# Clinical trial results:
# A Phase III Double-Blind, Randomized, Multicenter, Controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of Measles, Mumps, Rubella, Varicella (MMRV) Vaccine Made with an Alternative Manufacturing Process (AMP)

## Summary

| | |
|---|---|
| EudraCT number | 2017-001443-13 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 27 January 2014 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 15 June 2017 |
| First version publication date | 15 June 2017 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | V221-027 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01536405 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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 | 27 January 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 27 January 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

This study compared the safety, tolerability, and immunogenicity of measles, mumps, rubella, and varicella (MMRV) vaccine made with an alternative manufacturing process (MMRV [AMP]) with those of ProQuad™ (MMRV [2006 Process]). The primary hypothesis of the study was that MMRV (AMP) induces measles, mumps, rubella, and VZV antibody responses 6 weeks Postdose 1 that are non-inferior to those induced by MMRV (2006 Process).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 05 June 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 1412 |
| Worldwide total number of subjects | 1412 |
| 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) | 1412 |
| 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:

The study enrolled healthy children 12- to 23-months of age with no clinical history for measles, mumps, rubella, varicella, or zoster.

### Pre-assignment

Screening details:

One participant was inadvertently randomized twice, for a total of 1413 randomizations. The Subject Disposition tables below include this participant only once.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MMRV (AMP) |

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP])

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process. |
| Investigational medicinal product code | |
| Other name | V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| | |
|---|---|
| **Arm title** | MMRV (2006 Process) |

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process])

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process. |
| Investigational medicinal product code | |
| Other name | ProQuad™<br>V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| Number of subjects in period 1 | MMRV (AMP) | MMRV (2006 Process) |
|---|---|---|
| Started | 706 | 706 |
| Completed | 698 | 702 |
| Not completed | 8 | 4 |
| Not vaccinated | 8 | 4 |

## Period 2

| | |
|---|---|
| Period 2 title | Visit 1 (Day 1) to Visit 2 (Day 43) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MMRV (AMP) |

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP])

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process. |
| Investigational medicinal product code | |
| Other name | V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| | |
|---|---|
| **Arm title** | MMRV (2006 Process) |

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process])

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process. |
| Investigational medicinal product code | |
| Other name | ProQuad™<br>V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| Number of subjects in period 2 | MMRV (AMP) | MMRV (2006 Process) |
|---|---|---|
| Started | 698 | 702 |
| Received Vaccination 1 | 698 | 702 |
| Completed | 666 | 662 |
| Not completed | 32 | 40 |
| Consent withdrawn by subject | 12 | 18 |
| Lost to follow-up | 20 | 22 |

## Period 3

| | |
|---|---|
| Period 3 title | Visit 2 (Day 43) to Visit 3 (Day 91) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MMRV (AMP) |

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP])

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process. |
| Investigational medicinal product code | |
| Other name | V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| | |
|---|---|
| **Arm title** | MMRV (2006 Process) |

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process])

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process. |
| Investigational medicinal product code | |
| Other name | ProQuad™<br>V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| Number of subjects in period 3 | MMRV (AMP) | MMRV (2006 Process) |
|---|---|---|
| Started | 666 | 662 |
| Completed | 635 | 634 |
| Not completed | 31 | 28 |
| Consent withdrawn by subject | 17 | 13 |
| Adverse event, non-fatal | 3 | 3 |
| Lost to follow-up | 9 | 10 |
| Protocol deviation | 2 | 2 |

| Period 4 | |
|---|---|
| Period 4 title | Visit 3 (Day 91) to Visit 4 (Day 133) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

| Arms | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MMRV (AMP) |

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP])

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process. |
| Investigational medicinal product code | |
| Other name | V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| **Arm title** | MMRV (2006 Process) |
|---|---|

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process])

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process. |
| Investigational medicinal product code | |
| Other name | ProQuad™<br>V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| **Number of subjects in period 4** | MMRV (AMP) | MMRV (2006 Process) |
|---|---|---|
| Started | 635 | 634 |
| Received Vaccination 2 | 634 | 632 |
| Completed | 615 | 618 |
| Not completed | 20 | 16 |
| Consent withdrawn by subject | 3 | 2 |
| Adverse event, non-fatal | 1 | - |
| Lost to follow-up | 16 | 14 |

## Period 5

| | |
|---|---|
| Period 5 title | Visit 4 (Day 133) to Visit 5 (Day 271) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MMRV (AMP) |

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP])

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process. |
| Investigational medicinal product code | |
| Other name | V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| | |
|---|---|
| **Arm title** | MMRV (2006 Process) |

Arm description:

Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process])

| | |
|---|---|
| Arm type | Active comparator |

| | |
|---|---|
| Investigational medicinal product name | Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process. |
| Investigational medicinal product code | |
| Other name | ProQuad™<br>V221 |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two 0.5 mL subcutaneous injections administered at Day 1 and Day 91

| **Number of subjects in period 5** | MMRV (AMP) | MMRV (2006 Process) |
|---|---|---|
| Started | 615 | 618 |
| Completed | 595 | 595 |
| Not completed | 20 | 23 |
| Consent withdrawn by subject | - | 2 |
| Adverse event, non-fatal | - | 1 |
| Lost to follow-up | 20 | 20 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | MMRV (AMP) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP]) | |
| Reporting group title | MMRV (2006 Process) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process]) | |

| Reporting group values | MMRV (AMP) | MMRV (2006 Process) | Total |
|---|---|---|---|
| Number of subjects | 706 | 706 | 1412 |
| Age Categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 706 | 706 | 1412 |
| Age Continuous<br>Units: months | | | |
| arithmetic mean | 13.4 | 13.6 | |
| standard deviation | ± 2.2 | ± 2.5 | - |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 344 | 324 | 668 |
| Male | 362 | 382 | 744 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | MMRV (AMP) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP]) | |
| Reporting group title | MMRV (2006 Process) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process]) | |
| Reporting group title | MMRV (AMP) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP]) | |
| Reporting group title | MMRV (2006 Process) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process]) | |
| Reporting group title | MMRV (AMP) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP]) | |
| Reporting group title | MMRV (2006 Process) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process]) | |
| Reporting group title | MMRV (AMP) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP]) | |
| Reporting group title | MMRV (2006 Process) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process]) | |
| Reporting group title | MMRV (AMP) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP]) | |
| Reporting group title | MMRV (2006 Process) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process]) | |
| Subject analysis set title | MMRV (AMP) - Received at Least One Vaccination |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants received at least one 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella (MMRV) vaccine made with an alternative manufacturing process (AMP) | |
| Subject analysis set title | MMRV (2006 Process) - Received at Least one Vaccination |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants received at least one 0.5 mL subcutaneous injections of MMRV made with the 2006 manufacturing process | |

## Primary: Percentage of Participants With Varicella Zoster Virus (VZV) Antibody Levels >=5 gpELISA Units/mL

| End point title | Percentage of Participants With Varicella Zoster Virus (VZV) Antibody Levels >=5 gpELISA Units/mL |
|---|---|

End point description:

Sera were tested for VZV Immunoglobulin (IgG) antibody levels by a glycoprotein enzyme-linked immunosorbent assay (gpELISA). The population analyzed included participants who received >=1 dose of study vaccine, were seronegative at baseline and had postvaccination VZV serology results.

| End point type | Primary |
|---|---|

End point timeframe:

Six weeks after vaccination 1

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 586 | 589 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 97.3 (95.6 to 98.4) | 93 (90.7 to 95) | | |

### Statistical analyses

| Statistical analysis title | Non-inferiority Analysis |
|---|---|

Statistical analysis description:

The non-inferiority evaluation is based on the lower bound of the 2-sided 95% confidence interval (CI) on the risk difference excluding a decrease >= the prespecified criterion of 10 percentage points.

| Comparison groups | MMRV (AMP) - Received at Least One Vaccination v MMRV (2006 Process) - Received at Least one Vaccination |
|---|---|
| Number of subjects included in analysis | 1175 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[1] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 4.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.8 |
| upper limit | 6.8 |

Notes:

[1] - Risk Difference = MMRV (AMP) - MMRV (2006 process)

## Primary: Percentage of Participants With Measles Virus Antibody Levels >=255 mIU/mL

| End point title | Percentage of Participants With Measles Virus Antibody Levels |
|---|---|

| | |
|---|---|
| | >=255 mIU/mL |

End point description:

Sera were tested for measles virus IgG antibody levels by an ELISA. The population analyzed included participants who received >=1 dose of study vaccine, were seronegative at baseline and had postvaccination measles virus serology results.

| End point type | Primary |
|---|---|

End point timeframe:

Six weeks after vaccination 1

| **End point values** | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 629 | 621 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 96.7 (94.9 to 97.9) | 98.9 (97.7 to 99.5) | | |

**Statistical analyses**

| **Statistical analysis title** | Non-inferiority Analysis |
|---|---|

Statistical analysis description:

The non-inferiority evaluation is based on the lower bound of the 2-sided 95% CI on the risk difference excluding a decrease >= the prespecified criterion of 5 percentage points.

| Comparison groups | MMRV (AMP) - Received at Least One Vaccination v MMRV (2006 Process) - Received at Least one Vaccination |
|---|---|
| Number of subjects included in analysis | 1250 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[2] |
| P-value | = 0.003 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4 |
| upper limit | -0.6 |

Notes:

[2] - Risk Difference = MMRV (AMP) - MMRV (2006 process)

**Primary: Percentage of Participants With Mumps Virus Antibody Levels >=10 Mumps Ab Units/mL**

| End point title | Percentage of Participants With Mumps Virus Antibody Levels >=10 Mumps Ab Units/mL |
|---|---|

End point description:

Sera were tested for mumps virus IgG antibody levels by an enzyme-linked immunosorbent assay

(ELISA). The population analyzed included participants who received >=1 dose of study vaccine, were seronegative at baseline and had postvaccination mumps virus serology results.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Six weeks after vaccination 1

| **End point values** | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 618 | 610 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 98.2 (96.8 to 99.1) | 97.2 (95.6 to 98.4) | | |

## Statistical analyses

| **Statistical analysis title** | Non-inferiority Analysis |
|---|---|

Statistical analysis description:

The non-inferiority evaluation is based on the lower bound of the 2-sided 95% CI on the risk difference excluding a decrease >= the prespecified criterion of 5 percentage points.

| | |
|---|---|
| Comparison groups | MMRV (AMP) - Received at Least One Vaccination v MMRV (2006 Process) - Received at Least one Vaccination |
| Number of subjects included in analysis | 1228 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[3] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.7 |
| upper limit | 2.8 |

Notes:

[3] - Risk Difference = MMRV (AMP) - MMRV (2006 process)

## Primary: Percentage of Participants With Rubella Virus Antibody Levels >=10 International Units/mL (IU/mL)

| End point title | Percentage of Participants With Rubella Virus Antibody Levels >=10 International Units/mL (IU/mL) |
|---|---|

End point description:

Sera were tested for rubella virus IgG antibody levels by an ELISA. The population analyzed included participants who received >=1 dose of study vaccine, were seronegative at baseline and had postvaccination rubella serology results.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Six weeks after vaccination 1

| **End point values** | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 608 | 593 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 98.8 (97.6 to 99.5) | 99.3 (98.3 to 99.8) | | |

**Statistical analyses**

| **Statistical analysis title** | Non-inferiority Analysis |
|---|---|

Statistical analysis description:

The non-inferiority evaluation is based on the lower bound of the 2-sided 95% CI on the risk difference excluding a decrease >= the prespecified criterion of 5 percentage points.

| Comparison groups | MMRV (AMP) - Received at Least One Vaccination v MMRV (2006 Process) - Received at Least one Vaccination |
|---|---|
| Number of subjects included in analysis | 1201 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[4] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.8 |
| upper limit | 0.7 |

Notes:

[4] - Risk Difference = MMRV (AMP) - MMRV (2006 process)

**Primary: Geometric Mean Titer (GMT) of VZV Antibodies**

| End point title | Geometric Mean Titer (GMT) of VZV Antibodies |
|---|---|

End point description:

Sera were tested for VZV IgG antibody levels by gpELISA. The population analyzed included participants who received >=1 dose of study vaccine, were seronegative at baseline and had postvaccination VZV serology results.

| End point type | Primary |
|---|---|

End point timeframe:

Six weeks after vaccination 1

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 586 | 589 | | |
| Units: gpELISA Units/mL | | | | |
| geometric mean (confidence interval 95%) | 17.3 (16.4 to 18.3) | 14.4 (13.6 to 15.2) | | |

### Statistical analyses

| Statistical analysis title | Non-inferiority Analysis |
|---|---|

Statistical analysis description:

The non-inferiority evaluation is based on the lower bound of the 2-sided 95% CI on the GMT ratio, excluding a decrease of >=1.5 fold. Analysis was based on log-transformed titers.

| | |
|---|---|
| Comparison groups | MMRV (AMP) - Received at Least One Vaccination v MMRV (2006 Process) - Received at Least one Vaccination |
| Number of subjects included in analysis | 1175 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[5] |
| P-value | < 0.001 |
| Method | t-test, 2-sided |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.1 |
| upper limit | 1.3 |

Notes:

[5] - GMT ratio = MMRV (AMP) / MMRV (2006 process).

### Primary: Geometric Mean Titer (GMT) of Measles Virus Antibodies

| End point title | Geometric Mean Titer (GMT) of Measles Virus Antibodies |
|---|---|

End point description:

Sera were tested for measles virus IgG antibody levels by ELISA. The population analyzed included participants who received >=1 dose of study vaccine, were seronegative at baseline and had postvaccination measles virus serology results.

| End point type | Primary |
|---|---|

End point timeframe:

Six weeks after vaccination 1

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 629 | 621 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | 3426.5 (3162.5 to 3712.4) | 3719.5 (3506 to 3946) | | |

### Statistical analyses

| Statistical analysis title | Non-inferiority Analysis |
|---|---|

Statistical analysis description:

The non-inferiority evaluation is based on the lower bound of the 2-sided 95% CI on the GMT ratio, excluding a decrease of >=1.5 fold. Analysis was based on log-transformed titers.

| | |
|---|---|
| Comparison groups | MMRV (AMP) - Received at Least One Vaccination v MMRV (2006 Process) - Received at Least one Vaccination |
| Number of subjects included in analysis | 1250 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[6] |
| P-value | < 0.001 |
| Method | t-test, 2-sided |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 1 |

Notes:

[6] - GMT ratio = MMRV (AMP) / MMRV (2006 process).

### Primary: Geometric Mean Titer (GMT) of Mumps Virus Antibodies

| End point title | Geometric Mean Titer (GMT) of Mumps Virus Antibodies |
|---|---|

End point description:

Sera were tested for mumps virus IgG antibody levels by ELISA. The population analyzed included participants who received >=1 dose of study vaccine, were seronegative at baseline and had postvaccination mumps virus serology results.

| End point type | Primary |
|---|---|

End point timeframe:

Six weeks after vaccination 1

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 618 | 610 | | |
| Units: Mumps Ab units/mL | | | | |
| geometric mean (confidence interval 95%) | 112.1 (104.1 to 120.7) | 114 (105.8 to 122.8) | | |

### Statistical analyses

| Statistical analysis title | Non-inferiority Analysis |
|---|---|

Statistical analysis description:

The non-inferiority evaluation is based on the lower bound of the 2-sided 95% CI on the GMT ratio, excluding a decrease of >=1.5 fold. Analysis was based on log-transformed titers.

| | |
|---|---|
| Comparison groups | MMRV (AMP) - Received at Least One Vaccination v MMRV (2006 Process) - Received at Least one Vaccination |
| Number of subjects included in analysis | 1228 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[7] |
| P-value | < 0.001 |
| Method | t-test, 2-sided |
| Parameter estimate | GMT Ratio |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.1 |

Notes:

[7] - GMT ratio = MMRV (AMP) / MMRV (2006 process).

### Primary: Geometric Mean Titer (GMT) of Rubella Virus Antibodies

| End point title | Geometric Mean Titer (GMT) of Rubella Virus Antibodies |
|---|---|

End point description:

Sera were tested for rubella virus IgG antibody levels by ELISA. The population analyzed included participants who received >=1 dose of study vaccine, were seronegative at baseline and had postvaccination rubella virus serology results.

| End point type | Primary |
|---|---|

End point timeframe:

Six weeks after vaccination 1

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 608 | 593 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | 81.8 (76.8 to 87.2) | 80.7 (76.4 to 85.2) | | |

### Statistical analyses

| Statistical analysis title | Non-inferiority Analysis |
|---|---|

Statistical analysis description:

The non-inferiority evaluation is based on the lower bound of the 2-sided 95% CI on the GMT ratio, excluding a decrease of >=1.5 fold. Analysis was based on log-transformed titers.

| | |
|---|---|
| Comparison groups | MMRV (AMP) - Received at Least One Vaccination v MMRV (2006 Process) - Received at Least one Vaccination |
| Number of subjects included in analysis | 1201 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[8] |
| P-value | < 0.001 |
| Method | t-test, 2-sided |
| Parameter estimate | GMT Ratio |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.1 |

Notes:

[8] - GMT ratio = MMRV (AMP) / MMRV (2006 process).

### Primary: Percentage of Participants With Fever (>=102.2°F [39.0°C] or Oral Equivalent)

| End point title | Percentage of Participants With Fever (>=102.2°F [39.0°C] or Oral Equivalent) |
|---|---|

End point description:

Daily temperatures were recorded using a standardized Vaccination Report Card (VRC). The percentage of participants with fever (>=102.2°F [39.0°C] or oral equivalent) was assessed. The population analyzed included participants who received >=1 study vaccination and had follow-up safety data.

| End point type | Primary |
|---|---|

End point timeframe:

Up to 5 days after vaccination 1

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 645 | 648 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 0.9 | 0.8 | | |

### Statistical analyses

| Statistical analysis title | Non-inferiority Analysis |
|---|---|

Statistical analysis description:

The non-inferiority evaluation is based on the upper bound of the 2-sided 95% CI on the risk difference excluding an increase >= the prespecified criterion of 5 percentage points.

| Comparison groups | MMRV (AMP) - Received at Least One Vaccination v MMRV (2006 Process) - Received at Least one Vaccination |
|---|---|
| Number of subjects included in analysis | 1293 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[9] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 1.3 |

Notes:

[9] - Risk Difference = MMRV (AMP) - MMRV (2006 process)

### Secondary: Percentage of Participants With Fever (>=102.2°F [39.0°C] or Oral Equivalent)

| End point title | Percentage of Participants With Fever (>=102.2°F [39.0°C] or Oral Equivalent) |
|---|---|

End point description:

Daily temperatures were recorded using a standardized VRC. The percentage of participants with fever (>=102.2°F [39.0°C] or oral equivalent) was assessed. The population analyzed included participants who received >=1 study vaccination and had follow-up safety data.

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

End point timeframe:

Up to 42 days after each vaccination

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 650 | 649 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Vaccination 1: n=650, 649 | 10 | 10.6 | | |
| Vaccination 2: n=592, 597 | 5.7 | 8.4 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Zoster-like Rash

| End point title | Percentage of Participants With Zoster-like Rash |
|---|---|

End point description:

Zoster-like rash was solicited on the standardized VRC. The percentage of participants with zoster-like rash was assessed. The population analyzed included participants who received >=1 study vaccination and had follow-up safety data.

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

End point timeframe:

Up to 42 days after each vaccination

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 682 | 682 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Vaccination 1: n=682, 682 | 0 | 0 | | |
| Vaccination 2: n=634, 632 | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Mumps-like Symptoms

| End point title | Percentage of Participants With Mumps-like Symptoms |
|---|---|

End point description:

Mumps-like symptoms were solicited on the standardized VRC. The percentage of participants with mumps-like symptoms was assessed. The population analyzed included participants who received >=1

study vaccination and had follow-up safety data.

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

End point timeframe:

Up to 42 days after each vaccination

| **End point values** | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 682 | 682 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Vaccination 1: n=682, 682 | 0 | 0 | | |
| Vaccination 2: n=634, 632 | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Measles-like Rash

| End point title | Percentage of Participants With Measles-like Rash |
|---|---|

End point description:

Measles-like rash was solicited on the standardized VRC. The percentage of participants with measles-like rash was assessed. The population analyzed included participants who received >=1 study vaccination and had follow-up safety data.

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

End point timeframe:

Up to 42 days after each vaccination

| **End point values** | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 682 | 682 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Vaccination 1: n=682, 682 | 0.1 | 0.3 | | |
| Vaccination 2: n=634, 632 | 0.2 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Rubella-like Rash

| End point title | Percentage of Participants With Rubella-like Rash |
|---|---|

End point description:

Rubella-like rash was solicited on the standardized VRC. The percentage of participants with rubella-like rash was assessed. The population analyzed included participants who received >=1 study vaccination and had follow-up safety data.

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

End point timeframe:

Up to 42 days after each vaccination

| **End point values** | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 682 | 682 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Vaccination 1: n=682, 682 | 0 | 0 | | |
| Vaccination 2: n=634, 632 | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Varicella-like Rash

| End point title | Percentage of Participants With Varicella-like Rash |
|---|---|

End point description:

Varicella-like rash was solicited on the standardized VRC. The percentage of participants with varicella-like rash was assessed. The population analyzed included participants who received >=1 study vaccination and had follow-up safety data.

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

End point timeframe:

Up to 42 days after each vaccination

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 682 | 682 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Vaccination 1: n=682, 682 | 0.6 | 0 | | |
| Vaccination 2; n=634, 632 | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With an Injection-site Adverse Event

| End point title | Percentage of Participants With an Injection-site Adverse Event |
|---|---|

End point description:

An adverse event (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. Injection-site AEs were solicited on the standardized VRC. The percentage of participants with a VRC-solicited injection-site AE was assessed. The population analyzed included participants who received >=1 study vaccination and had follow-up safety data.

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

End point timeframe:

Up to 5 days after each vaccination

| End point values | MMRV (AMP) - Received at Least One Vaccination | MMRV (2006 Process) - Received at Least one Vaccination | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 682 | 682 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Vaccination 1: n=682, 682 | 36.4 | 29.8 | | |
| Vaccination 2: n=634, 632 | 35.5 | 29.6 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Up to 6 months (180 days) after vaccination 2 | |
| Adverse event reporting additional description: | |
| The population analyzed included randomized participants who received >=1 dose of study vaccine and had safety follow-up results. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 16 |

| Reporting groups | |
|---|---|
| Reporting group title | MMRV (2006 Process) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with the 2006 manufacturing process (MMRV [2006 Process]) | |
| Reporting group title | MMRV (AMP) |
| Reporting group description: | |
| Participants were to received two 0.5 mL subcutaneous injections of Mumps, Measles, Rubella, Varicella vaccine made with an alternative manufacturing process (MMRV [AMP]) | |

| Serious adverse events | MMRV (2006 Process) | MMRV (AMP) | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 18 / 683 (2.64%) | 21 / 682 (3.08%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Exposure via direct contact | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Exposure via ingestion | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body aspiration | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Skull fracture | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Kawasaki's disease | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 4 / 682 (0.59%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 3 / 683 (0.44%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial hyperreactivity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Status asthmaticus | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Juvenile idiopathic arthritis | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 2 / 683 (0.29%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis staphylococcal | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (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 | 2 / 683 (0.29%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 2 / 682 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Groin abscess | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lobar pneumonia | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (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 | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (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 | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 2 / 683 (0.29%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 0 / 682 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal abscess | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 683 (0.15%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vulval abscess | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 683 (0.00%) | 2 / 682 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 683 (0.00%) | 1 / 682 (0.15%) | |
| 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** | MMRV (2006 Process) | MMRV (AMP) | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 572 / 683 (83.75%) | 574 / 682 (84.16%) | |
| General disorders and administration site conditions | | | |
| Injection site pain | | | |
| subjects affected / exposed | 187 / 683 (27.38%) | 208 / 682 (30.50%) | |
| occurrences (all) | 243 | 267 | |
| Injection site erythema | | | |
| subjects affected / exposed | 199 / 683 (29.14%) | 254 / 682 (37.24%) | |
| occurrences (all) | 258 | 344 | |
| Pyrexia | | | |
| subjects affected / exposed | 235 / 683 (34.41%) | 225 / 682 (32.99%) | |
| occurrences (all) | 360 | 349 | |
| Injection site swelling | | | |
| subjects affected / exposed | 123 / 683 (18.01%) | 156 / 682 (22.87%) | |
| occurrences (all) | 146 | 190 | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 46 / 683 (6.73%) | 48 / 682 (7.04%) | |
| occurrences (all) | 47 | 52 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 91 / 683 (13.32%) | 77 / 682 (11.29%) | |
| occurrences (all) | 107 | 98 | |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 61 / 683 (8.93%) | 60 / 682 (8.80%) | |
| occurrences (all) | 72 | 77 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 53 / 683 (7.76%) | 58 / 682 (8.50%) | |
| occurrences (all) | 64 | 78 | |
| Cough | | | |
| subjects affected / exposed | 101 / 683 (14.79%) | 87 / 682 (12.76%) | |
| occurrences (all) | 118 | 113 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis diaper | | | |
| subjects affected / exposed | 77 / 683 (11.27%) | 62 / 682 (9.09%) | |
| occurrences (all) | 106 | 76 | |
| Rash | | | |
| subjects affected / exposed | 47 / 683 (6.88%) | 48 / 682 (7.04%) | |
| occurrences (all) | 55 | 50 | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 41 / 683 (6.00%) | 29 / 682 (4.25%) | |
| occurrences (all) | 43 | 32 | |
| Otitis media acute | | | |
| subjects affected / exposed | 44 / 683 (6.44%) | 56 / 682 (8.21%) | |
| occurrences (all) | 57 | 72 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 66 / 683 (9.66%) | 55 / 682 (8.06%) | |
| occurrences (all) | 76 | 65 | |
| Otitis media | | | |
| subjects affected / exposed | 128 / 683 (18.74%) | 128 / 682 (18.77%) | |
| occurrences (all) | 179 | 177 | |
| Pharyngitis | | | |
| subjects affected / exposed | 35 / 683 (5.12%) | 40 / 682 (5.87%) | |
| occurrences (all) | 43 | 47 | |
| Viral infection | | | |
| subjects affected / exposed | 57 / 683 (8.35%) | 44 / 682 (6.45%) | |
| occurrences (all) | 64 | 52 | |
| Upper respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 163 / 683 (23.87%)<br>212 | 159 / 682 (23.31%)<br>210 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 15 May 2012 | Amendment 1: The amendment incorporated a new primary objective for safety and a new co-primary hypothesis for immunogenicity. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported