



Clinical trial results:

A phase IIIA, randomized, observer-blind, controlled, multinational consistency study to evaluate the immunogenicity and safety of GSK Biologicals' MMR vaccine (209762) (Priorix®) compared to Merck & Co., Inc.'s MMR vaccine (M-M-R®II), as a first dose, both co-administered with Varivax, Havrix and Prevnar 13 (subset of children) to healthy children 12 to 15 months of age.

Summary

EudraCT number	2011-004891-12
Trial protocol	EE FI ES
Global end of trial date	16 April 2015

Results information

Result version number	v1
This version publication date	30 July 2016
First version publication date	30 July 2016

Trial information

Trial identification

Sponsor protocol code	115648
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01702428
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	Interim
Date of interim/final analysis	18 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 November 2014
Global end of trial reached?	Yes
Global end of trial date	16 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the consistency of three manufacturing lots of Inv_MMR vaccine in terms of seroresponse rates to measles, mumps and rubella viruses at Day 42.
- To demonstrate the consistency of three manufacturing lots of Inv_MMR vaccine in terms of geometric mean concentrations (GMCs) for antibodies to measles, mumps and rubella viruses at Day 42.
- To demonstrate the non-inferiority of Inv_MMR (for the three pooled lots) compared to Com_MMR (for the two pooled lots) vaccine in terms of seroresponse rates for measles, mumps and rubella viruses at Day 42.
- To demonstrate non-inferiority of Inv_MMR (for the three pooled lots) compared to Com_MMR (for the two pooled lots) vaccine in terms of GMCs for antibodies to measles, mumps and rubella viruses at Day 42.
- To demonstrate an acceptable immune response for Inv_MMR in terms of seroresponse rates for measles, mumps and rubella viruses at Day 42.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 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	Spain: 256
Country: Number of subjects enrolled	Estonia: 501
Country: Number of subjects enrolled	Finland: 1350
Country: Number of subjects enrolled	Mexico: 394
Country: Number of subjects enrolled	United States: 2515
Worldwide total number of subjects	5016
EEA total number of subjects	2107

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	5016
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:

13 subjects from 5016 were allocated subject number but no study vaccine was administered. Therefore, the number of subjects started is 5003.

Pre-assignment

Screening details:

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.

Period 1

Period 1 title	Day-42 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	No
Arm title	INV_MMR _Lot1 Group

Arm description:

Subjects received 1 dose of INV_MMR lot 1 vaccine (i.e., MMR_MMR_L1) co administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13.

The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Arm type	Experimental
Investigational medicinal product name	Priorix
Investigational medicinal product code	
Other name	GSK Biologicals measles, mumps and rubella vaccine live (GSK 209762)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 1 dose of MMR vaccine which was administered subcutaneously in the triceps region of the left arm.

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

Dosage and administration details:

Subjects received 1 dose of varicella vaccine which was administered subcutaneously in the triceps region of the right arm.

Investigational medicinal product name	Havrix 720 Junior
Investigational medicinal product code	
Other name	HEPATITIS A VIRUS HM175 STRAIN (INACTIVATED)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 1 dose of HAV vaccine which was administered intramuscularly in the anterolateral region of the right thigh.

Investigational medicinal product name	Pprevnar 13
Investigational medicinal product code	
Other name	PCV 13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

US subjects received 1 dose of PCV vaccine which was administered intramuscularly in the anterolateral region of the left thigh.

Arm title	INV_MMR _Lot2 Group
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Arm description:

Subjects received 1 dose of INV_MMR lot 2 vaccine (i.e., MMR_MMR_L2) co administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Pprevnar 13.

The MMR vaccine was administered subcutaneously in the in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Arm type	Experimental
Investigational medicinal product name	Priorix
Investigational medicinal product code	
Other name	GSK Biologicals measles, mumps and rubella vaccine live (GSK 209762)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 1 dose of MMR vaccine which was administered subcutaneously in the triceps region of the left arm.

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

Dosage and administration details:

Subjects received 1 dose of varicella vaccine which was administered subcutaneously in the triceps region of the right arm.

Investigational medicinal product name	Havrix 720 Junior
Investigational medicinal product code	
Other name	HEPATITIS A VIRUS HM175 STRAIN (INACTIVATED)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 1 dose of HAV vaccine which was administered intramuscularly in the anterolateral region of the right thigh.

Investigational medicinal product name	Pprevnar 13
Investigational medicinal product code	
Other name	PCV 13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

US subjects received 1 dose of PCV vaccine which was administered intramuscularly in the anterolateral region of the left thigh.

Arm title	INV_MMR _Lot3 Group
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Arm description:

Subjects received 1 dose of INV_MMR lot 3 vaccine (i.e., MMR_MMR_L3) co-administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Pprevnar 13.

The MMR vaccine was administered subcutaneously in the in the triceps region of the left arm while the

VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Arm type	Experimental
Investigational medicinal product name	Priorix
Investigational medicinal product code	
Other name	GSK Biologicals measles, mumps and rubella vaccine live (GSK 209762)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 1 dose of MMR vaccine which was administered subcutaneously in the triceps region of the left arm.

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

Dosage and administration details:

Subjects received 1 dose of varicella vaccine which was administered subcutaneously in the triceps region of the right arm.

Investigational medicinal product name	Havrix 720 Junior
Investigational medicinal product code	
Other name	HEPATITIS A VIRUS HM175 STRAIN (INACTIVATED)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 1 dose of HAV vaccine which was administered intramuscularly in the anterolateral region of the right thigh.

Investigational medicinal product name	Prevnar 13
Investigational medicinal product code	
Other name	PCV 13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

US subjects received 1 dose of PCV vaccine which was administered intramuscularly in the anterolateral region of the left thigh.

Arm title	INV_MMR Group
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Arm description:

This group included subjects from INV_MMR _L1, INV_MMR _L2 and INV_MMR _L3 groups for whom pooled analysis was conducted in addition to lot-to-lot consistency.

Arm type	Experimental
Investigational medicinal product name	Priorix
Investigational medicinal product code	
Other name	GSK Biologicals measles, mumps and rubella vaccine live (GSK 209762)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 1 dose of MMR vaccine which was administered subcutaneously in the triceps region of the left arm.

Arm title	COM_MMR Group
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Arm description:

Subjects in this group received one dose of COM_MMR from Lot 1 and Lot 2 for whom pooled analysis was conducted.

Arm type	Active comparator
Investigational medicinal product name	M-M-R VaxPro
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 1 dose of MMR vaccine which was administered subcutaneously in the triceps region of the left arm.

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

Dosage and administration details:

Subjects received 1 dose of varicella vaccine which was administered subcutaneously in the triceps region of the right arm.

Investigational medicinal product name	Havrix 720 Junior
Investigational medicinal product code	
Other name	HEPATITIS A VIRUS HM175 STRAIN (INACTIVATED)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 1 dose of HAV vaccine which was administered intramuscularly in the anterolateral region of the right thigh.

Investigational medicinal product name	Pevnar 13
Investigational medicinal product code	
Other name	PCV 13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

US subjects received 1 dose of PCV vaccine which was administered intramuscularly in the anterolateral region of the left thigh.

Number of subjects in period 1	INV_MMR_Lot1 Group	INV_MMR_Lot2 Group	INV_MMR_Lot3 Group
Started	1239	1232	1243
Completed	1199	1192	1211
Not completed	40	40	32
Consent withdrawn by subject	19	19	13
Adverse event, non-fatal	2	-	-
Migrated/moved from study area	4	1	3
Lost to follow-up	13	20	16
Protocol deviation	2	-	-

Number of subjects in period 1	INV_MMR Group	COM_MMR Group
Started	3714	1289

Completed	3602	1258
Not completed	112	31
Consent withdrawn by subject	51	8
Adverse event, non-fatal	2	-
Migrated/moved from study area	-	2
Lost to follow-up	57	21
Protocol deviation	2	-

Baseline characteristics

Reporting groups^[1]

Reporting group title	INV_MMR_Lot1 Group
Reporting group description:	
Subjects received 1 dose of INV_MMR lot 1 vaccine (i.e., MMR_MMR_L1) co administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.	
Reporting group title	INV_MMR_Lot2 Group
Reporting group description:	
Subjects received 1 dose of INV_MMR lot 2 vaccine (i.e., MMR_MMR_L2) co administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13. The MMR vaccine was administered subcutaneously in the in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.	
Reporting group title	INV_MMR_Lot3 Group
Reporting group description:	
Subjects received 1 dose of INV_MMR lot 3 vaccine (i.e., MMR_MMR_L3) co-administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13. The MMR vaccine was administered subcutaneously in the in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.	
Reporting group title	INV_MMR Group
Reporting group description:	
This group included subjects from INV_MMR_L1, INV_MMR_L2 and INV_MMR_L3 groups for whom pooled analysis was conducted in addition to lot-to-lot consistency.	
Reporting group title	COM_MMR Group
Reporting group description:	
Subjects in this group received one dose of COM_MMR from Lot 1 and Lot 2 for whom pooled analysis was conducted.	

Notes:

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

Justification: 13 subjects from 5016 were allocated subject number but no study vaccine was administered. Therefore, the number of subjects started is 5003.

Reporting group values	INV_MMR_Lot1 Group	INV_MMR_Lot2 Group	INV_MMR_Lot3 Group
Number of subjects	1239	1232	1243
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age continuous Units: months arithmetic mean standard deviation	12.3 ± 0.7	12.3 ± 0.7	12.3 ± 0.7
Gender categorical Units: Subjects			
Female	607	594	615
Male	632	638	628

Reporting group values	INV_MMR Group	COM_MMR Group	Total
Number of subjects	3714	1289	5003
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: months arithmetic mean standard deviation	12.3 ± 0.7	12.3 ± 0.7	-
Gender categorical Units: Subjects			
Female	1816	618	2434
Male	1898	671	2569

End points

End points reporting groups

Reporting group title	INV_MMR_Lot1 Group
Reporting group description: Subjects received 1 dose of INV_MMR lot 1 vaccine (i.e., MMR_MMR_L1) co administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.	
Reporting group title	INV_MMR_Lot2 Group
Reporting group description: Subjects received 1 dose of INV_MMR lot 2 vaccine (i.e., MMR_MMR_L2) co administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13. The MMR vaccine was administered subcutaneously in the in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.	
Reporting group title	INV_MMR_Lot3 Group
Reporting group description: Subjects received 1 dose of INV_MMR lot 3 vaccine (i.e., MMR_MMR_L3) co-administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13. The MMR vaccine was administered subcutaneously in the in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.	
Reporting group title	INV_MMR Group
Reporting group description: This group included subjects from INV_MMR_L1, INV_MMR_L2 and INV_MMR_L3 groups for whom pooled analysis was conducted in addition to lot-to-lot consistency.	
Reporting group title	COM_MMR Group
Reporting group description: Subjects in this group received one dose of COM_MMR from Lot 1 and Lot 2 for whom pooled analysis was conducted.	

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 ≥ 200 milli International Unit/Milliliter (mIU/mL) among children who were seronegative (antibody concentration < 150 mIU/mL) before vaccination.	
End point type	Primary
End point timeframe: 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.	

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1083	1069	1096	
Units: Subjects				
Anti-measles \geq 150 mIU/mL	1064	1057	1075	
Anti-measles \geq 200 mIU/mL	1062	1054	1072	

Statistical analyses

Statistical analysis title	Serostatus for Anti-Measles antibodies
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2152
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	0.58

Statistical analysis title	Serostatus for Anti-Measles antibodies
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	1.5

Statistical analysis title	Serostatus for Anti-measles antibodies
Comparison groups	INV_MMR _Lot2 Group v INV_MMR _Lot3 Group

Number of subjects included in analysis	2165
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	1.98

Primary: Anti-measles Virus Antibody Concentrations

End point title	Anti-measles Virus Antibody Concentrations ^[2]
End point description:	Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL.
End point type	Primary
End point timeframe:	At Day 42

Notes:

[2] - 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1083	1069	1096	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Measles antibody concentration	2970.3 (2813.2 to 3136.2)	3023.6 (2864.5 to 3191.6)	3058.3 (2893.9 to 3232)	

Statistical analyses

Statistical analysis title	GMC ratio for Anti-measles antibodies
Statistical analysis description:	
Ratio order:	INV_MMR _Lot1 / INV_MMR _ Lot2
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2152
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.06

Statistical analysis title	GMC ratio for Anti-measles antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot1 / Inv_ MMR_ Lot3	
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.05

Statistical analysis title	GMC ratio for Anti-measles antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot2 / INV_MMR _ Lot1	
Comparison groups	INV_MMR _Lot2 Group v INV_MMR _Lot1 Group
Number of subjects included in analysis	2152
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.09

Statistical analysis title	GMC ratio for Anti-measles antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot2 / INV_MMR _ Lot3	
Comparison groups	INV_MMR _Lot2 Group v INV_MMR _Lot3 Group

Number of subjects included in analysis	2165
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.06

Statistical analysis title	GMC ratio for Anti-measles antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot3 / INV_MMR _ Lot1	
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.11

Statistical analysis title	GMC ratio for Anti-measles antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot3 / INV_MMR _ Lot2	
Comparison groups	INV_MMR _Lot2 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2165
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.09

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

End point description:

Seroresponse was defined as post-vaccination anti-mumps virus antibody concentration ≥ 10 EL.U/mL among children who were seronegative (antibody concentrations < 5 EL.U/mL before vaccination).

End point type

Primary

End point timeframe:

At Day 42

Notes:

[3] - 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1062	1047	1078	
Units: Subjects				
Anti-mumps ≥ 5 EL.U/mL	1059	1040	1069	
Anti-mumps ≥ 10 EL.U/mL	1047	1032	1056	

Statistical analyses

Statistical analysis title	Serostatus for Anti-mumps antibodies
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2109
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	1.09

Statistical analysis title	Serostatus for Anti-mumps antibodies
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2140
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	0.63

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.81

Statistical analysis title	Serostatus for Anti-mumps antibodies
Comparison groups	INV_MMR _Lot2 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	1.79

Primary: Anti-mumps virus antibody concentration

End point title	Anti-mumps virus antibody concentration ^[4]
End point description:	
Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL.	
End point type	Primary
End point timeframe:	
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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1062	1047	1078	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Mumps antibody concentration	71.7 (68.3 to 75.2)	76.9 (73.2 to 80.8)	69 (65.5 to 72.7)	

Statistical analyses

Statistical analysis title	GMC ratio for Anti-mumps antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot1 /MMR_Lot2	
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2109
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1

Statistical analysis title	GMC ratio for Anti-mumps antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot1 /MMR_ Lot3	
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2140
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.11

Statistical analysis title	GMC ratio for Anti-mumps antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot2 /MMR_ Lot1	
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2109
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.15

Statistical analysis title	GMC ratio for Anti-mumps antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot2 /MMR_ Lot3	
Comparison groups	INV_MMR _Lot2 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.19

Statistical analysis title	GMC ratio for Anti-mumps antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot3 /MMR_ Lot1	
Comparison groups	INV_MMR _Lot3 Group v INV_MMR _Lot1 Group
Number of subjects included in analysis	2140
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.03

Statistical analysis title	GMC ratio for Anti-mumps antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot3 /MMR_ Lot2	
Comparison groups	INV_MMR _Lot3 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	0.96

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 ^[5]
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End point description:

Seroresponse was defined as post-vaccination anti-rubella virus antibody concentration ≥ 10 IU/mL among children who were seronegative (antibody concentrations < 4 IU/mL) before vaccination.

End point type	Primary
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End point timeframe:

At Day 42

Notes:

[5] - 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1083	1067	1095	
Units: Subjects				
Anti-rubella ≥ 4 IU/mL	1077	1064	1088	
Anti-rubella ≥ 10 IU/mL	1053	1036	1070	

Statistical analyses

Statistical analysis title	Serostatus for Anti-rubella antibodies
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2150
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.58

Statistical analysis title	Serostatus for Anti-rubella antibodies
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2178
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.86
upper limit	0.86

Statistical analysis title	Serostatus for Anti-rubella antibodies
Comparison groups	INV_MMR _Lot3 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2162
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.02
upper limit	0.74

Primary: Anti-rubella virus antibody concentration

End point title	Anti-rubella virus antibody concentration ^[6]
End point description:	
Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL.	
End point type	Primary
End point timeframe:	
At Day 42	

Notes:

[6] - 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1083	1067	1095	
Units: Titers				
geometric mean (confidence interval 95%)				

Anti-Rubella antibody concentration	57.2 (54.4 to 60.1)	53.1 (50.5 to 55.7)	57 (54.3 to 59.8)	
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Statistical analyses

Statistical analysis title	GMC ratio for Anti-rubella antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot1 / INV_MMR _ Lot2	
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2150
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.15

Statistical analysis title	GMC ratio for Anti-rubella antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot1 / INV_MMR _ Lot3	
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2178
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.07

Statistical analysis title	GMC ratio for Anti-rubella antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot2 / INV_MMR _ Lot1	
Comparison groups	INV_MMR _Lot1 Group v INV_MMR _Lot2 Group

Number of subjects included in analysis	2150
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	0.99

Statistical analysis title	GMC ratio for Anti-rubella antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot2 / INV_MMR _ Lot3	
Comparison groups	INV_MMR _Lot2 Group v INV_MMR _Lot3 Group
Number of subjects included in analysis	2162
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	0.99

Statistical analysis title	GMC ratio for Anti-rubella antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot3 / INV_MMR _ Lot1	
Comparison groups	INV_MMR _Lot3 Group v INV_MMR _Lot1 Group
Number of subjects included in analysis	2178
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.07

Statistical analysis title	GMC ratio for Anti-rubella antibodies
Statistical analysis description:	
Ratio order: INV_MMR _ Lot3 / INV_MMR _ Lot2	

Comparison groups	INV_MMR _Lot3 Group v INV_MMR _Lot2 Group
Number of subjects included in analysis	2162
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.15

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

End point title	Number of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value in pooled MMR groups ^[7]
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End point description:

Seroresponse was defined as post-vaccination anti-measles virus antibody concentration \geq 200 milli International Unit/Milliliter (mIU/mL) among children who were seronegative (antibody concentration $<$ 150 mIU/mL) before vaccination.

End point type	Primary
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End point timeframe:

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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3248	1137		
Units: Subjects				
Anti-measles \geq 150 mIU/mL	3196	1115		
Anti-measles \geq 200 mIU/mL	3188	1114		

Statistical analyses

Statistical analysis title	Serostatus for Anti-measles antibodies
Comparison groups	INV_MMR Group v COM_MMR Group

Number of subjects included in analysis	4385
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	1.25

Primary: Anti-measles Virus Antibody Concentrations in pooled MMR groups

End point title	Anti-measles Virus Antibody Concentrations in pooled MMR groups ^[8]
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End point description:

Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL.

End point type	Primary
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End point timeframe:

At Day 42

Notes:

[8] - 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3248	1137		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Measles antibody concentration	3017.4 (2923.9 to 3113.8)	3074.4 (2911 to 3246.9)		

Statistical analyses

Statistical analysis title	GMC ratio for Anti-measles antibodies
Comparison groups	INV_MMR Group v COM_MMR Group
Number of subjects included in analysis	4385
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.98

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.05

Primary: Number of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value in pooled MMR groups

End point title	Number of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value in pooled MMR groups ^[9]
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End point description:

Seroresponse was defined as post-vaccination anti-mumps virus antibody concentration ≥ 10 EL.U/mL among children who were seronegative (antibody concentrations < 5 EL.U/mL).

End point type	Primary
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End point timeframe:

At Day 42

Notes:

[9] - 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3187	1107		
Units: Subjects				
Anti-mumps ≥ 5 EL.U/mL	3168	1099		
Anti-mumps ≥ 10 EL.U/mL	3135	1080		

Statistical analyses

Statistical analysis title	Serostatus for Anti-mumps antibodies
Comparison groups	INV_MMR Group v COM_MMR Group
Number of subjects included in analysis	4294
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	1.96

Primary: Anti-mumps virus antibody concentration in pooled MMR groups

End point title	Anti-mumps virus antibody concentration in pooled MMR groups ^[10]
End point description: Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL.	
End point type	Primary
End point timeframe: 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3187	1107		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Mumps antibody concentration	72.4 (70.4 to 74.5)	69.1 (65.7 to 72.7)		

Statistical analyses

Statistical analysis title	GMC ratio for Anti-mumps antibodies
Comparison groups	INV_MMR Group v COM_MMR Group
Number of subjects included in analysis	4294
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.11

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

End point title	Number of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value in pooled MMR groups ^[11]
End point description: Seroreponse was defined as post-vaccination anti-rubella virus antibody concentration ≥ 10 IU/mL among children who were seronegative (antibody concentrations < 4 IU/mL) before vaccination.	
End point type	Primary

End point timeframe:

At Day 42

Notes:

[11] - 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3245	1135		
Units: Subjects				
Anti-rubella ≥ 4 IU/mL	3229	1130		
Anti-rubella ≥ 10 IU/mL	3159	1118		

Statistical analyses

Statistical analysis title	Serostatus for Anti-rubella antibodies
Comparison groups	INV_MMR Group v COM_MMR Group
Number of subjects included in analysis	4380
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in seroresponse rate
Point estimate	-1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-0.15

Primary: Anti-rubella virus antibody concentration in pooled MMR groups

End point title	Anti-rubella virus antibody concentration in pooled MMR
End point description:	
Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL.	
End point type	Primary
End point timeframe:	
At Day 42	

Notes:

[12] - 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 results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3245	1135		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Rubella antibody concentration	55.7 (54.2 to 57.3)	64 (61.1 to 67)		

Statistical analyses

Statistical analysis title	GMC ratio for Anti-rubella antibodies
Comparison groups	INV_MMR Group v COM_MMR Group
Number of subjects included in analysis	4380
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted GMC ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	0.92

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.
End point type	Secondary
End point timeframe:	During the 4-day (Days 0-3) post-vaccination period

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	INV_MMR Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1186	1175	1194	3555
Units: Subjects				
Any Pain	331	315	273	919
Grade 3 Pain	6	9	9	24
Any Redness	296	273	301	870
Grade 3 Redness	6	2	6	14
Any Swelling	116	99	103	318
Grade 3 Swelling	1	5	6	12

End point values	COM_MMR Group			
Subject group type	Reporting group			
Number of subjects analysed	1242			
Units: Subjects				
Any Pain	349			
Grade 3 Pain	12			
Any Redness	313			
Grade 3 Redness	8			
Any Swelling	133			
Grade 3 Swelling	5			

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
End point description:	
Assessed solicited general symptoms were drowsiness, irritability and loss of appetite. Any = occurrence of the symptom regardless of intensity grade. Grade 3 Drowsiness = drowsiness that prevented normal activity. Grade 3 Irritability/Fussiness = crying that could not be comforted/ prevented normal activity. Grade 3 Loss of appetite = did not eat at all.	
End point type	Secondary
End point timeframe:	
During the 15-day (Days 0-14) post-vaccination period	

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	INV_MMR Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1190	1176	1200	3566
Units: Subjects				
Any Drowsiness	533	535	533	1601
Grade 3 Drowsiness	23	39	23	85
Any Irritability / fussiness	764	729	765	2258
Grade 3 Irritability / fussiness	56	63	57	176
Any Loss of appetite	546	536	526	1608
Grade 3 Loss of appetite	24	29	19	72

End point values	COM_MMR Group			
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Subject group type	Reporting group			
Number of subjects analysed	1243			
Units: Subjects				
Any Drowsiness	586			
Grade 3 Drowsiness	22			
Any Irritability / fussiness	819			
Grade 3 Irritability / fussiness	58			
Any Loss of appetite	548			
Grade 3 Loss of appetite	31			

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:	
Fever was assessed for temperature $\geq 38^{\circ}\text{C}/100.4^{\circ}\text{F}$ and $> 39.5^{\circ}\text{C}/103.1^{\circ}\text{F}$ as measured rectally.	
End point type	Secondary
End point timeframe:	
During the 43 days (Days 0-42) post-vaccination period	

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	INV_MMR Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1190	1176	1200	3566
Units: Subjects				
Any Fever	404	422	418	1244
Grade 3 Fever	36	37	32	105

End point values	COM_MMR Group			
Subject group type	Reporting group			
Number of subjects analysed	1243			
Units: Subjects				
Any Fever	412			
Grade 3 Fever	32			

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
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End point description:

Assessed MMR specific symptoms were rash, parotid gland swelling, and any suspected signs of meningism including febrile convulsions. Any = occurrence of the symptom regardless of intensity grade. Grade 3 Parotid/salivary gland swelling = Swelling accompanied with general symptoms. Grade 3 Febrile convulsion = Prevented normal, everyday activities. Related = symptom assessed by the investigator as causally related to study vaccination.

End point type	Secondary
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End point timeframe:

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

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	INV_MMR Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1190	1176	1200	3566
Units: Subjects				
Any Febrile convulsion	4	1	5	10
Grade 3 Febrile convulsion	2	0	2	4
Related Febrile convulsion	1	1	2	4
Any Parotid/ salivary gland swelling	0	0	0	0
Grade 3 Parotid/ salivary gland swelling	0	0	0	0
Related Parotid/ salivary gland swelling	0	0	0	0

End point values	COM_MMR Group			
Subject group type	Reporting group			
Number of subjects analysed	1243			
Units: Subjects				
Any Febrile convulsion	3			
Grade 3 Febrile convulsion	0			
Related Febrile convulsion	2			
Any Parotid/ salivary gland swelling	0			
Grade 3 Parotid/ salivary gland swelling	0			
Related Parotid/ salivary gland swelling	0			

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
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End point description:

Assessed any rash, measles/rubella-like rash and varicella-like rash. Grade 3 Measles/rubella/varicella-like rash = rash with more than 150 lesions. Other Grade 3 Rash = rash that prevented normal,

everyday activities.

End point type	Secondary
End point timeframe:	
During the 43 days (Days 0-42) post-vaccination period	

End point values	INV_MMR _Lot1 Group	INV_MMR _Lot2 Group	INV_MMR _Lot3 Group	INV_MMR Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1190	1176	1200	3566
Units: Subjects				
Any Localized or generalized	352	331	360	1043
Any With fever	106	123	118	347
Any Varicella like	87	78	85	250
Any Measles/ Rubella like	71	88	76	235
Any Grade 3	33	37	36	106
Localized Any	230	224	251	705
Localized Administration site	10	16	12	38
Localized Other site	225	213	242	680
Localized With fever	48	67	67	182
Localized Varicella like	68	57	55	180
Localized Measles/ Rubella like	25	34	34	93
Localized Grade 3	6	10	9	25
Generalized Any	143	138	133	414
Generalized With fever	66	65	55	186
Generalized Varicella like	20	23	31	74
Generalized Measles/ Rubella like	47	55	44	146
Generalized Grade 3	29	27	27	83

End point values	COM_MMR Group			
Subject group type	Reporting group			
Number of subjects analysed	1243			
Units: Subjects				
Any Localized or generalized	378			
Any With fever	104			
Any Varicella like	85			
Any Measles/ Rubella like	77			
Any Grade 3	25			
Localized Any	266			
Localized Administration site	16			
Localized Other site	252			
Localized With fever	54			
Localized Varicella like	61			
Localized Measles/ Rubella like	35			
Localized Grade 3	5			
Generalized Any	143			
Generalized With fever	55			

Generalized Varicella like	25			
Generalized Measles/ Rubella like	42			
Generalized Grade 3	20			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events: From Day 0 through the end of study (Day-42); Solicited local and general symptoms: During the 4-day (Days 0-3) and 15 days (Day 0-14) post-vaccination period; Unsolicited adverse events: During the 43-days post-vaccination period.

Adverse event reporting additional description:

The analysis of the solicited symptoms was based on the Total Vaccinated cohort which included only children/doses with documented safety data (i.e., symptom screen/sheet completed).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	INV_MMR_Lot1 Group
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Reporting group description:

Subjects received 1 dose of INV_MMR lot 1 vaccine (i.e., MMR_MMR_L1) co administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13.

The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Reporting group title	INV_MMR_Lot2 Group
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Reporting group description:

Subjects received 1 dose of INV_MMR lot 2 vaccine (i.e., MMR_MMR_L2) co administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13.

The MMR vaccine was administered subcutaneously in the in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Reporting group title	INV_MMR_Lot3 Group
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Reporting group description:

Subjects received 1 dose of INV_MMR lot 3 vaccine (i.e., MMR_MMR_L3) co-administered with Varivax and Havrix vaccines at Visit 1 (Day 0). All US subjects were also given Prevnar 13.

The MMR vaccine was administered subcutaneously in the in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV 13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Reporting group title	INV_MMR Group
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Reporting group description:

This group included subjects from INV_MMR_L1, INV_MMR_L2 and INV_MMR_L3 groups for whom pooled analysis was conducted in addition to lot-to-lot consistency.

Reporting group title	COM_MMR Group
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Reporting group description:

Subjects in this group received one dose of COM_MMR from Lot 1 and Lot 2 for whom pooled analysis was conducted.

Serious adverse events	INV_MMR_Lot1 Group	INV_MMR_Lot2 Group	INV_MMR_Lot3 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1190 (0.00%)	0 / 1176 (0.00%)	0 / 1200 (0.00%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events	0	0	0
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Serious adverse events	INV_MMR Group	COM_MMR Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3566 (0.00%)	0 / 1243 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	INV_MMR_Lot1 Group	INV_MMR_Lot2 Group	INV_MMR_Lot3 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	764 / 1190 (64.20%)	729 / 1176 (61.99%)	765 / 1200 (63.75%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed ^[1]	331 / 1186 (27.91%)	315 / 1175 (26.81%)	273 / 1194 (22.86%)
occurrences (all)	331	315	273
Redness			
subjects affected / exposed ^[2]	296 / 1186 (24.96%)	273 / 1175 (23.23%)	301 / 1194 (25.21%)
occurrences (all)	296	273	301
Swelling			
subjects affected / exposed ^[3]	116 / 1186 (9.78%)	99 / 1175 (8.43%)	103 / 1194 (8.63%)
occurrences (all)	116	99	103
Drowsiness			
subjects affected / exposed	533 / 1190 (44.79%)	535 / 1176 (45.49%)	533 / 1200 (44.42%)
occurrences (all)	533	535	533
Irritability / fussiness			
subjects affected / exposed	764 / 1190 (64.20%)	729 / 1176 (61.99%)	765 / 1200 (63.75%)
occurrences (all)	764	729	765
Loss of appetite			
subjects affected / exposed	546 / 1190 (45.88%)	536 / 1176 (45.58%)	526 / 1200 (43.83%)
occurrences (all)	546	536	526
Fever			

subjects affected / exposed	404 / 1190 (33.95%)	422 / 1176 (35.88%)	418 / 1200 (34.83%)
occurrences (all)	404	422	418
Localized rash			
subjects affected / exposed	230 / 1190 (19.33%)	224 / 1176 (19.05%)	251 / 1200 (20.92%)
occurrences (all)	230	224	251
Generalized rash			
subjects affected / exposed	143 / 1190 (12.02%)	138 / 1176 (11.73%)	133 / 1200 (11.08%)
occurrences (all)	143	138	133

Non-serious adverse events	INV_MMR Group	COM_MMR Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2258 / 3566 (63.32%)	819 / 1243 (65.89%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed ^[1]	919 / 3555 (25.85%)	349 / 1242 (28.10%)	
occurrences (all)	919	349	
Redness			
subjects affected / exposed ^[2]	870 / 3555 (24.47%)	313 / 1242 (25.20%)	
occurrences (all)	870	313	
Swelling			
subjects affected / exposed ^[3]	318 / 3555 (8.95%)	133 / 1242 (10.71%)	
occurrences (all)	318	133	
Drowsiness			
subjects affected / exposed	1601 / 3566 (44.90%)	586 / 1243 (47.14%)	
occurrences (all)	1601	586	
Irritability / fussiness			
subjects affected / exposed	2258 / 3566 (63.32%)	819 / 1243 (65.89%)	
occurrences (all)	2258	819	
Loss of appetite			
subjects affected / exposed	1608 / 3566 (45.09%)	548 / 1243 (44.09%)	
occurrences (all)	1608	548	
Fever			

subjects affected / exposed	1244 / 3566 (34.89%)	412 / 1243 (33.15%)	
occurrences (all)	1244	412	
Localized rash			
subjects affected / exposed	705 / 3566 (19.77%)	266 / 1243 (21.40%)	
occurrences (all)	705	266	
Generalized rash			
subjects affected / exposed	414 / 3566 (11.61%)	143 / 1243 (11.50%)	
occurrences (all)	414	143	

Notes:

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

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

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

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

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

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets 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