Clinical trial results:
A phase IIIA, randomized, observer-blind, controlled, multinational study to evaluate the safety and immunogenicity of GlaxoSmithKline (GSK) Biologicals' measles, mumps, rubella (MMR) vaccine (209762) (Priorix) compared to Merck & Co., Inc.’s MMR vaccine (M-M-R II or VaxPro), as a first dose, both co-administered with Varivax, Havrix (all subjects) and Prevnar 13 (US subset) in healthy children 12 to 15 months of age

Summary

EudraCT number	2011-006161-18
Trial protocol	EE FI
Global end of trial date	22 December 2015

Results information

Result version number	v2 (current)
This version publication date	17 June 2018
First version publication date	12 January 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	115650

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02184572
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut, 89, Rixensart, Belgium, 1330
Public contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44(2089) 904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44(2089) 904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To demonstrate the safety profile (fever > 39.0°C (> 102.2°F)) of INV_MMR compared to COM_MMR (pooled lots) when co-administered with Varivax and Havrix (to all children) and Prevnar 13 (only to children enrolled in the US).
• To demonstrate the safety profile (fever ≥ 38.0°C (≥ 100.4°F)) of INV_MMR compared to COM_MMR (pooled lots) when co-administered with Varivax and Havrix (to all children) and Prevnar 13 (children enrolled in the US).

Protection of trial subjects:

All subjects were observed closely for at least 30 minutes with appropriate medical treatment readily available in case of anaphylaxis following the administration of vaccines. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 240
Country: Number of subjects enrolled	Finland: 220
Country: Number of subjects enrolled	Taiwan: 185
Country: Number of subjects enrolled	United States: 1097
Worldwide total number of subjects	1742
EEA total number of subjects	460

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)	1742

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:

6 subjects from 1742 were allocated subject number but no study vaccine was administered. Therefore, the number of subjects started in 1736.

Pre-assignment

Screening details:

US sub-cohort: Subjects recruited in US received INV_MMR (Priorix) or COM_MMR (M-M-R II/M-M-R VaxPro) co-administered with Varivax, Havrix & Prevnar 13 vaccines (Day 0). Non-US sub-cohort: Subjects recruited outside the US received INV_MMR (Priorix) or COM_MMR (M-M-R II/M-M-R VaxPro) co-administered with Varivax & Havrix vaccines (Day 0).

Pre-assignment period milestones

Number of subjects started	1742
Number of subjects completed	1736

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Subject no. allocated vaccine not administered: 6

Period 1

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

Blinding implementation details:

Observer blinded study

Arms

Are arms mutually exclusive?	Yes
Arm title	INV_MMR

Arm description:

Subjects received 1 dose of the study vaccine Priorix co-administered with Varivax and Havrix vaccines at Day 0. Subjects recruited in the US also received Prevnar 13 at Day 0.

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

Dosage and administration details:

1 dose administered subcutaneously in the triceps region of left arm at Day 0

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	GSK Biologicals' Hepatitis A vaccine, inactivated
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly in the anterolateral region of the right thigh at Day 0

Investigational medicinal product name	Varivax
Investigational medicinal product code	
Other name	Merck & Co. Inc.'s Varicella virus vaccine, live
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose administered subcutaneously in the triceps region of right arm at Day 0

Investigational medicinal product name	Prevnar 13
Investigational medicinal product code	
Other name	Pfizer Inc.'s Pneumococcal 13-valent conjugate vaccine (diphtheria CRM197 protein)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly in the anterolateral region of the left thigh at Day 0 to subjects recruited in US

Arm title	COM_MMR

Arm description:

Subjects received 1 dose of the licensed vaccine M-M-R II or M-M-R VaxPro Lot 1 or Lot 2 co-administered with Varivax and Havrix vaccines at Day 0. Subjects recruited in the US also received Prevnar 13 at Day 0.

Arm type	Active comparator
Investigational medicinal product name	M-M-R II
Investigational medicinal product code	
Other name	MMR vaccine live (M-M R II, Merck & Co., Inc., or M-M-R VaxPro, Sanofi Pasteur/Merck Sharp and Dohme [SPMSD])
Pharmaceutical forms	Powder and solvent for suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose administered subcutaneously in the triceps region of left arm at Day 0

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	GSK Biologicals' Hepatitis A vaccine, inactivated
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly in the anterolateral region of the right thigh at Day 0

Investigational medicinal product name	Varivax
Investigational medicinal product code	
Other name	Merck & Co. Inc.'s Varicella virus vaccine, live
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose administered subcutaneously in the triceps region of right arm at Day 0

Investigational medicinal product name	Prevnar 13
Investigational medicinal product code	
Other name	Pfizer Inc.'s Pneumococcal 13-valent conjugate vaccine (diphtheria CRM197 protein)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly in the anterolateral region of the left thigh at Day 0 to subjects recruited in US

Notes:

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

Justification: Study was conducted in an observer-blind manner.

Number of subjects in period 1[2]	INV_MMR	COM_MMR
Started	1164	572
Completed	1117	542
Not completed	47	30
Consent withdrawn by subject	14	9
Loss Of Kaiser Insurance	1	-
2nd blooddraw & diary card incomplete	1	-
Traveling Outside The Country	1	-
Lost to follow-up	29	21
Family Out Of Country Until 9/29/2015	1	-

Notes:

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

Justification: 6 subjects from 1742 were allocated subject number but no study vaccine was administered. Therefore, the number of subjects started in 1736.

Baseline characteristics

Reporting groups	
Reporting group title	INV_MMR
Reporting group description:	
Subjects received 1 dose of the study vaccine Priorix co-administered with Varivax and Havrix vaccines at Day 0. Subjects recruited in the US also received Prevnar 13 at Day 0.	
Reporting group title	COM_MMR
Reporting group description:	
Subjects received 1 dose of the licensed vaccine M-M-R II or M-M-R VaxPro Lot 1 or Lot 2 co-administered with Varivax and Havrix vaccines at Day 0. Subjects recruited in the US also received Prevnar 13 at Day 0.	

Reporting group values	INV_MMR	COM_MMR	Total
Number of subjects	1164	572	1736
Age categorical			
Units: Subjects			
Age continuous			
Age continuous description			
Units: months			
arithmetic mean	12.3	12.3	
standard deviation	± 0.7	± 0.7	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	551	270	821
Male	613	302	915
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage / African American	64	38	102
American Indian or Alaskan Native	29	16	45
Asian - Central/South Asian Heritage	9	4	13
Asian - East Asian Heritage	131	65	196
Asian - Japanese Heritage	2	0	2
Asian - South East Asian Heritage	28	12	40
Native Hawaiian or Other Pacific Islander	1	2	3
White - Arabic / North African Heritage	3	3	6
White - Caucasian / European Heritage	808	385	1193
Other	89	47	136

End points

End points reporting groups

Reporting group title	INV_MMR
Reporting group description:	
Subjects received 1 dose of the study vaccine Priorix co-administered with Varivax and Havrix vaccines at Day 0. Subjects recruited in the US also received Prevnar 13 at Day 0.	
Reporting group title	COM_MMR
Reporting group description:	
Subjects received 1 dose of the licensed vaccine M-M-R II or M-M-R VaxPro Lot 1 or Lot 2 co-administered with Varivax and Havrix vaccines at Day 0. Subjects recruited in the US also received Prevnar 13 at Day 0.	

Primary: Number of subjects reporting fever after MMR (Priorix or M-M-R II/M-M-R VaxPro [Lot 1 or Lot 2]) vaccination

End point title	Number of subjects reporting fever after MMR (Priorix or M-M-R II/M-M-R VaxPro [Lot 1 or Lot 2]) vaccination
End point description:	
Fever was assessed for temperature equal to/above (≥) 38.0°C and above (>) 39.0°C. The safety profile for fever was assessed based on the group difference (INV_MMR minus COM_MMR) in incidence of fever equal to or below the cut-off value.	
End point type	Primary
End point timeframe:	
During Day 5 to Day 12 post-vaccination period	

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1126	555		
Units: Participants				
> 39.0°C	47	17		
≥ 38.0°C	205	95		

Statistical analyses

Statistical analysis title	Difference in incidence of fever (> 39.0°C)
Statistical analysis description:	
Difference between groups (INV_MMR Group minus COM_MMR Group) in incidence of fever > 39.0°C.	
Comparison groups	INV_MMR v COM_MMR
Number of subjects included in analysis	1681
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in incidence of fever
Point estimate	1.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	2.89

Notes:

[1] - The upper limit of the 2-sided standardized asymptotic 95% Confidence Interval (CI) for the group difference (INV_MMR minus COM_MMR) in incidence of fever ≥ 39.0°C (≥ 102.2°F) should be equal to or below 5%.

Statistical analysis title	Difference in incidence of fever (> 38.0°C)

Statistical analysis description:

Difference between groups (INV_MMR Group minus COM_MMR Group) in incidence of fever > 38.0°C.

Comparison groups	INV_MMR v COM_MMR
Number of subjects included in analysis	1681
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in incidence of fever
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.89
upper limit	4.85

Notes:

[2] - The upper limit of the 2-sided standardized asymptotic 95% CI for the group difference (INV_MMR minus COM_MMR) in incidence of fever ≥ 38.0°C (≥ 100.4°F) should be equal to or below 10%.

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

End point title	Percentage of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value

End point description:

Seroresponse was defined as post-vaccination anti-measles virus antibody concentration greater than or equal to [≥] 200 milli International Units per milliliter [mIU/mL] (Enzyme-Linked Immunosorbent Assay [ELISA], Enzygnost) among subjects who were seronegative (antibody concentration less than [<] 150 mIU/mL) before vaccination.

End point type	Secondary

End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1043	521		
Units: Percentage of subjects				
number (confidence interval 95%)				
≥ 150 mIU/mL	99.3 (98.6 to 99.7)	96.7 (94.8 to 98.1)		
≥ 200 mIU/mL	99.0 (98.2 to 99.5)	96.5 (94.6 to 97.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-measles virus antibody concentrations

End point title	Anti-measles virus antibody concentrations

End point description:

Antibody concentrations were expressed as Geometric Mean Concentrations (GMCs) in mIU/mL. Analyses included initially seronegative subjects only.

End point type	Secondary

End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1043	521		
Units: mIU/mL				
geometric mean (confidence interval 95%)	2751.9 (2618.3 to 2892.2)	3133.3 (2878.6 to 3410.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value

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

End point description:

Seroresponse was defined as post-vaccination anti-mumps virus antibody concentration ≥ 10 ELISA Unit per milliliter [EU/mL] (ELISA, Pharmaceutical Product Development, Inc.[PPD]) among subjects who were seronegative (antibody concentration < 5 EU/mL) before vaccination.

End point type	Secondary

End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	964	483		
Units: Percentage of subjects				
number (confidence interval 95%)				
≥ 5 EU/mL	99.8 (99.3 to 100)	99.4 (98.2 to 99.9)		
≥ 10 EU/mL	99.4 (98.7 to 99.8)	97.9 (96.2 to 99.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-mumps virus antibody concentrations

End point title	Anti-mumps virus antibody concentrations

End point description:

Antibody concentrations were expressed as GMCs in EU/mL. Analyses included initially seronegative subjects only.

End point type	Secondary

End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	964	483		
Units: EU/mL				
geometric mean (confidence interval 95%)	86.0 (82.0 to 90.3)	82.6 (76.5 to 89.2)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Seroresponse was defined as post-vaccination anti-rubella virus antibody concentration ≥ 10 International Unit per milliliter [IU/mL] (ELISA, Enzygnost) among subjects who were seronegative (antibody concentration < 4 IU/mL) before vaccination.

End point type	Secondary

End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1043	521		
Units: Percentage of subjects				
number (confidence interval 95%)				
≥ 4 IU/mL	99.6 (99.0 to 99.9)	99.8 (98.9 to 100)		
≥ 10 IU/mL	95.7 (94.3 to 96.8)	98.3 (96.7 to 99.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rubella virus antibody concentrations

End point title	Anti-rubella virus antibody concentrations

End point description:

Antibody concentrations were expressed as GMCs in IU/mL. Analyses included initially seronegative subjects only.

End point type	Secondary

End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1043	521		
Units: IU/mL				
geometric mean (confidence interval 95%)	45.0 (42.8 to 47.2)	66.8 (62.3 to 71.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local adverse events (AEs)

End point title	Number of subjects with any solicited local adverse events (AEs)

End point description:

Assessed solicited local AEs were injection site pain, redness and swelling. Any = Occurrence of AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

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

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1123	553		
Units: Participants				
Any pain	312	131		
Any redness (mm)	260	137		
Any swelling (mm)	96	58		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general AEs

End point title	Number of subjects with any solicited general AEs

End point description:

Assessed solicited general AEs were drowsiness, irritability/fussiness and loss of appetite. Any = Occurrence of AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 15-day (Days 0-14) post-vaccination period

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1126	555		
Units: Participants				
Any drowsiness	527	238		
Any irritability/fussiness	722	345		
Any loss of appetite	493	232		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any fever

End point title	Number of subjects reporting any fever

End point description:

Any fever (≥ 38°C) = Occurrence of fever 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	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1126	555		
Units: Participants	350	179		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rash

End point title	Number of subjects reporting any rash

End point description:

Any rash = Occurrence of 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	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1126	555		
Units: Participants				
Any localized or generalized	275	152		
Any with fever	100	48		
Any varicella like	40	22		
Any measles/rubella like	65	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting MMR specific solicited general AEs

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

End point description:

Assessed MMR specific solicited general AEs were parotid gland swelling and any suspected signs of meningism including febrile convulsions. Any = Occurrence of 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	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1126	555		
Units: Participants				
Any parotid gland swelling	0	0		
Any febrile convulsion	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited AEs

End point title	Number of subjects reporting any unsolicited AEs

End point description:

Unsolicited AE included any AE reported in addition to those solicited during the clinical study and any 'solicited' AE with onset outside the specified period of follow-up for solicited AEs. Any = Occurrence of 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	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1164	572		
Units: Participants	598	277		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting AEs of specific interest

End point title	Number of subjects reporting AEs of specific interest

End point description:

AEs of specific interest included new onset chronic disease (NOCD) (e.g., autoimmune disorders, asthma, type I diabetes, vasculitis, celiac disease, conditions associated with sub-acute or chronic thrombocytopenia and allergies) and AEs prompting emergency room (ER) visits.

End point type	Secondary

End point timeframe:

Day 0 through the end of the study (Day 180)

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1164	572		
Units: Participants				
NOCDs	29	11		
AEs prompting ER visits	166	55		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs)

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

End point description:

SAE included any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization or resulted in disability/incapacity. Any = Occurrence of AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

Day 0 through the end of the study (Day 180)

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1164	572		
Units: Participants	24	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting measles-like illness

End point title	Number of subjects reporting measles-like illness

End point description:

Measles-like illness was defined as the occurrence of the following signs/symptoms in the absence of another confirmed diagnosis: maculopapular rash (includes measles/rubella-like rash), fever (≥ 38°C) and at least one of the symptoms: cough, coryza (runny nose), conjunctivitis or diarrhea, with fever or rash. Other event must be one of cough, coryza, conjunctivitis, or diarrhea.

End point type	Secondary

End point timeframe:

During Day 5 to Day 12 post-vaccination period

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1164	572		
Units: Participants				
Measles-like illness	18	5		
Maculopapular rash plus fever and one other event	26	9		
Maculopapular rash and fever	90	43		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs = From Day 0 to study end (Day 180); Solicited local and general AEs = During the 4-day (Day 0-3) and 15-day (Day 0-14) post vaccination period, respectively; Unsolicited adverse events = During the 43-day (Day 0-42) post vaccination period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	INV_MMR Group

Reporting group description:

Subjects received 1 dose of the study vaccine Priorix co-administered with Varivax and Havrix vaccines at Day 0. Subjects recruited in the US also received Prevnar 13 at Day 0.

Reporting group title	COM_MMR Group

Reporting group description:

Subjects received 1 dose of the licensed vaccine M-M-R II or M-M-R VaxPro Lot 1 or Lot 2 co-administered with Varivax and Havrix vaccines at Day 0. Subjects recruited in the US also received Prevnar 13 at Day 0.

Serious adverse events	INV_MMR Group	COM_MMR Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 1164 (2.06%)	9 / 572 (1.57%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 1164 (0.00%)	1 / 572 (0.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 1164 (0.00%)	1 / 572 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	0 / 1164 (0.00%)	1 / 572 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 1164 (0.09%)	1 / 572 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Joint effusion			

subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	0 / 1164 (0.00%)	1 / 572 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 1164 (0.09%)	1 / 572 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 1164 (0.09%)	2 / 572 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal skin infection			

subjects affected / exposed	0 / 1164 (0.00%)	1 / 572 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 1164 (0.00%)	1 / 572 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			

subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 1164 (0.34%)	1 / 572 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			

subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 1164 (0.26%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 1164 (0.09%)	0 / 572 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	INV_MMR Group	COM_MMR Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	980 / 1164 (84.19%)	477 / 572 (83.39%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	529 / 1164 (45.45%)	238 / 572 (41.61%)	
occurrences (all)	529	238	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	284 / 1164 (24.40%)	143 / 572 (25.00%)	
occurrences (all)	297	149	

Injection site pain			
subjects affected / exposed	313 / 1164 (26.89%)	133 / 572 (23.25%)	
occurrences (all)	314	133	
Injection site swelling			
subjects affected / exposed	105 / 1164 (9.02%)	61 / 572 (10.66%)	
occurrences (all)	108	62	
Pyrexia			
subjects affected / exposed	350 / 1164 (30.07%)	180 / 572 (31.47%)	
occurrences (all)	350	180	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	95 / 1164 (8.16%)	46 / 572 (8.04%)	
occurrences (all)	105	53	
Teething			
subjects affected / exposed	59 / 1164 (5.07%)	15 / 572 (2.62%)	
occurrences (all)	71	17	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	80 / 1164 (6.87%)	30 / 572 (5.24%)	
occurrences (all)	85	31	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	275 / 1164 (23.63%)	152 / 572 (26.57%)	
occurrences (all)	275	152	
Psychiatric disorders			
Irritability			
subjects affected / exposed	723 / 1164 (62.11%)	348 / 572 (60.84%)	
occurrences (all)	740	350	
Infections and infestations			
Otitis media			
subjects affected / exposed	86 / 1164 (7.39%)	35 / 572 (6.12%)	
occurrences (all)	95	36	
Upper respiratory tract infection			
subjects affected / exposed	111 / 1164 (9.54%)	73 / 572 (12.76%)	
occurrences (all)	119	75	
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	495 / 1164 (42.53%)	233 / 572 (40.73%)	
occurrences (all)	497	234	

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