Clinical trial results:
Phase IIIa, observer-blind, randomized study to evaluate non-inferiority of second dose of GSK Biologicals' measles-mumps-rubella vaccine vs second dose of Merck & Co., Inc.'s MMR vaccine when administered with and without diphtheria, tetanus, acellular pertussis and inactivated polio (DTaP-IPV) vaccine and varicella vaccine (VV) to healthy children 4 to 6 years of age

Summary

EudraCT number	2011-004638-32
Trial protocol	Outside EU/EEA
Global end of trial date	09 November 2015

Results information

Result version number	v1 (current)
This version publication date	30 August 2017
First version publication date	30 August 2017

Trial information

Trial identification

Sponsor protocol code	115158

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01621802
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 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 July 2015
Global end of trial reached?	Yes
Global end of trial date	09 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the non-inferiority of Priorix vaccine to M-M-R II (M-M-R Vax Pro) vaccine, when administered with VV and DTaP-IPV vaccines in terms of seroresponse rates to measles, mumps and rubella viruses at Day 42.

- To demonstrate the non-inferiority of Priorix vaccine to M-M-R II (M-M-R Vax Pro) vaccine, when administered with VV and DTaP-IPV vaccines in terms of antibody concentrations to measles, mumps and rubella viruses at Day 42.

- To demonstrate the non-inferiority of Priorix vaccine to M-M-R II (M-M-R Vax Pro) vaccine, when administered without VV and DTaP-IPV vaccines in terms of seroresponse rates to measles, mumps and rubella viruses at Day 42.

- To demonstrate the non-inferiority of Priorix vaccine to M-M-R II (M-M-R Vax Pro) vaccine, when administered without VV and DTaP-IPV vaccines in terms of antibody concentrations to measles, mumps and rubella viruses at Day 42.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of vaccine(s), with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 June 2012
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	Korea, Republic of: 359
Country: Number of subjects enrolled	Taiwan: 968
Country: Number of subjects enrolled	United States: 2684
Worldwide total number of subjects	4011
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)	0
Children (2-11 years)	4011
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:

Subjects were enrolled in 3 sub-cohorts. Sub-cohort 1: Inv_MMR_CO and Com_MMR_CO (Lot 1 or Lot 2), Sub-cohort 2: Inv_MMR_I and Com_MMR_I (Lot 1 or Lot 2) and Sub-cohort 3: Inv_MMR_S and Com_MMR_S (Lot 1 or Lot 2).

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 Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

Blinding implementation details:

Data were collected in an observer-blind manner. By observer-blind, it is meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g. safety, reactogenicity, and immunogenicity) will all be unaware of which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	Inv_MMR_CO Group

Arm description:

Subjects received one dose of the study vaccine Priorix along with Kinrix and ProQuad vaccines at Visit 1 (Day 0).

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

Dosage and administration details:

One dose administered subcutaneously in the triceps region of the right arm.

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

Dosage and administration details:

One dose administered by deep intramuscular injection in the upper left deltoid.

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:

One dose administered subcutaneously in the triceps region of the left arm.

Arm title	Com_MMR_CO Group

Arm description:

Subjects received one dose of the licensed vaccine M-M-R II (also known as M-M-R Vax Pro) Lot 1 or Lot 2 along with Kinrix and ProQuad vaccines at Visit 1 (Day 0).

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:

One dose administered subcutaneously in the triceps region of the left arm.

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

Dosage and administration details:

One dose administered by deep intramuscular injection in the upper left deltoid.

Investigational medicinal product name	M-M-R II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose administered subcutaneously in the triceps region of the right arm.

Arm title	Inv_MMR_I Group

Arm description:

Subjects received one dose of Priorix at Visit 1 (Day 0).

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

Dosage and administration details:

One dose administered subcutaneously in the triceps region of the right arm.

Arm title	Com_MMR_I Group

Arm description:

Subjects received one dose of M-M-R II (also known as M-M-R Vax Pro) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).

Arm type	Active comparator
Investigational medicinal product name	M-M-R II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose administered subcutaneously in the triceps region of the right arm.

Arm title	Inv_MMR_S Group

Arm description:

Subjects in this safety cohort received one dose of Priorix at Visit 1 (Day 0).

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

Dosage and administration details:

One dose administered subcutaneously in the triceps region of the right arm.

Arm title	Com_MMR_S Group

Arm description:

Subjects in this safety cohort received one dose of M-M-R II (also known as M-M-R Vax Pro) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).

Arm type	Active comparator
Investigational medicinal product name	M-M-R II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose administered subcutaneously in the triceps region of the right arm.

Number of subjects in period 1[1]	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group
Started	802	298	796
Completed	755	275	763
Not completed	47	23	33
Consent withdrawn by subject	8	4	4
Others	3	3	3
Migrated/moved from study area	-	-	2
Lost to follow-up	36	16	24
Protocol deviation	-	-	-

Number of subjects in period 1[1]	Com_MMR_I Group	Inv_MMR_S Group	Com_MMR_S Group
Started	303	1319	489
Completed	292	1284	477
Not completed	11	35	12
Consent withdrawn by subject	2	2	-
Others	2	1	-
Migrated/moved from study area	-	1	-
Lost to follow-up	7	31	11
Protocol deviation	-	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: While 4011 subjects were enrolled in the study, only 4007 eligible subjects received a study vaccination.

Baseline characteristics

Reporting groups	
Reporting group title	Inv_MMR_CO Group
Reporting group description:	
Subjects received one dose of the study vaccine Priorix along with Kinrix and ProQuad vaccines at Visit 1 (Day 0).	
Reporting group title	Com_MMR_CO Group
Reporting group description:	
Subjects received one dose of the licensed vaccine M-M-R II (also known as M-M-R Vax Pro) Lot 1 or Lot 2 along with Kinrix and ProQuad vaccines at Visit 1 (Day 0).	
Reporting group title	Inv_MMR_I Group
Reporting group description:	
Subjects received one dose of Priorix at Visit 1 (Day 0).	
Reporting group title	Com_MMR_I Group
Reporting group description:	
Subjects received one dose of M-M-R II (also known as M-M-R Vax Pro) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).	
Reporting group title	Inv_MMR_S Group
Reporting group description:	
Subjects in this safety cohort received one dose of Priorix at Visit 1 (Day 0).	
Reporting group title	Com_MMR_S Group
Reporting group description:	
Subjects in this safety cohort received one dose of M-M-R II (also known as M-M-R Vax Pro) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).	

Reporting group values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group
Number of subjects	802	298	796
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	4.1	4.1	4.4
standard deviation	± 0.3	± 0.3	± 0.6
Gender categorical Units: Subjects			
Female	398	134	361
Male	404	164	435
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	96	39	48
American Indian or Alaskan Native	130	38	15
Asian - Central/South Asian Heritage	12	5	7
Asian - East Asian Heritage	28	6	384
Asian - Japanese Heritage	3	0	0
Asian - South East Asian Heritage	49	25	11
Native Hawaiian or Other Pacific Islander	4	2	2

Other	112	45	35
White - Arabic / North African Heritage	5	3	3
White - Caucasian / European Heritage	363	135	291

Reporting group values	Com_MMR_I Group	Inv_MMR_S Group	Com_MMR_S Group
Number of subjects	303	1319	489
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	4.3	4.4	4.4
standard deviation	± 0.6	± 0.6	± 0.6
Gender categorical			
Units: Subjects			
Female	153	632	225
Male	150	687	264
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage / African American	19	94	32
American Indian or Alaskan Native	3	4	0
Asian - Central/South Asian Heritage	1	8	0
Asian - East Asian Heritage	146	565	209
Asian - Japanese Heritage	1	1	0
Asian - South East Asian Heritage	4	16	8
Native Hawaiian or Other Pacific Islander	0	3	0
Other	9	52	22
White - Arabic / North African Heritage	3	1	0
White - Caucasian / European Heritage	117	575	218

Reporting group values	Total		
Number of subjects	4007		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	1903		
Male	2104		
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage / African American	328		
American Indian or Alaskan Native	190		

Asian - Central/South Asian Heritage	33		
Asian - East Asian Heritage	1338		
Asian - Japanese Heritage	5		
Asian - South East Asian Heritage	113		
Native Hawaiian or Other Pacific Islander	11		
Other	275		
White - Arabic / North African Heritage	15		
White - Caucasian / European Heritage	1699		

End points

End points reporting groups

Reporting group title	Inv_MMR_CO Group
Reporting group description:	
Subjects received one dose of the study vaccine Priorix along with Kinrix and ProQuad vaccines at Visit 1 (Day 0).	
Reporting group title	Com_MMR_CO Group
Reporting group description:	
Subjects received one dose of the licensed vaccine M-M-R II (also known as M-M-R Vax Pro) Lot 1 or Lot 2 along with Kinrix and ProQuad vaccines at Visit 1 (Day 0).	
Reporting group title	Inv_MMR_I Group
Reporting group description:	
Subjects received one dose of Priorix at Visit 1 (Day 0).	
Reporting group title	Com_MMR_I Group
Reporting group description:	
Subjects received one dose of M-M-R II (also known as M-M-R Vax Pro) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).	
Reporting group title	Inv_MMR_S Group
Reporting group description:	
Subjects in this safety cohort received one dose of Priorix at Visit 1 (Day 0).	
Reporting group title	Com_MMR_S Group
Reporting group description:	
Subjects in this safety cohort received one dose of M-M-R II (also known as M-M-R Vax Pro) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).	

Primary: Number of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value

End point title	Number of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value[1]
End point description:	
Seroresponse was defined as post-vaccination anti-measles virus antibody concentration equal to or above (≥) 200 milli-international Units per milliliter (mIU/mL). Analysis was done in sub-cohorts 1 and 2 only.	
End point type	Primary
End point timeframe:	
42 days post vaccination (At Day 42)	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, with and without co-administration with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO, Com_MMR_CO, Inv_MMR_I and Com_MMR_I Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	697	249	736	283
Units: Subjects				
Anti-measles	697	249	736	281

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Power obtained using PASS 2005 (Likelihood Score [Miettienen and Nurminen approach]), one-sided non-inferiority test for the difference of two independent proportions, under the alternative associated to the reference value & alpha=1.25%. The global power to reach all non-inferiority objectives of Priorix vs. M-M-R II in sub-cohort 1 should be at least 94.04% (=100%- the sum of type II errors associated to cohort 1.

Comparison groups	Inv_MMR_CO Group v Com_MMR_CO Group
Number of subjects included in analysis	946
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in seroresponse rate (%)
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.72
upper limit	1.98

Notes:

[2] - Non-inferiority criterion for sub cohort 1: Lower limit (LL) of the 2-sided 97.5% confidence interval (CI) for group difference (Inv_MMR_CO Group minus pooled Com_MMR_CO Group) in seroresponse rates to measles, mumps and rubella viruses is ≥ -5%.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Power obtained using PASS 2005 (Likelihood Score [Miettienen and Nurminen approach]), one-sided non-inferiority test for the difference of two independent proportions, under the alternative associated to the reference value & alpha=1.25%. The global power to reach all non-inferiority objectives of Priorix vs. M-M-R II in sub-cohort 2 should be at least 98.88% (=100%- the sum of type II error associated to cohort 2.

Comparison groups	Inv_MMR_I Group v Com_MMR_I Group
Number of subjects included in analysis	1019
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in Seroresponse rate (%)
Point estimate	0.71
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.02
upper limit	2.97

Notes:

[3] - Non-inferiority criterion for sub cohort 2: The LL of the 2-sided 97.5% CI for group difference (Inv_MMR_I group minus pooled Com_MMR_I group) in seroresponse rates to measles, mumps and rubella viruses was ≥ -5%.

Primary: Number of subjects with anti-mumps virus antibody concentration equal to

or above the cut-off-value	
End point title	Number of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value[4]

End point description:

Seroresponse was defined as post-vaccination anti-mumps virus antibody concentration ≥ 10 ELISA Units per milliliter (EU/mL). Analysis was done in sub-cohorts 1 and 2 only.

End point type	Primary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, with and without co-administration with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO, Com_MMR_CO, Inv_MMR_I and Com_MMR_I Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	698	250	736	283
Units: Subjects				
Anti-mumps	698	250	736	283

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Power obtained using PASS 2005 (Likelihood Score [Miettienen and Nurminen approach]), one-sided non-inferiority test for the difference of two independent proportions, under the alternative associated to the reference value & alpha =1.25%. The global power to reach all non-inferiority objectives of Priorix vs. M-M-R II in sub-cohort 1 should be at least 94.04% (=100%- the sum of type II errors associated to cohort 1.

Comparison groups	Inv_MMR_CO Group v Com_MMR_CO Group
Number of subjects included in analysis	948
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in seroresponse rate (%)
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.72
upper limit	1.97

Notes:

[5] - Non-inferiority criterion for sub cohort 1: The LL of the 2-sided 97.5% CI for group difference (Inv_MMR_CO Group minus pooled Com_MMR_CO Group) in seroresponse rates to measles, mumps and rubella viruses was ≥ -5%.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Power obtained using PASS 2005 (Likelihood Score [Miettienen and Nurminen approach]), one-sided non-inferiority test for the difference of two independent proportions, under the alternative associated to the reference value & alpha=1.25%. The global power to reach all non-inferiority objectives of Priorix

vs. M-M-R II in sub-cohort 2 should be at least 98.88% (=100%- the sum of type II error associated to cohort 2.

Comparison groups	Inv_MMR_I Group v Com_MMR_I Group
Number of subjects included in analysis	1019
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in Seroresponse rate (%)
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.68
upper limit	1.75

Notes:

[6] - Non-inferiority criterion for sub cohort 2: The LL of the 2-sided 97.5% CI for group difference (Inv_MMR_I group minus pooled Com_MMR_I group) in seroresponse rates to measles, mumps and rubella viruses was ≥ -5%.

Primary: Number of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value

End point title	Number of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value[7]

End point description:

Seroresponse was defined as post-vaccination anti-rubella virus antibody concentration ≥ 10 International Units per milliliter (IU/mL). Analysis was done in sub-cohorts 1 and 2 only.

End point type	Primary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, with and without co-administration with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO, Com_MMR_CO, Inv_MMR_I and Com_MMR_I Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	697	249	736	283
Units: Subjects				
Anti-rubella	696	249	736	283

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Power obtained using PASS 2005 (Likelihood Score [Miettienen and Nurminen approach]), one-sided non-inferiority test for the difference of two independent proportions, under the alternative associated to the reference value & alpha =1.25%. The global power to reach all non-inferiority objectives of Priorix vs. M-M-R II in sub-cohort 1 should be at least 94.04% (=100%- the sum of type II errors associated to cohort 1.

Comparison groups	Inv_MMR_CO Group v Com_MMR_CO Group

Number of subjects included in analysis	946
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Difference in seroresponse rate (%)
Point estimate	-0.14
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.98
upper limit	1.84

Notes:

[8] - Non-inferiority criterion for sub cohort 1: The LL of the 2-sided 97.5% CI for group difference (Inv_MMR_CO group minus pooled Com_MMR_CO group) in seroresponse rates to measles, mumps and rubella viruses was ≥ -5%.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Power obtained using PASS 2005 (Likelihood Score [Miettienen and Nurminen approach]), one-sided non-inferiority test for the difference of two independent proportions, under the alternative associated to the reference value & alpha=1.25%. The global power to reach all non-inferiority objectives of Priorix vs. M-M-R II in sub-cohort 2 should be at least 98.88% (=100%- the sum of type II error associated to cohort 2.

Comparison groups	Inv_MMR_I Group v Com_MMR_I Group
Number of subjects included in analysis	1019
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	Difference in seroresponse rate (%)
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.68
upper limit	1.75

Notes:

[9] - Non-inferiority criterion for sub cohort 2: The LL of the 2-sided 97.5% CI for group difference (Inv_MMR_I group minus pooled Com_MMR_I group) in seroresponse rates to measles, mumps and rubella viruses was ≥ -5%.

Primary: Evaluation of immunogenicity in terms of anti-measles virus antibody concentrations

End point title	Evaluation of immunogenicity in terms of anti-measles virus antibody concentrations[10]

End point description:

Antibody concentrations were expressed as Geometric Mean Concentrations (GMCs) in mIU/mL. Analysis was done in sub-cohorts 1 and 2 only.

End point type	Primary

End point timeframe:

42 days after vaccination (At Day 42)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, with and without co-administration with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO, Com_MMR_CO, Inv_MMR_I and Com_MMR_I Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	697	249	736	283
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-measles	4335 (4089.7 to 4594.9)	4215.6 (3806.7 to 4668.4)	3646.6 (3453.5 to 3850.4)	3503.9 (3174.6 to 3867.4)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Inv_MMR_CO Group v Com_MMR_CO Group
Number of subjects included in analysis	946
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.99
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.92
upper limit	1.06

Notes:

[11] - Non-inferiority criterion for sub cohort 1: The LL of the 2-sided 97.5% CI for the adjusted GMC ratio (Inv_MMR_CO group divided by pooled Com_MMR_CO group) was ≥ 0.67 for antibodies to measles, mumps and rubella viruses.

Statistical analysis title	Statistical analysis 2
Comparison groups	Inv_MMR_I Group v Com_MMR_I Group
Number of subjects included in analysis	1019
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	1.03
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.96
upper limit	1.1

Notes:

[12] - Non-inferiority criterion for sub cohort 2: The LL of the 2-sided 97.5% CI for the adjusted GMC ratio (Inv_MMR_I group divided by pooled Com_MMR_I group) was ≥ 0.67 for antibodies to measles, mumps and rubella viruses.

Primary: Evaluation of immunogenicity in terms of anti-mumps virus antibody concentrations

End point title	Evaluation of immunogenicity in terms of anti-mumps virus antibody concentrations[13]

End point description:

Antibody concentrations were expressed as GMCs in EU/mL. Analysis was done in sub-cohorts 1 and 2 only.

End point type	Primary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, with and without co-administration with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO, Com_MMR_CO, Inv_MMR_I and Com_MMR_I Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	698	250	736	283
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-mumps	170.5 (161.6 to 179.9)	190.1 (174.7 to 206.8)	167.2 (158.6 to 176.3)	176.2 (161.5 to 192.2)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Inv_MMR_CO Group v Com_MMR_CO Group
Number of subjects included in analysis	948
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.91
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.83
upper limit	1

Notes:

[14] - The LL of the 2-sided 97.5% CI for the adjusted GMC ratio (Inv_MMR_CO group divided by pooled Com_MMR_CO group) was ≥ 0.67 for antibodies to measles, mumps and rubella viruses.

Statistical analysis title	Statistical analysis 2
Comparison groups	Inv_MMR_I Group v Com_MMR_I Group
Number of subjects included in analysis	1019
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.96

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.87
upper limit	1.06

Notes:

[15] - The LL of the 2-sided 97.5% CI for the adjusted GMC ratio (Inv_MMR_I group divided by pooled Com_MMR_I group) was ≥ 0.67 for antibodies to measles, mumps and rubella viruses.

Primary: Evaluation of immunogenicity in terms of anti-rubella virus antibody concentrations

End point title	Evaluation of immunogenicity in terms of anti-rubella virus antibody concentrations[16]

End point description:

Antibody concentrations were expressed as GMCs in IU/mL. Analysis was done in sub-cohorts 1 and 2 only.

End point type	Primary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, with and without co-administration with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO, Com_MMR_CO, Inv_MMR_I and Com_MMR_I Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	697	249	736	283
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-rubella	96.4 (92.6 to 100.4)	96 (89.5 to 103)	98.9 (95.3 to 102.8)	98.7 (93.2 to 104.5)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Adjusted geometric mean concentration (GMC) ratio (Inv_MMR_CO group divided by Com_MMR_CO group) for antibodies to rubella virus.

Comparison groups	Inv_MMR_CO Group v Com_MMR_CO Group
Number of subjects included in analysis	946
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	1.03

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.97
upper limit	1.09

Notes:

[17] - Non-inferiority criterion for sub cohort 1: The LL of the 2-sided 97.5% CI for the adjusted GMC ratio (Inv_MMR_CO group divided by pooled Com_MMR_CO group) was ≥ 0.67 for antibodies to measles, mumps and rubella viruses.

Statistical analysis title	Statistical analysis 2
Comparison groups	Inv_MMR_I Group v Com_MMR_I Group
Number of subjects included in analysis	1019
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	1.01
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.95
upper limit	1.07

Notes:

[18] - Non-inferiority criterion for sub cohort 2: The LL of the 2-sided 97.5% CI for the adjusted GMC ratio (Inv_MMR_I group divided by pooled Com_MMR_I group) was ≥ 0.67 for antibodies to measles, mumps and rubella viruses.

Secondary: Number of subjects with anti-varicella zoster virus (VZV) antibody concentration equal to or above the cut-off-value

End point title	Number of subjects with anti-varicella zoster virus (VZV) antibody concentration equal to or above the cut-off-value[19]

End point description:

Seroresponse was defined as post-vaccination anti-VZV antibody concentration ≥ 75 mIU/mL. Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	695	247		
Units: Subjects				
Anti-VZV	693	247		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of immunogenicity in terms of anti-VZV antibody concentrations

End point title	Evaluation of immunogenicity in terms of anti-VZV antibody concentrations[20]

End point description:

Antibody concentrations were expressed as GMCs in mIU/mL. Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	695	247		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-VZV	887.7 (834.3 to 944.4)	820.4 (749.3 to 898.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody booster response to diphtheria toxin (anti-D) and tetanus toxin (anti-T)

End point title	Number of subjects with antibody booster response to diphtheria toxin (anti-D) and tetanus toxin (anti-T)[21]

End point description:

Booster response was defined as: For subjects with pre-vaccination antibody concentration less than (<) 0.1 IU/mL, antibody concentration ≥ 0.4 IU/ml at Day 42. For subjects with pre-vaccination antibody concentration ≥ 0.1 IU/mL: antibody concentration at Day 42 ≥ 4 fold the pre-vaccination antibody concentration. Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	661	234		
Units: Subjects				
Anti-D (N=659;233)	657	233		
Anti-T (N=661;234)	621	224		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody booster response to pertussis toxin (PT)

End point title	Number of subjects with antibody booster response to pertussis toxin (PT)[22]

End point description:

Booster response was defined as: For initially seronegative subjects, antibody concentration ≥ 10.772 IU/mL at Day 42. For initially seropositive subjects with pre-vaccination antibody concentration < 10.772 IU/mL: antibody concentration at Day 42 ≥ 4 fold the pre-vaccination antibody concentration. For initially seropositive subjects with pre-vaccination antibody concentration ≥ 10.772 IU/mL: antibody concentration at Day 42 ≥ 2 fold the pre-vaccination antibody concentration. Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	659	233		
Units: Subjects				
Anti-PT	643	225		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody booster response to filamentous hemagglutinin (FHA)

End point title	Number of subjects with antibody booster response to filamentous hemagglutinin (FHA)[23]

End point description:

Booster response was defined as: For initially seronegative subjects, antibody concentration ≥ 8.184

IU/ml at Day 42. For initially seropositive subjects with pre-vaccination antibody concentration < 8.184 IU/mL: antibody concentration at Day 42 ≥ 4 fold the pre-vaccination antibody concentration. For initially seropositive subjects with pre-vaccination antibody concentration ≥ 8.184 IU/mL: antibody concentration at Day 42 ≥ 2 fold the pre-vaccination antibody concentration. Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	659	234		
Units: Subjects				
Anti-FHA	620	221		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody booster response to pertactin (PRN)

End point title	Number of subjects with antibody booster response to pertactin (PRN)[24]

End point description:

Booster response was defined as: For initially seronegative subjects, antibody concentration ≥ 8.748 IU/mL at Day 42. For initially seropositive subjects with pre-vaccination antibody concentration < 8.748 IU/mL: antibody concentration at Day 42 ≥ 4 fold the pre-vaccination antibody concentration. For initially seropositive subjects with pre-vaccination antibody concentration ≥ 8.748 IU/mL: antibody concentration at Day 42 ≥ 2 fold the pre-vaccination antibody concentration. Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	660	234		
Units: Subjects				
Anti-PRN	657	233		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of immunogenicity in terms of anti-D and anti-T antibody concentrations

End point title	Evaluation of immunogenicity in terms of anti-D and anti-T antibody concentrations[25]

End point description:

Antibody concentrations were expressed as GMCs in IU/mL. Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	684	243		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D	17.2 (16.2 to 18.1)	17.8 (16.1 to 19.6)		
Anti-T	7.4 (6.9 to 7.8)	8.4 (7.6 to 9.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of immunogenicity in terms of anti-PT, anti-FHA and anti-PRN antibody concentrations

End point title	Evaluation of immunogenicity in terms of anti-PT, anti-FHA and anti-PRN antibody concentrations[26]

End point description:

Antibody concentrations were expressed as GMCs in EU/mL. Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	684	243		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PT (N=684;243)	76.6 (71.6 to 82)	73.9 (66.2 to 82.4)		
Anti-FHA (N=684;243)	316.2 (299.4 to 334)	319.3 (293.1 to 347.9)		
Anti-PRN (N=682;243)	402.2 (370.4 to 436.8)	427.3 (377.6 to 483.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-D and anti-T antibody concentrations ≥ 0.1 IU/mL

End point title	Number of subjects with anti-D and anti-T antibody concentrations ≥ 0.1 IU/mL[27]

End point description:

Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	684	243		
Units: Subjects				
Anti-D	684	243		
Anti-T	684	243		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-D and anti-T antibody concentrations ≥ 1.0 IU/mL

End point title	Number of subjects with anti-D and anti-T antibody concentrations ≥ 1.0 IU/mL[28]

End point description:

Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	684	243		
Units: Subjects				
Anti-D	683	242		
Anti-T	678	243		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of immunogenicity in terms of anti-polio virus types 1, 2 and 3 antibody titers

End point title	Evaluation of immunogenicity in terms of anti-polio virus types 1, 2 and 3 antibody titers[29]

End point description:

Antibody titers were expressed as Geometric Mean Titers (GMTs) in ED50. Analysis was done in sub-cohort 1 only.

End point type	Secondary

End point timeframe:

42 days post vaccination (At Day 42)

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	669	238		
Units: ED50				
geometric mean (confidence interval 95%)				
Anti-Polio 1 (N=669;238)	1618.7 (1499.8 to 1747)	1587.3 (1387.3 to 1816.1)		
Anti-Polio 2 (N=653;233)	2026.4 (1881.2 to 2182.7)	2206.1 (1955.2 to 2489.3)		
Anti-Polio 3 (N=590;214)	2753.5 (2512.4 to 3017.6)	3040.6 (2613 to 3538.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with 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 and swelling = greater than 50 millimeters (m m) i.e . > 50mm.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	727	267	766	289
Units: Subjects				
Any Pain	295	109	152	64
Grade 3 Pain	22	4	6	2
Any Redness	157	69	146	53
Grade 3 Redness	9	4	0	0
Any Swelling	82	28	64	23
Grade 3 Swelling	3	3	0	0

End point values	Inv_MMR_S Group	Com_MMR_S Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1289	480		

Units: Subjects				
Any Pain	278	123		
Grade 3 Pain	5	2		
Any Redness	242	90		
Grade 3 Redness	0	0		
Any Swelling	108	42		
Grade 3 Swelling	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms[30]

End point description:

Assessed solicited general symptoms were drowsiness and loss of appetite. Any = occurrence of the symptom regardless of intensity grade. Grade 3 Drowsiness = Drowsiness that prevented normal activity, Grade 3 Loss of appetite = Not eating at all. Related = symptom assessed by the investigator as causally related to study vaccination. Analysis was done for sub-cohort 1 only.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point was aimed at assessing non-inferiority of Priorix vaccine to M-M-R II vaccine, when co-administered with Kinrix and ProQuad vaccines. This endpoint therefore presents the results for groups applicable for this analysis (i.e., Inv_MMR_CO and Com_MMR_CO Groups).

End point values	Inv_MMR_CO Group	Com_MMR_CO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	731	268		
Units: Subjects				
Any Drowsiness	199	72		
Grade 3 Drowsiness	10	3		
Related Drowsiness	180	63		
Any Loss of appetite	154	59		
Grade 3 Loss of appetite	2	2		
Related Loss of appetite	135	56		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting fever

End point title	Number of subjects reporting fever

End point description:

Any fever = fever ≥ 38°C. Grade 3 fever = fever > 39.5°C. Related = fever assessed by the investigator as causally related to study vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	731	268	767	291
Units: Subjects				
Any fever	177	67	146	58
Grade 3 fever	7	6	14	9
Related fever	100	32	27	11

End point values	Inv_MMR_S Group	Com_MMR_S Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1291	481		
Units: Subjects				
Any fever	257	96		
Grade 3 fever	21	8		
Related fever	52	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting MMR specific solicited general symptoms

End point title	Number of subjects reporting MMR specific solicited general symptoms

End point description:

Assessed MMR specific symptoms were parotid gland swelling and any suspected signs of meningism including febrile convulsions. Any = occurrence of any general symptoms regardless of their intensity grade or relationship to vaccination. Grade 3 Parotid/salivary gland swelling = Swelling accompanied with general symptoms. Grade 3 Sign of meningism (any suspected signs including febrile convulsions) = An event which prevented normal, everyday activities. Related = symptom assessed by the investigator as causally related to study vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	731	268	767	291
Units: Subjects				
Any Sign of meningism	0	2	1	0
Grade 3 Sign of meningism	0	0	0	0
Related Sign of meningism	0	2	0	0
Any Parotid gland swelling	0	0	0	1
Grade 3 Parotid gland swelling	0	0	0	0
Related Parotid gland swelling	0	0	0	1

End point values	Inv_MMR_S Group	Com_MMR_S Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1291	481		
Units: Subjects				
Any Sign of meningism	0	0		
Grade 3 Sign of meningism	0	0		
Related Sign of meningism	0	0		
Any Parotid gland swelling	1	1		
Grade 3 Parotid gland swelling	0	0		
Related Parotid gland swelling	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting investigator-confirmed rash

End point title	Number of subjects reporting investigator-confirmed rash

End point description:

Assessed any rash, varicella-like rash, measles/rubella-like rash, Grade 3, related. Any= occurrence of rash regardless of their intensity grade. Grade 3 measles/rubella/varicella-like rash = Rash with more than 150 lesions. Other Grade 3 Rash = Rash that prevented normal, everyday activities. Related= Rash assessed by the investigator as causally related to study vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	731	268	767	291
Units: Subjects				
Any localized or generalized	61	28	37	12
Any with fever	11	7	5	1
Any Varicella like	4	3	0	0
Any Measles/Rubella like	14	5	3	2
Any grade 3	3	0	1	0
Any related	25	11	2	2
Localized any	50	24	27	9
Localized administration site	9	2	1	0
Localized other site	41	22	26	9
Localized with fever	8	6	4	0
Localized Varicella like	2	2	0	0
Localized Measles/Rubella like	12	4	3	2
Localized Grade 3	2	0	1	0
Localized related	18	10	2	2
Generalized any	12	4	10	3
Generalized with fever	3	1	1	1
Generalized Varicella like	2	1	0	0
Generalized Measles/Rubella like	2	1	0	0
Generalized Grade 3	1	0	0	0
Generalized Related	7	1	0	0

End point values	Inv_MMR_S Group	Com_MMR_S Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1291	481		
Units: Subjects				
Any localized or generalized	56	23		
Any with fever	6	1		
Any Varicella like	0	0		
Any Measles/Rubella like	4	2		
Any grade 3	3	0		
Any related	8	3		
Localized any	42	19		
Localized administration site	8	0		
Localized other site	36	19		
Localized with fever	4	1		
Localized Varicella like	0	0		
Localized Measles/Rubella like	4	1		
Localized Grade 3	0	0		
Localized related	7	2		
Generalized any	15	4		
Generalized with fever	2	0		
Generalized Varicella like	0	0		
Generalized Measles/Rubella like	0	1		
Generalized Grade 3	3	0		

Generalized Related	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new onset chronic diseases (NOCDs)

End point title	Number of subjects with new onset chronic diseases (NOCDs)

End point description:

NOCDs include autoimmune disorders, asthma, type I diabetes, allergies.

End point type	Secondary

End point timeframe:

During the entire study period (from Day 0 up to Day 180)

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	802	298	796	303
Units: Subjects				
Any NOCD(s)	8	4	6	0

End point values	Inv_MMR_S Group	Com_MMR_S Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1319	489		
Units: Subjects				
Any NOCD(s)	11	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting adverse events resulting in Emergency Room (ER) visits

End point title	Number of subjects reporting adverse events resulting in Emergency Room (ER) visits

End point description:

The number of subjects reporting adverse events resulting in Emergency Room (ER) visits is reported.

End point type	Secondary

End point timeframe:

During the entire study period (from Day 0 up to Day 180)

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	802	298	796	303
Units: Subjects				
Any AE(s) with ER visits	61	29	64	22

End point values	Inv_MMR_S Group	Com_MMR_S Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1319	489		
Units: Subjects				
Any AE(s) with ER visits	102	36		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)

End point description:

An unsolicited 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 and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	802	298	796	303
Units: Subjects				
Any AE(s)	276	90	314	112

End point values	Inv_MMR_S Group	Com_MMR_S Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1319	489		
Units: Subjects				
Any AE(s)	508	186		

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 included medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity. Any SAE = occurrence of SAE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (from Day 0 up to Day 180)

End point values	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group	Com_MMR_I Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	802	298	796	303
Units: Subjects				
Any SAE(s)	4	0	14	1

End point values	Inv_MMR_S Group	Com_MMR_S Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1319	489		
Units: Subjects				
Any SAE(s)	25	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local symptoms: during the 4-day (Days 0-3) post-vaccination period; Solicited general symptoms and Unsolicited AEs: during the 43-day (Days 0-42) post-vaccination period; SAEs: during the entire study period (from Day 0 up to Day 180).

Adverse event reporting additional description:

Drowsiness and loss of appetite symptoms were collected during the 4-day (Days 0-3) post-vaccination period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Inv_MMR_CO Group

Reporting group description:

Subjects received one dose of the study vaccine Priorix along with Kinrix and ProQuad vaccines at Visit 1 (Day 0).

Reporting group title	Com_MMR_CO Group

Reporting group description:

Subjects received one dose of the licensed vaccine M-M-R II (also known as M-M-R Vax Pro) Lot 1 or Lot 2 along with Kinrix and ProQuad vaccines at Visit 1 (Day 0).

Reporting group title	Inv_MMR_I Group

Reporting group description:

Subjects received one dose of Priorix at Visit 1 (Day 0).

Reporting group title	Com_MMR_I Group

Reporting group description:

Subjects received one dose of M-M-R II (also known as M-M-R Vax Pro) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).

Reporting group title	Inv_MMR_S Group

Reporting group description:

Subjects in this safety cohort received one dose of Priorix at Visit 1 (Day 0).

Reporting group title	Com_MMR_S Group

Reporting group description:

Subjects in this safety cohort received one dose of M-M-R II (also known as M-M-R Vax Pro) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).

Serious adverse events	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 802 (0.50%)	0 / 298 (0.00%)	14 / 796 (1.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Accidental exposure to product			

subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
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 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 802 (0.12%)	0 / 298 (0.00%)	0 / 796 (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
Abdominal pain			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cyclic vomiting syndrome			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	2 / 802 (0.25%)	0 / 298 (0.00%)	4 / 796 (0.50%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchial hyperreactivity			
subjects affected / exposed	1 / 802 (0.12%)	0 / 298 (0.00%)	0 / 796 (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
Sleep apnoea syndrome			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status asthmaticus			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema vesicular			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash generalised			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenovirus infection			

subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	1 / 802 (0.12%)	0 / 298 (0.00%)	0 / 796 (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
Bronchitis			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	2 / 796 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpangina			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			

subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	2 / 796 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	0 / 796 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
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 upper respiratory tract infection			

subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
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			
Dehydration			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 802 (0.00%)	0 / 298 (0.00%)	1 / 796 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Com_MMR_I Group	Inv_MMR_S Group	Com_MMR_S Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 303 (0.33%)	25 / 1319 (1.90%)	9 / 489 (1.84%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	1 / 489 (0.20%)
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			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Road traffic accident			

subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	1 / 489 (0.20%)
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			
Abdominal discomfort			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Cyclic vomiting syndrome			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Gastritis			
subjects affected / exposed	0 / 303 (0.00%)	2 / 1319 (0.15%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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

Inguinal hernia			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	1 / 489 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	0 / 303 (0.00%)	2 / 1319 (0.15%)	0 / 489 (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
Asthma			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	2 / 489 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Status asthmaticus			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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

Tonsillar hypertrophy			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema vesicular			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Rash generalised			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	1 / 489 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	1 / 489 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Gastroenteritis			
subjects affected / exposed	0 / 303 (0.00%)	5 / 1319 (0.38%)	1 / 489 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Herpangina			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	3 / 489 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 303 (0.00%)	2 / 1319 (0.15%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 303 (0.00%)	2 / 1319 (0.15%)	0 / 489 (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			
subjects affected / exposed	1 / 303 (0.33%)	0 / 1319 (0.00%)	3 / 489 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			

subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Pyelonephritis			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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
Tonsillitis			
subjects affected / exposed	0 / 303 (0.00%)	2 / 1319 (0.15%)	1 / 489 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 303 (0.00%)	2 / 1319 (0.15%)	0 / 489 (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
Viral infection			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 303 (0.00%)	2 / 1319 (0.15%)	0 / 489 (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
Hypovolaemia			
subjects affected / exposed	0 / 303 (0.00%)	1 / 1319 (0.08%)	0 / 489 (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	Inv_MMR_CO Group	Com_MMR_CO Group	Inv_MMR_I Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	544 / 802 (67.83%)	198 / 298 (66.44%)	410 / 796 (51.51%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	199 / 802 (24.81%)	73 / 298 (24.50%)	1 / 796 (0.13%)
occurrences (all)	199	73	1
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	170 / 802 (21.20%)	73 / 298 (24.50%)	147 / 796 (18.47%)
occurrences (all)	173	75	147
Injection site pain			
subjects affected / exposed	309 / 802 (38.53%)	118 / 298 (39.60%)	153 / 796 (19.22%)
occurrences (all)	321	125	153
Injection site swelling			
subjects affected / exposed	97 / 802 (12.09%)	31 / 298 (10.40%)	64 / 796 (8.04%)
occurrences (all)	97	32	64
Pyrexia			
subjects affected / exposed	177 / 802 (22.07%)	67 / 298 (22.48%)	146 / 796 (18.34%)
occurrences (all)	177	67	146
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	38 / 802 (4.74%)	16 / 298 (5.37%)	37 / 796 (4.65%)
occurrences (all)	41	17	41
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	61 / 802 (7.61%)	28 / 298 (9.40%)	37 / 796 (4.65%)
occurrences (all)	61	28	37
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	25 / 802 (3.12%)	3 / 298 (1.01%)	77 / 796 (9.67%)
occurrences (all)	27	3	100
Upper respiratory tract infection			

subjects affected / exposed	27 / 802 (3.37%)	11 / 298 (3.69%)	55 / 796 (6.91%)
occurrences (all)	28	11	66
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	156 / 802 (19.45%)	61 / 298 (20.47%)	2 / 796 (0.25%)
occurrences (all)	159	61	2

Non-serious adverse events	Com_MMR_I Group	Inv_MMR_S Group	Com_MMR_S Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	156 / 303 (51.49%)	702 / 1319 (53.22%)	279 / 489 (57.06%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 303 (0.00%)	0 / 1319 (0.00%)	0 / 489 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	53 / 303 (17.49%)	242 / 1319 (18.35%)	90 / 489 (18.40%)
occurrences (all)	53	242	90
Injection site pain			
subjects affected / exposed	64 / 303 (21.12%)	278 / 1319 (21.08%)	123 / 489 (25.15%)
occurrences (all)	64	278	123
Injection site swelling			
subjects affected / exposed	23 / 303 (7.59%)	108 / 1319 (8.19%)	42 / 489 (8.59%)
occurrences (all)	23	108	42
Pyrexia			
subjects affected / exposed	58 / 303 (19.14%)	257 / 1319 (19.48%)	96 / 489 (19.63%)
occurrences (all)	58	257	96
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 303 (2.64%)	47 / 1319 (3.56%)	21 / 489 (4.29%)
occurrences (all)	8	50	22
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	12 / 303 (3.96%)	56 / 1319 (4.25%)	23 / 489 (4.70%)
occurrences (all)	12	56	23
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	28 / 303 (9.24%)	112 / 1319 (8.49%)	45 / 489 (9.20%)
occurrences (all)	32	143	57
Upper respiratory tract infection			
subjects affected / exposed	27 / 303 (8.91%)	92 / 1319 (6.97%)	21 / 489 (4.29%)
occurrences (all)	35	107	22
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 303 (0.33%)	3 / 1319 (0.23%)	0 / 489 (0.00%)
occurrences (all)	1	3	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported