



## Clinical trial results:

**A phase II, randomized, double-blind study of Priorix-Tetra (combined measles-mumps-rubella-varicella vaccine), one lot using new measles and rubella working seeds and one lot using old working seeds, in healthy subjects aged 11 to 21 months**

### Summary

EudraCT number	2011-005881-38
Trial protocol	Outside EU/EEA
Global end of trial date	13 December 2010

### Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	30 July 2015

### Trial information

#### Trial identification

Sponsor protocol code	108760
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00892775
WHO universal trial number (UTN)	-

Notes:

### Sponsors

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

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 September 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 September 2010
Global end of trial reached?	Yes
Global end of trial date	13 December 2010
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of MeMuRu-OKAnew WS to MeMuRu-OKA in terms of seroconversion rate to the measles, mumps, rubella, varicella components after the first dose.

Criterion for non-inferiority (43 days after dose 1): For each antibody to mumps (ELISA), measles (ELISA), rubella (ELISA), varicella (IFA), lower limit of the standardized asymptotic 95% CI for the group difference (MeMuRu OKAnew WS minus MeMuRu-OKA) in the percentage of subjects with seroconversion is -10% (clinical limit for non-inferiority).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 June 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Singapore: 250
Country: Number of subjects enrolled	Taiwan: 251
Worldwide total number of subjects	501
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	501
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:

Three subjects were enrolled but not vaccinated, of which one subject was assigned to the MMRVnew WS Group, and remaining two subjects were not assigned a treatment group.

### Pre-assignment

Screening details:

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

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	MMRVnew WS Group

Arm description:

Subjects received 2 doses of GlaxoSmithKline (GSK) Biologicals' live attenuated measles mumps rubella varicella vaccine formulated with new measles and rubella working seeds (MMRVnew WS) at Day 0 and Week 12

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

Dosage and administration details:

Two doses of MMRVnew WS vaccine administered by subcutaneous injections in the upper arm

<b>Arm title</b>	MMRV Group
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Arm description:

Subjects received 2 doses of GSK Biologicals' live attenuated measles-mumps-rubella-varicella (MMRV) vaccine manufactured with current working seed virus or new measles and rubella working seeds at Day 0 and Week 12

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

Dosage and administration details:

Two doses of MMRV vaccine administered subcutaneously in the upper arm

<b>Number of subjects in period 1<sup>[1]</sup></b>	MMRVnew WS Group	MMRV Group
Started	332	166
Completed	327	165
Not completed	5	1
Consent withdrawn by subject	-	1
Migrated/moved from study area	1	-
The subject had difficulty with blood drawing	1	-
Because of H1N1 the parents give up participating	1	-
Lost to follow-up	1	-
Protocol deviation	1	-

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Notes:

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

Justification: Three subjects were enrolled but not vaccinated, of which one subject was assigned to the MMRVnew WS Group, and remaining two subjects were not assigned a treatment group.

## Baseline characteristics

### Reporting groups

Reporting group title	MMRVnew WS Group
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Reporting group description:

Subjects received 2 doses of GlaxoSmithKline (GSK) Biologicals' live attenuated measles mumps rubella varicella vaccine formulated with new measles and rubella working seeds (MMRVnew WS) at Day 0 and Week 12

Reporting group title	MMRV Group
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Reporting group description:

Subjects received 2 doses of GSK Biologicals' live attenuated measles-mumps-rubella-varicella (MMRV) vaccine manufactured with current working seed virus or new measles and rubella working seeds at Day 0 and Week 12

Reporting group values	MMRVnew WS Group	MMRV Group	Total
Number of subjects	332	166	498
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: months			
arithmetic mean	13	12.9	
standard deviation	± 1.94	± 1.7	-
Gender categorical Units: Subjects			
Female	166	84	250
Male	166	82	248

## End points

### End points reporting groups

Reporting group title	MMRVnew WS Group
Reporting group description: Subjects received 2 doses of GlaxoSmithKline (GSK) Biologicals' live attenuated measles mumps rubella varicella vaccine formulated with new measles and rubella working seeds (MMRVnew WS) at Day 0 and Week 12	
Reporting group title	MMRV Group
Reporting group description: Subjects received 2 doses of GSK Biologicals' live attenuated measles-mumps-rubella-varicella (MMRV) vaccine manufactured with current working seed virus or new measles and rubella working seeds at Day 0 and Week 12	

### Primary: Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies above the cut-off value.

End point title	Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies above the cut-off value.
End point description: Seroconversion was defined as the appearance of antibodies (i.e. titre greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. The cut-off values for seroconversion was 150 mIU/mL, 231 U/mL, 4 IU/mL and 1:4 dilution for measles, mumps, rubella and varicella, respectively.	
End point type	Primary
End point timeframe: At 42-56 days after the first dose of study vaccine (Week 6).	

End point values	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	314	157		
Units: Subjects				
Anti-measles $\geq$ 150 mIU/mL	312	157		
Anti-mumps $\geq$ 231 U/ML	279	142		
Anti-rubella $\geq$ 4 IU/mL	313	157		
IgG varicella antibodies $\geq$ 1:4 dilution	284	131		

### Statistical analyses

Statistical analysis title	Non-inferiority of MMRVnew WS to MMRV
Statistical analysis description: Non-inferiority of GSK Biologicals' MMRV new formulation vaccine (MMRVnew WS) compared to MMRV vaccine after the first dose in terms of anti-measles seroconversion rates, 42 – 56 days after the first dose. Non-inferiority with respect to seroconversion rates for measles 42-56 days after vaccination was concluded if the lower limit of the 95% CI around the difference in seroconversion rates between groups would be $[-10\%]$ or higher.	
Comparison groups	MMRVnew WS Group v MMRV Group

Number of subjects included in analysis	471
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.29
upper limit	1.76

<b>Statistical analysis title</b>	Non-inferiority of MMRVnew WS to MMRV
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Statistical analysis description:

Non-inferiority of GSK Biologicals' MMRV new formulation vaccine (MMRVnew WS) compared to MMRV vaccine after the first dose in terms of anti-mumps seroconversion rates, 42 – 56 days after the first dose. Non-inferiority with respect to seroconversion rates for mumps 42-56 days after vaccination was concluded if the lower limit of the 95% CI around the difference in seroconversion rates between groups would be [-10%] or higher.

Comparison groups	MMRVnew WS Group v MMRV Group
Number of subjects included in analysis	471
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.14
upper limit	5.58

<b>Statistical analysis title</b>	Non-inferiority of MMRVnew WS to MMRV
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Statistical analysis description:

Non-inferiority of GSK Biologicals' MMRV new formulation vaccine (MMRVnew WS) compared to MMRV vaccine after the first dose in terms of anti-rubella seroconversion rates, 42 – 56 days after the first dose. Non-inferiority with respect to seroconversion rates for rubella 42-56 days after vaccination was concluded if the lower limit of the 95% CI around the difference in seroconversion rates between groups would be [-10%] or higher.

Comparison groups	MMRVnew WS Group v MMRV Group
Number of subjects included in analysis	471
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.78
upper limit	2.08



<b>Statistical analysis title</b>	Non-inferiority of MMRVnew WS to MMRV
Statistical analysis description:	
Non-inferiority of GSK Biologicals' MMRV new formulation vaccine (MMRVnew WS) compared to MMRV vaccine after the first dose in terms of anti-varicella seroconversion rates, 42 – 56 days after the first dose. Non-inferiority with respect to seroconversion rates for varicella 42-56 days after vaccination was concluded if the lower limit of the 95% CI around the difference in seroconversion rates between groups would be [-10%] or higher.	
Comparison groups	MMRVnew WS Group v MMRV Group
Number of subjects included in analysis	471
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	4.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	10.34

**Secondary: Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies above the cut-off value.**

End point title	Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies above the cut-off value.
End point description:	
Seroconversion was defined as the appearance of antibodies (i.e. titre greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. The cut-off values for seroconversion was 150 mIU/mL, 231 U/mL, 4 IU/mL and 1:4 dilution for measles, mumps, rubella and varicella, respectively.	
End point type	Secondary
End point timeframe:	
At 42-56 days after the second dose of study vaccine (week 18)	

<b>End point values</b>	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	308	156		
Units: Subjects				
Anti-measles $\geq$ 150 mIU/mL	308	156		
Anti-mumps $\geq$ 231 U/ML	307	155		
Anti-rubella $\geq$ 4 IU/mL	308	156		
IgG varicella antibodies $\geq$ 1:4 dilution	286	138		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody titers against measles, mumps, rubella and varicella viruses

End point title	Antibody titers against measles, mumps, rubella and varicella viruses
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End point description:

Antibody titers were summarized by geometric mean titers (GMTs) with their 95% CIs.

End point type	Secondary
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End point timeframe:

At 42-56 days after the first and second dose of study vaccine(s).

End point values	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	314	157		
Units: Titres				
geometric mean (confidence interval 95%)				
Anti-Measles (mIU/mL); Dose 1 [N=314,157]	3291.2 (3054 to 3546.8)	3460.1 (3145.6 to 3806)		
Anti-Mumps (U/mL); Dose 1 [N=311, 157]	924.4 (821.9 to 1039.7)	994.4 (851.7 to 1161)		
Anti-Rubella (IU/mL); Dose 1 [N=314, 157]	71.7 (66.1 to 77.9)	66.6 (59.3 to 74.9)		
Anti-Varicella (1/dil); Dose 1 [N=291, 141]	104.8 (90.8 to 120.9)	69.6 (53.6 to 90.2)		
Anti-Measles (mIU/mL); Dose 2 [N= 308, 156]	4247.6 (3911.5 to 4612.6)	4297.1 (3867.9 to 4774)		
Anti-Mumps (U/mL); Dose 2 [N=307, 155]	3379.5 (3121.3 to 3659)	3216.2 (2870.9 to 3603)		
Anti-Rubella (IU/mL); Dose 2 [N= 308, 156]	125.7 (117.4 to 134.5)	115.2 (104.2 to 127.4)		
Anti-Varicella (1/dil); Dose 2 [N= 286, 138]	6570.6 (5746.7 to 7512.7)	5134.8 (4153.8 to 6347.4)		

## Statistical analyses

No statistical analyses for this end point

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

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

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

End point type	Secondary
End point timeframe:	
Within 4 days after each vaccination (Days 0-3)	

End point values	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	166		
Units: Subjects				
Any Pain; Dose 1 [N=330, 166]	62	28		
Grade 3 Pain; Dose 1 [N=330, 166]	0	0		
Any Redness; Dose 1 [N=330, 166]	92	44		
Grade 3 Redness; Dose 1 [N=330, 166]	2	3		
Any Swelling; Dose 1 [N=330, 166]	22	11		
Grade 3 Swelling; Dose 1 [N=330, 166]	0	0		
Any Pain; Dose 2 [N=327, 164]	46	24		
Grade 3 Pain; Dose 2 [N=327, 164]	0	0		
Any Redness; Dose 2 [N=327, 164]	79	43		
Grade 3 Redness; Dose 2 [N=327, 164]	4	5		
Any Swelling; Dose 2 [N=327, 164]	37	25		
Grade 3 Swelling; Dose 2 [N=327, 164]	1	0		

## Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting any and grade 3 solicited general symptoms
End point description:	
Assessed solicited general symptoms were meningism and parotid gland swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 meningism and parotid gland swelling = meningism/parotid gland swelling which prevented normal everyday activities.	
End point type	Secondary
End point timeframe:	
Within 43 days (Days 0-42) after each vaccination	

End point values	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	166		
Units: Subjects				
Any Meningism; Dose 1 [N=330, 166]	2	1		
Grade 3 Meningism; Dose 1 [N=330, 166]	0	0		

Any Parotid gland; Dose 1 [N=330, 166]	0	0		
Grade 3 Parotid gland; Dose 1 [N=330, 166]	0	0		
Any Meningism; Dose 2 [N=327, 164]	2	0		
Grade 3 Meningism; Dose 2 [N=327, 164]	1	0		
Any Parotid gland; Dose 2 [N=327, 164]	0	0		
Grade 3 Parotid gland; Dose 2 [N=327, 164]	0	0		

## Statistical analyses

No statistical analyses for this end point

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

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

Any fever was defined as fever  $\geq 38.0^{\circ}\text{C}$  and grade 3 fever  $> 39.5^{\circ}\text{C}$  after vaccination. Related fever was defined as fever assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

Within 43 days (Days 0-42) after each vaccination.

End point values	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	166		
Units: Subjects				
Any temperature; Dose 1 [N=330, 166]	231	104		
Grade 3 temperature; Dose 1 [N=330, 166]	54	23		
Related temperature; Dose 1 [N=330, 166]	160	70		
Any temperature; Dose 2 [N=327, 164]	115	62		
Grade 3 temperature; Dose 2 [N=327, 164]	31	13		
Related temperature; Dose 2 [N=327, 164]	29	28		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any (localised or generalised), grade 3 and related rashes

End point title	Number of subjects reporting any (localised or generalised),
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## End point description:

Rash/exanthem was defined as:

1) measles/ rubella rashes (macular or maculo-papular rashes): presence of macules, discolored small patches or spots of the skin, neither elevated nor depressed below the skin's surface.

2) varicella rash (maculo-papulo-vesicular): simultaneous presence of macules, papules and vesicles raised above the skin's surface or

3) other types of rash (heat rash, diaper rash etc.). Any rash = occurrence of rash regardless of intensity grade or relationship to vaccination Grade 3 rash = > 150 lesions and Related = rash assessed by the investigator as related to the vaccination.

## End point type

Secondary

## End point timeframe:

Within 43 days (Days 0-42) after each vaccination.

End point values	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	166		
Units: Subjects				
Any, rash type; Dose 1 [N=330, 166]	88	42		
Grade 3 rash type; Dose 1 [N=330, 166]	9	6		
Related rash type; Dose 1 [N=330, 166]	37	23		
Any, rash type; Dose 2 [N=327, 164]	40	17		
Grade 3 rash type; Dose 2 [N=327, 164]	6	1		
Related rash type; Dose 2 [N=327, 164]	12	7		

## Statistical analyses

No statistical analyses for this end point

**Secondary: Number of subjects reporting any, grade 3 and related unsolicited adverse event (AEs)**

## End point title

Number of subjects reporting any, grade 3 and related unsolicited adverse event (AEs)

## End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event. Grade 3 was defined as an event that prevented normal activity and Related was defined as an event assessed by the investigator as causally related to the study vaccination

## End point type

Secondary

## End point timeframe:

Within 43 days (Days 0-42) after first vaccination dose.

End point values	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	166		
Units: Subjects				
Any AE(s)	165	73		
Grade 3 AE(s)	8	5		
Related AE(s)	21	8		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any, grade 3 and related unsolicited adverse event (AEs)

End point title	Number of subjects reporting any, grade 3 and related unsolicited adverse event (AEs)
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End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event. Grade 3 was defined as an event that prevented normal activity and Related was defined as an event assessed by the investigator as causally related to the study vaccination

End point type	Secondary
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End point timeframe:

Within 43 days (Days 86-128) after second vaccination dose.

End point values	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	166		
Units: Subjects				
Any AE(s)	146	76		
Grade 3 AE(s)	6	6		
Related AE(s)	10	6		

### Statistical analyses

No statistical analyses for this end point

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

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

Serious adverse events (SAEs) assessed included medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of existing hospitalization, resulted in

disability/incapacity or is a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary
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End point timeframe:

From first study dose until study end (Day 0 to Day 129-171)

End point values	MMRVnew WS Group	MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	166		
Units: Subjects				
Any SAE(s)	27	12		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local symptoms were collected within 4 days after each vaccination. Solicited general symptoms & unsolicited AEs were collected within 43 days after each vaccination. SAEs were collected throughout the entire study period

Adverse event reporting additional description:

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

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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### Reporting groups

Reporting group title	MMRVnew WS Group
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Reporting group description:

Subjects received 2 doses of GlaxoSmithKline (GSK) Biologicals' live attenuated measles mumps rubella varicella vaccine formulated with new measles and rubella working seeds (MMRVnew WS) at Day 0 and Week 12

Reporting group title	MMRV Group
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Reporting group description:

Subjects received 2 doses of GSK Biologicals' live attenuated measles-mumps-rubella-varicella (MMRV) vaccine manufactured with current working seed virus or new measles and rubella working seeds at Day 0 and Week 12

Serious adverse events	MMRVnew WS Group	MMRV Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 332 (8.13%)	12 / 166 (7.23%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Band neutrophil count increased			
subjects affected / exposed	0 / 332 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			



Kawasaki's disease			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	4 / 332 (1.20%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Hypochromic anaemia			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 332 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	2 / 332 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal discomfort			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 332 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			

subjects affected / exposed	0 / 332 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 332 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular retraction			
subjects affected / exposed	0 / 332 (0.00%)	1 / 166 (0.60%)	
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			
Asthma			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	0 / 332 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	4 / 332 (1.20%)	4 / 166 (2.41%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute tonsillitis			
subjects affected / exposed	4 / 332 (1.20%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	2 / 332 (0.60%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	2 / 332 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	2 / 332 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpangina			
subjects affected / exposed	2 / 332 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	3 / 332 (0.90%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	3 / 332 (0.90%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	1 / 332 (0.30%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 332 (0.30%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			

subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis orbital			
subjects affected / exposed	0 / 332 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis viral			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovirus infection			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (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 / 332 (0.30%)	0 / 166 (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 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (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	1 / 332 (0.30%)	0 / 166 (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 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rash			
subjects affected / exposed	1 / 332 (0.30%)	0 / 166 (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			
Hypovolaemia			
subjects affected / exposed	0 / 332 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	MMRVnew WS Group	MMRV Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	231 / 332 (69.58%)	104 / 166 (62.65%)	
General disorders and administration site conditions			
Pain; Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[1]</sup>	62 / 330 (18.79%)	28 / 166 (16.87%)	
occurrences (all)	62	28	
Redness; Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[2]</sup>	92 / 330 (27.88%)	44 / 166 (26.51%)	
occurrences (all)	92	44	
Swelling; Dose 1			
alternative assessment type: Systematic			

<p>subjects affected / exposed<sup>[3]</sup></p> <p>occurrences (all)</p> <p>Pain; Dose 2</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed<sup>[4]</sup></p> <p>occurrences (all)</p> <p>Redness; Dose 2</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed<sup>[5]</sup></p> <p>occurrences (all)</p> <p>Swelling; Dose 2</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed<sup>[6]</sup></p> <p>occurrences (all)</p>	<p>22 / 330 (6.67%)</p> <p>22</p> <p>46 / 327 (14.07%)</p> <p>46</p> <p>79 / 327 (24.16%)</p> <p>79</p> <p>37 / 327 (11.31%)</p> <p>37</p>	<p>11 / 166 (6.63%)</p> <p>11</p> <p>24 / 164 (14.63%)</p> <p>24</p> <p>43 / 164 (26.22%)</p> <p>43</p> <p>25 / 164 (15.24%)</p> <p>25</p>	
<p>Gastrointestinal disorders</p> <p>Diarrhoea; Dose 1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>17 / 332 (5.12%)</p> <p>17</p>	<p>11 / 166 (6.63%)</p> <p>11</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Rhinorrhoea; Dose 1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough; Dose 1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough; Dose 2</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rhinorrhoea; Dose 2</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>31 / 332 (9.34%)</p> <p>31</p> <p>24 / 332 (7.23%)</p> <p>24</p> <p>24 / 332 (7.23%)</p> <p>24</p> <p>24 / 332 (7.23%)</p> <p>24</p>	<p>10 / 166 (6.02%)</p> <p>10</p> <p>10 / 166 (6.02%)</p> <p>10</p> <p>12 / 166 (7.23%)</p> <p>12</p> <p>10 / 166 (6.02%)</p> <p>10</p>	
<p>Skin and subcutaneous tissue disorders</p> <p>Rash; Dose 1</p> <p>subjects affected / exposed<sup>[7]</sup></p> <p>occurrences (all)</p> <p>Rash; Dose 2</p>	<p>88 / 330 (26.67%)</p> <p>88</p>	<p>42 / 166 (25.30%)</p> <p>42</p>	

subjects affected / exposed <sup>[8]</sup>	40 / 327 (12.23%)	17 / 164 (10.37%)	
occurrences (all)	40	17	
Infections and infestations			
Fever; Dose 1			
subjects affected / exposed <sup>[9]</sup>	231 / 330 (70.00%)	104 / 166 (62.65%)	
occurrences (all)	231	104	
Fever; Dose 2			
subjects affected / exposed <sup>[10]</sup>	115 / 327 (35.17%)	62 / 164 (37.80%)	
occurrences (all)	115	62	
Upper respiratory tract infection; Dose 1			
subjects affected / exposed	50 / 332 (15.06%)	22 / 166 (13.25%)	
occurrences (all)	50	22	
Upper respiratory tract infection; Dose 2			
subjects affected / exposed	30 / 332 (9.04%)	31 / 166 (18.67%)	
occurrences (all)	30	31	

Notes:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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



## **More information**

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

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported