# 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 | v2 (current) |
| This version publication date | 12 August 2022 |
| First version publication date | 30 July 2015 |
| Version creation reason | • Correction of full data set<br>Correction of full data set and alignment between registries. |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 108760 |

**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% confidence interval (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 Priorix-Tetra new 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 | Subject, Investigator, Carer, Assessor |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Priorix-Tetra new WS Group |

Arm description:

Subjects received 2 doses of Priorix-Tetra vaccine formulated with new measles and rubella working seeds 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.

| | |
|---|---|
| **Arm title** | Priorix-Tetra current WS Group |

Arm description:

Subjects received 2 doses of Priorix-Tetra vaccine manufactured with current working seed virus 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.

| **Number of subjects in period 1[1]** | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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 | - |

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 Priorix-Tetra new WS Group, and remaining two subjects were not assigned a treatment group.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Priorix-Tetra new WS Group |
| Reporting group description: | |
| Subjects received 2 doses of Priorix-Tetra vaccine formulated with new measles and rubella working seeds at Day 0 and Week 12. | |
| Reporting group title | Priorix-Tetra current WS Group |
| Reporting group description: | |
| Subjects received 2 doses of Priorix-Tetra vaccine manufactured with current working seed virus at Day 0 and Week 12. | |

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

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Priorix-Tetra new WS Group |
| Reporting group description: | |
| Subjects received 2 doses of Priorix-Tetra vaccine formulated with new measles and rubella working seeds at Day 0 and Week 12. | |
| Reporting group title | Priorix-Tetra current WS Group |
| Reporting group description: | |
| Subjects received 2 doses of Priorix-Tetra vaccine manufactured with current working seed virus at Day 0 and Week 12. | |

### Primary: Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies greater than or equal to (>=) the cut-off value

| | |
|---|---|
| End point title | Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies greater than or equal to (>=) the cut-off value |
| End point description: | |
| Seroconversion was defined as the appearance of antibodies in the serum of subjects seronegative before vaccination. The cut-off values for seroconversion were 150 milli international units per milliliter (mIU/mL), 231 units per milliliter (U/mL), 4 international units per milliliter (IU/mL) and 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 | Priorix-Tetra new WS Group | Priorix-Tetra current WS Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 314 | 157 | | |
| Units: Subjects | | | | |
| Anti-measles ≥ 150 mIU/mL | 312 | 157 | | |
| Anti-mumps ≥ 231 U/ML | 279 | 142 | | |
| Anti-rubella ≥ 4 IU/mL | 313 | 157 | | |
| IgG varicella antibodies ≥ 1:4 dilution | 284 | 131 | | |

### Statistical analyses

| Statistical analysis title | Priorix-Tetra New WS vs Priorix-Tetra Current WS |
|---|---|
| Statistical analysis description: | |
| Non-inferiority of GSK Biologicals' MMRV new formulation vaccine (Priorix-Tetra new WS) compared to Priorix-Tetra current WS 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 | Priorix-Tetra current WS Group v Priorix-Tetra new WS 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 |

| **Statistical analysis title** | Priorix-Tetra New WS vs Priorix-Tetra Current WS |
|---|---|

Statistical analysis description:

Non-inferiority of GSK Biologicals' MMRV new formulation vaccine (Priorix-Tetra new WS) compared to Priorix-Tetra current WS 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 | Priorix-Tetra new WS Group v Priorix-Tetra current WS 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 |

| **Statistical analysis title** | Priorix-Tetra New WS vs Priorix-Tetra Current WS |
|---|---|

Statistical analysis description:

Non-inferiority of GSK Biologicals' MMRV new formulation vaccine (Priorix-Tetra new WS) compared to Priorix-Tetra current WS 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 | Priorix-Tetra new WS Group v Priorix-Tetra current WS 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 |

| **Statistical analysis title** | Priorix-Tetra New WS vs Priorix-Tetra Current WS |
|---|---|

Statistical analysis description:

Non-inferiority of GSK Biologicals' MMRV new formulation vaccine (Priorix-Tetra new WS) compared to Priorix-Tetra current WS 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 | Priorix-Tetra new WS Group v Priorix-Tetra current WS 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 >= the cut-off value

| | |
|---|---|
| End point title | Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies >= the cut-off value |

End point description:

Seroconversion was defined as the appearance of antibodies 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)

| **End point values** | Priorix-Tetra new WS Group | Priorix-Tetra current WS Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 308 | 156 | | |
| Units: Subjects | | | | |
| Anti-measles ≥ 150 mIU/mL | 308 | 156 | | |
| Anti-mumps ≥ 231 U/ML | 307 | 155 | | |
| Anti-rubella ≥ 4 IU/mL | 308 | 156 | | |
| IgG varicella antibodies ≥ 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 |
|---|---|

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

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

| End point values | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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 |
|---|---|

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** | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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 | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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 |
|---|---|

End point description:

Any fever was defined as fever >= 38.0°C and grade 3 fever greater than (>) 39.5°C after vaccination. Related fever was defined as fever assessed by the investigator as related to the vaccination.

| End point type | Secondary |
|---|---|

End point timeframe:

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

| End point values | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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 (local or general), grade 3 and related rashes

| End point title | Number of subjects reporting any (local or general), grade 3 and related rashes |
|---|---|

End point description:

Rash 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; 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 | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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** | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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) |
|---|---|

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 86-128) after second vaccination dose

| End point values | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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) |
|---|---|

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 |
|---|---|

End point timeframe:

From first study dose (Day 0) until study end (Week 18)

| End point values | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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. The solicited local and general symptoms were only collected for those subjects who filled-in their symptom sheets.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 14.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Priorix-Tetra new WS Group |

Reporting group description:

Subjects received 2 doses of vaccine formulated with new measles and rubella working seeds at Day 0 and Week 12.

| | |
|---|---|
| Reporting group title | Priorix-Tetra current WS Group |

Reporting group description:

Subjects received 2 doses of Priorix-Tetra vaccine manufactured with current working seed virus at Day 0 and Week 12

| Serious adverse events | Priorix-Tetra new WS Group | Priorix-Tetra current WS 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|---|---|
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non- | | | |

| | | | |
|---|---|---|---|
| systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |

| | | | |
|---|---|---|---|
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|---|---|
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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<br>alternative assessment type: Non-systematic | | | |
| 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<br>alternative assessment type: Non-systematic | | | |
| 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<br>alternative assessment type: Non-systematic | | | |
| 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<br>alternative assessment type: Non-systematic | | | |
| 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<br>alternative assessment type: Non-systematic | | | |
| 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<br>alternative assessment type: Non-systematic | | | |
| 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<br>alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|---|---|
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 | | | |
| alternative assessment type: Non-systematic | | | |
| 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 %

| **Non-serious adverse events** | Priorix-Tetra new WS Group | Priorix-Tetra current WS Group | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 246 / 332 (74.10%) | 117 / 166 (70.48%) | |
| General disorders and administration site conditions | | | |
| Pain; Dose 1 | | | |
| subjects affected / exposed[1] | 62 / 330 (18.79%) | 28 / 166 (16.87%) | |
| occurrences (all) | 62 | 28 | |
| Redness; Dose 1 | | | |
| subjects affected / exposed[2] | 92 / 330 (27.88%) | 44 / 166 (26.51%) | |
| occurrences (all) | 92 | 44 | |
| Swelling; Dose 1 | | | |

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

| | | | |
|---|---|---|---|
| Rash; Dose 1 | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed[7] | 88 / 330 (26.67%) | 42 / 166 (25.30%) | |
| occurrences (all) | 88 | 42 | |
| Rash; Dose 2 | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed[8] | 40 / 327 (12.23%) | 17 / 164 (10.37%) | |
| occurrences (all) | 40 | 17 | |
| Infections and infestations | | | |
| Fever; Dose 1 | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed[9] | 231 / 330 (70.00%) | 104 / 166 (62.65%) | |
| occurrences (all) | 231 | 104 | |
| Fever; Dose 2 | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed[10] | 115 / 327 (35.17%) | 62 / 164 (37.80%) | |
| occurrences (all) | 115 | 62 | |
| Upper respiratory tract infection; Dose 1 | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 50 / 332 (15.06%) | 22 / 166 (13.25%) | |
| occurrences (all) | 50 | 22 | |
| Upper respiratory tract infection; Dose 2 | | | |
| alternative assessment type: Non-systematic | | | |
| 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: 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.

[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: The analysis was performed on the Total vaccinated cohort, only on subjects with their

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