 0	± 0.11	± 0
Gender categorical Units: Subjects			
Female	79	89	49
Male	101	91	41
Race/Ethnicity Units: Subjects			
Asian - central/south Asian heritage	177	175	88
Asian - south east Asian heritage	2	5	2
American Indian or Alaskan native	1	0	0

Reporting group values	Total		
Number of subjects	450		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	450		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	217		
Male	233		
Race/Ethnicity			
Units: Subjects			
Asian - central/south Asian heritage	440		
Asian - south east Asian heritage	9		
American Indian or Alaskan native	1		

End points

End points reporting groups

Reporting group title	Priorix-Tetra Group
Reporting group description:	
Subjects received 2 doses of Priorix-Tetra vaccine, 1 at Day 0 and 1 at Month 6, administered subcutaneously in the left anterolateral thigh.	
Reporting group title	Priorix/Priorix-Tetra Group
Reporting group description:	
Subjects received 1 dose of Priorix vaccine at Day 0 and 1 dose of Priorix-Tetra vaccine at Month 6, both administered subcutaneously in the left anterolateral thigh.	
Reporting group title	Control Group
Reporting group description:	
Subjects received 1 dose of Priorix vaccine at Day 0 and 1 dose of Priorix vaccine co-administered with Varilrix vaccine at Month 6, administered subcutaneously in the left and right anterolateral thigh.	

Primary: Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies

End point title	Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies
End point description:	
Seroconversion was defined as the appearance of antibodies [i.e. concentration/titre greater than or equal to (≥) the cut-off value] in the serum of subjects seronegative before vaccination. The cut-off values for seroconversion were 150 milli-international units per milliliter (mIU/mL), 231 units per milliliter (U/mL), 4 international units per milliliter (IU/mL) and for immunoglobulin G (IgG) varicella antibodies 1:4 dilution for measles, mumps, rubella and varicella, respectively.	
End point type	Primary
End point timeframe:	
At 42 – 56 days after the second vaccination dose at week 30	

End point values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	153	73	
Units: Subjects				
Anti-measles ≥ 150 mIU/mL [N=149, 153, 72]	149	153	72	
Anti-mumps ≥ 231 U/ML [N=149, 152, 72]	149	152	72	
Anti-rubella ≥ 4 IU/mL [N=150, 152, 73]	150	152	73	
IgG varicella antibodies ≥ 1:4 [N= 138, 143, 72]	138	141	69	

Statistical analyses

Statistical analysis title	Non-inferiority of 2 doses MMRV vs Control group

Statistical analysis description:

Non-inferiority of 2 doses of MMRV vaccine compared to MMR vaccine followed by MMR vaccine co-administered with V vaccine in terms of anti-measles seroconversion rates. Non-inferiority with respect to seroconversion rates for measles 42-56 days after second vaccination dose was concluded if the lower limit (LL) of the two-sided standardised asymptotic 95% CI on the difference in the seroconversion rates between the two groups (MMRV Group minus Control Group) was greater than or equal to -10%.

Comparison groups	Priorix-Tetra Group v Control Group
Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.52
upper limit	5.09

Statistical analysis title	Non-inferiority of 2 doses MMRV vs Control group

Statistical analysis description:

Non-inferiority of 2 doses of MMRV vaccine compared to MMR vaccine followed by MMR vaccine co-administered with V vaccine in terms of anti-mumps seroconversion rates. Non-inferiority with respect to seroconversion rates for mumps 42-56 days after second vaccination dose was concluded if the LL of the two-sided standardised asymptotic 95% CI on the difference in the seroconversion rates between the two groups (MMRV Group minus Control Group) was greater than or equal to -10%.

Comparison groups	Control Group v Priorix-Tetra Group
Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.52
upper limit	5.09

Statistical analysis title	Non-inferiority of 2 doses MMRV vs Control group

Statistical analysis description:

Non-inferiority of 2 doses of MMRV vaccine compared to MMR vaccine followed by MMR vaccine co-administered with V vaccine in terms of anti-rubella seroconversion rates. Non-inferiority with respect to seroconversion rates for rubella 42-56 days after second vaccination dose was concluded if the LL of the two-sided standardised asymptotic 95% CI on the difference in the seroconversion rates between the two groups (MMRV Group minus Control Group) was greater than or equal to -10%.

Comparison groups	Priorix-Tetra Group v Control Group

Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	5.02

Statistical analysis title	Non-inferiority of 2 doses MMRV vs Control group

Statistical analysis description:

Non-inferiority of 2 doses of MMRV vaccine compared to MMR vaccine followed by MMR vaccine co-administered with V vaccine in terms of anti-varicella seroconversion rates. Non-inferiority with respect to seroconversion rates for varicella 42-56 days after second vaccination dose was concluded if the LL of the two-sided standardised asymptotic 95% CI on the difference in the seroconversion rates between the two groups (MMRV Group minus Control Group) was greater than or equal to -10%.

Comparison groups	Priorix-Tetra Group v Control Group
Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	4.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	11.57

Statistical analysis title	Non-inferiority of MMR/MMRV vs Control group

Statistical analysis description:

Non-inferiority of MMR vaccine followed by MMRV vaccine compared to MMR vaccine followed by MMR vaccine co-administered with V vaccine in terms of anti-measles seroconversion rates. Non-inferiority with respect to seroconversion rates for measles 42-56 days after second vaccination dose was concluded if the LL of the 2-sided standardised asymptotic 95% CI on the difference in the seroconversion rates between the 2 groups (MMR/MMRV Group minus Control Group) was ≥ -10%.

Comparison groups	Control Group v Priorix/Priorix-Tetra Group
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.46
upper limit	5.09

Statistical analysis title	Non-inferiority of MMR/MMRV vs Control group

Statistical analysis description:

Non-inferiority of MMR vaccine followed by MMRV vaccine compared to MMR vaccine followed by MMR vaccine co-administered with V vaccine in terms of anti-mumps seroconversion rates. Non-inferiority with respect to seroconversion rates for mumps 42-56 days after second vaccination dose was concluded if the LL of the 2-sided standardised asymptotic 95% CI on the difference in the seroconversion rates between the 2 groups (MMR/MMRV Group minus Control Group) was ≥ -10%.

Comparison groups	Control Group v Priorix/Priorix-Tetra Group
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.48
upper limit	5.09

Statistical analysis title	Non-inferiority of MMR/MMRV vs Control group

Statistical analysis description:

Non-inferiority of MMR vaccine followed by MMRV vaccine compared to MMR vaccine followed by MMR vaccine co-administered with V vaccine in terms of anti-rubella seroconversion rates. Non-inferiority with respect to seroconversion rates for rubella 42-56 days after second vaccination dose was concluded if the LL of the 2-sided standardised asymptotic 95% CI on the difference in the seroconversion rates between the 2 groups (MMR/MMRV Group minus Control Group) was ≥ -10%.

Comparison groups	Priorix/Priorix-Tetra Group v Control Group
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.48
upper limit	5.02

Statistical analysis title	Non-inferiority of MMR/MMRV vs Control group

Statistical analysis description:

Non-inferiority of MMR vaccine followed by MMRV vaccine compared to MMR vaccine followed by MMR vaccine co-administered with V vaccine in terms of anti-varicella seroconversion rates. Non-inferiority with respect to seroconversion rates for varicella 42-56 days after second vaccination dose was concluded if the LL of the 2-sided standardised asymptotic 95% CI on the difference in the seroconversion rates between the 2 groups (MMR/MMRV Group minus Control Group) was ≥ -10%.

Comparison groups	Priorix/Priorix-Tetra Group v Control Group

Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	2.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.59
upper limit	10.29

Secondary: Number of seroconverted subjects for measles, mumps, rubella and varicella antibodies

End point title	Number of seroconverted subjects for measles, mumps, rubella and varicella antibodies

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. concentration/titre ≥ the cut-off value) in the serum of subjects seronegative before vaccination. The cut-off values for seroconversion was 150 mIU/mL, 231 U/mL, 4 IU/mL and for IgG varicella antibodies 1:4 dilution for measles, mumps, rubella and varicella, respectively.

End point type	Secondary

End point timeframe:

Approximately 42 to 56 days after the first vaccine dose at week 6

End point values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	149	153	73	
Units: Subjects				
Anti-measles ≥ 150 mIU/mL [N= 148, 153, 72]	138	135	63	
Anti-mumps ≥ 231 U/ML [N= 144, 152, 72]	124	128	60	
Anti-rubella ≥ 4 IU/mL [N= 149, 152, 73]	147	151	73	
IgG varicella antibodies ≥ 1:4 [N= 138, 142, 72]	130	4	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against measles, mumps, rubella and varicella viruses

End point title	Antibody concentrations against measles, mumps, rubella and varicella viruses

End point description:

Antibody concentrations were summarized by geometric mean concentrations (GMCs) with their 95% confidence intervals (CIs).

End point type	Secondary

End point timeframe:

At 42 – 56 days after the first (at Week 6) and second (at Week 30) vaccination dose

End point values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	153	73	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-measles; W6 [N= 148, 153, 72]	2013.6 (1662.2 to 2439.3)	1180.4 (963 to 1446.7)	1200 (887.9 to 1621.8)	
Anti-mumps; W6 [N= 144, 152, 72]	991.9 (819.7 to 1200.3)	746.6 (628 to 887.6)	775.1 (600.9 to 999.7)	
Anti-rubella; W6 [N= 149, 152, 73]	45.4 (38.3 to 53.7)	63.8 (55.9 to 72.8)	62 (51.3 to 74.9)	
IgG varicella antibodies; W6 [N= 138, 142, 72]	120.5 (90.8 to 160)	2.2 (2 to 2.4)	2.2 (1.8 to 2.6)	
Anti-measles; W30 [N=149, 153, 72]	4471.3 (3975.3 to 5029.2)	3358.7 (3017.5 to 3738.4)	2495 (2064.5 to 3015.2)	
Anti-mumps; W30 [N=149, 152, 72]	6428 (5774.9 to 7154.9)	10108.5 (9223.9 to 11078)	4925.3 (4200.9 to 5774.7)	
Anti-rubella; W30 [N=150, 152, 73]	148.4 (136.1 to 161.8)	164.8 (152.1 to 178.6)	173 (153 to 195.6)	
IgG varicella antibodies; W30 [N= 138, 143, 72]	5318.5 (4318.7 to 6549.8)	198 (158.2 to 247.7)	128 (91.7 to 178.7)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = Cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 20 millimeters (mm) of injection site.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose (Dose 1 and Dose 2)

End point values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	174	172	84	
Units: Subjects				
Any Pain; Dose 1 [N= 174, 172, 84]	20	12	9	
Grade 3 Pain; Dose 1 [N= 174, 172, 84]	0	0	0	
Any Redness; Dose 1 [N= 174, 172, 84]	15	8	3	
Grade 3 Redness; Dose 1 [N= 174, 172, 84]	0	0	0	
Any Swelling; Dose 1 [N= 174, 172, 84]	8	5	3	
Grade 3 Swelling; Dose 1 [N= 174, 172, 84]	0	0	0	
Any Pain; Dose 2 [N= 155, 159, 79]	9	10	3	
Grade 3 Pain; Dose 2 [N= 155, 159, 79]	0	0	0	
Any Redness; Dose 2 [N= 155, 159, 79]	10	6	0	
Grade 3 Redness; Dose 2 [N= 155, 159, 79]	3	0	0	
Any Swelling; Dose 2 [N= 155, 159, 79]	9	6	0	
Grade 3 Swelling; Dose 2 [N= 155, 159, 79]	0	0	0	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Assessed solicited general symptoms were meningism and parotid gland swelling. Any = occurrence of the symptom regardless of intensity grade or relationship to vaccination. Grade 3 (G3) meningism and parotid gland swelling = meningism/parotid gland swelling which prevented normal everyday activities. Related (Rel) = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period following each dose (Dose 1 and Dose 2)

End point values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	174	172	83	
Units: Subjects				
Any Meningism; D1 [N= 174, 172, 83]	0	0	0	
G3 Meningism; D1 [N= 174, 172, 83]	0	0	0	

Rel Meningism; D1 [N= 174, 172, 83]	0	0	0	
Any Parotid gland swelling; D1 [N= 174, 172, 83]	0	0	0	
G3 Parotid gland swelling; D1 [N= 174, 172, 83]	0	0	0	
Rel Parotid gland swelling; D1 [N= 174, 172, 83]	0	0	0	
Any Meningism; D2 [N= 155, 159, 79]	0	0	0	
G3 Meningism; D2 [N= 155, 159, 79]	0	0	0	
Rel Meningism; D2 [N= 155, 159, 79]	0	0	0	
Any Parotid gland swelling; D2 [N= 155, 159, 79]	0	0	0	
G3 Parotid gland swelling; D2 [N= 155, 159, 79]	0	0	0	
Rel Parotid gland swelling; D2 [N= 155, 159, 79]	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related fever

End point title	Number of subjects reporting any, grade 3 and related fever

End point description:

Any fever was defined as fever ≥ 38.0°C and grade 3 fever > 39.5°C after vaccination. Related fever was defined as fever assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period following each dose (Dose 1 and Dose 2)

End point values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	174	172	83	
Units: Subjects				
Any temperature; Dose 1 [N= 174, 172, 83]	76	70	27	
Grade 3 temperature; Dose 1 [N= 174, 172, 83]	11	5	1	
Related temperature; Dose 1 [N= 174, 172, 83]	53	48	15	
Any temperature; Dose 2 [N= 155, 159, 79]	41	37	22	
Grade 3 temperature; Dose 2 [N= 155, 159, 79]	2	6	2	
Related temperature; Dose 2 [N= 155, 159, 79]	22	21	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related rash

End point title	Number of subjects reporting any, grade 3 and related rash

End point description:

Any rash was defined as incidence of a rash regardless of intensity grade or relationship to vaccination and grade 3 rash greater than (>) 150 lesions. Related rash was defined as rash assessed by the investigator as causally related to the vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period following each dose (Dose 1 and Dose 2)

End point values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	174	172	83	
Units: Subjects				
Any Rash; Dose 1 [N= 174, 172, 83]	1	2	1	
Grade 3 Rash; Dose 1 [N= 174, 172, 83]	0	0	0	
Related Rash; Dose 1 [N= 174, 172, 83]	1	0	0	
Any Rash; Dose 2 [N= 155, 159, 79]	0	1	0	
Grade 3 Rash; Dose 2 [N= 155, 159, 79]	0	0	0	
Related Rash; Dose 2 [N= 155, 159, 79]	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse event

End point title	Number of subjects reporting any unsolicited adverse event

End point description:

An unsolicited adverse event (AE) covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any was defined as an AE reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

Within 43-day (Days 0-42) after the first and second vaccination dose

End point values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	180	90	
Units: Subjects				
Any AE(s); Dose 1	37	39	18	
Any AE(s); Dose 2	19	18	11	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

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

End point type	Secondary

End point timeframe:

From the first study dose up to study end (Month 0 to Month 7.5 approximately)

End point values	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	180	90	
Units: Subjects				
Any SAE(s)	7	6	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms were collected during the 4-day and 43-day after each vaccination dose, respectively. Unsolicited AEs were collected during the 43-day after each vaccination dose. SAEs were collected from Month 0 to Month 7.5.

Adverse event reporting additional description:

The number of occurrences reported for solicited symptoms, adverse events, and serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Priorix-Tetra Group

Reporting group description:

Subjects received 2 doses of Priorix-Tetra vaccine, 1 at Day 0 and 1 at Month 6, administered subcutaneously in the left anterolateral thigh.

Reporting group title	Priorix/Priorix-Tetra Group

Reporting group description:

Subjects received 1 dose of Priorix vaccine at Day 0 and 1 dose of Priorix-Tetra vaccine at Month 6, both administered subcutaneously in the left anterolateral thigh.

Reporting group title	Control Group

Reporting group description:

Subjects received 1 dose of Priorix vaccine at Day 0 and 1 dose of Priorix vaccine co-administered with Varilrix vaccine at Month 6, administered subcutaneously in the left and right anterolateral thigh.

Serious adverse events	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 180 (3.89%)	6 / 180 (3.33%)	0 / 90 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 180 (0.00%)	1 / 180 (0.56%)	0 / 90 (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	1 / 180 (0.56%)	0 / 180 (0.00%)	0 / 90 (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, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 180 (0.56%)	0 / 180 (0.00%)	0 / 90 (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 inflammation			
subjects affected / exposed	0 / 180 (0.00%)	1 / 180 (0.56%)	0 / 90 (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
Wheezing			
subjects affected / exposed	1 / 180 (0.56%)	0 / 180 (0.00%)	0 / 90 (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
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 180 (1.11%)	3 / 180 (1.67%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	2 / 180 (1.11%)	1 / 180 (0.56%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 180 (0.56%)	1 / 180 (0.56%)	0 / 90 (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
Bronchiolitis			
subjects affected / exposed	0 / 180 (0.00%)	1 / 180 (0.56%)	0 / 90 (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

Pneumonia			
subjects affected / exposed	0 / 180 (0.00%)	1 / 180 (0.56%)	0 / 90 (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			
Dehydration			
subjects affected / exposed	0 / 180 (0.00%)	1 / 180 (0.56%)	0 / 90 (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	Priorix-Tetra Group	Priorix/Priorix-Tetra Group	Control Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	114 / 180 (63.33%)	116 / 180 (64.44%)	55 / 90 (61.11%)
General disorders and administration site conditions			
Pain; Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed	20 / 180 (11.11%)	12 / 180 (6.67%)	9 / 90 (10.00%)
occurrences (all)	20	12	9
Redness; Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed[1]	15 / 174 (8.62%)	8 / 172 (4.65%)	3 / 84 (3.57%)
occurrences (all)	15	8	3
Pain; Dose 2			
alternative assessment type: Systematic			
subjects affected / exposed[2]	9 / 155 (5.81%)	10 / 159 (6.29%)	3 / 79 (3.80%)
occurrences (all)	9	10	3
Redness; Dose 2			
alternative assessment type: Systematic			
subjects affected / exposed[3]	10 / 155 (6.45%)	6 / 159 (3.77%)	0 / 79 (0.00%)
occurrences (all)	10	6	0
Swelling; Dose 2			
alternative assessment type: Systematic			

subjects affected / exposed[4]	9 / 155 (5.81%)	6 / 159 (3.77%)	0 / 79 (0.00%)
occurrences (all)	9	6	0
Fever; Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed[5]	76 / 174 (43.68%)	70 / 172 (40.70%)	27 / 83 (32.53%)
occurrences (all)	76	70	27
Fever; Dose 2			
alternative assessment type: Systematic			
subjects affected / exposed[6]	41 / 155 (26.45%)	37 / 159 (23.27%)	22 / 79 (27.85%)
occurrences (all)	41	37	22
Respiratory, thoracic and mediastinal disorders			
Cough; Dose 1			
subjects affected / exposed	6 / 180 (3.33%)	10 / 180 (5.56%)	6 / 90 (6.67%)
occurrences (all)	6	10	6
Infections and infestations			
Rhinitis; Dose 1			
subjects affected / exposed	7 / 180 (3.89%)	9 / 180 (5.00%)	6 / 90 (6.67%)
occurrences (all)	7	9	6
Nasopharyngitis; Dose 1			
subjects affected / exposed	4 / 180 (2.22%)	8 / 180 (4.44%)	6 / 90 (6.67%)
occurrences (all)	4	8	6
Upper respiratory tract infection; Dose 1			
subjects affected / exposed	10 / 180 (5.56%)	7 / 180 (3.89%)	1 / 90 (1.11%)
occurrences (all)	10	7	1
Rhinitis; Dose 2			
subjects affected / exposed	6 / 180 (3.33%)	7 / 180 (3.89%)	5 / 90 (5.56%)
occurrences (all)	6	7	5

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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen 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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen 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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen 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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen 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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen completed).

[6] - 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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen completed).

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