



## Clinical trial results:

### Post-marketing, Randomized, Open-label Study to Assess the Immunogenicity and Safety of Concomitant Administration of V260 and Diphtheria, Tetanus, Pertussis and Inactivated Poliovirus Vaccine (DTP-IPV) in Japanese Healthy Infants

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-000277-37 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 06 June 2014   |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 26 May 2017  |
| First version publication date | 26 May 2017  |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | V260-060 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01926015 |
| 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,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp,<br>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                       | 09 September 2014 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 06 June 2014      |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

The study evaluated the immunogenicity of DTP-IPV (Tetrabik<sup>TM</sup>) with concomitant administration of RotaTeq<sup>TM</sup> (V260) in healthy Japanese infants. The hypothesis to be tested was that the antibody response rates to DTP-IPV with concomitant administration of RotaTeq<sup>TM</sup> were non-inferior to those with staggered administration of RotaTeq<sup>TM</sup>.

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                          | 19 September 2013 |
| 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 | Japan: 192 |
| Worldwide total number of subjects   | 192        |
| 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)  | 192 |
| 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: -

### Pre-assignment

Screening details:

A total of 193 participants' parents/legal guardians agreed to participate by giving written informed consent for study participation. Of these, a total of 192 participants were randomised and 190 participants received study vaccinations; 2 participants were randomised but did not receive study vaccination.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Randomisation and Overall Treatment (overall period) |
| Is this the baseline period? | Yes  |
| Allocation method            | Randomised - controlled                              |
| Blinding used                | Not blinded  |

### Arms

|                              |                                 |
|------------------------------|---------------------------------|
| Are arms mutually exclusive? | Yes                             |
| <b>Arm title</b>             | Concomitant RotaTeqTM + DTP-IPV |

Arm description:

RotaTeqTM (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | RotaTeqTM     |
| Investigational medicinal product code |               |
| Other name                             | V260          |
| Pharmaceutical forms                   | Oral solution |
| Routes of administration               | Oral use      |

Dosage and administration details:

Live, oral, pentavalent vaccine containing 5 human-bovine reassortant rotavirus strains. 2 mL oral administration at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

|  |                  |
|--|------------------|
| Investigational medicinal product name | DTP-IPV          |
| Investigational medicinal product code |                  |
| Other name                             | TetrabikTM       |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Diphtheria, tetanus, pertussis, inactivated polio vaccine used as part of the Japanese vaccination schedule. 0.5 mL subcutaneous injection at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | Staggered RotaTeqTM + DTP-IPV |
|------------------|-------------------------------|

Arm description:

RotaTeqTM (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | RotaTeqTM     |
| Investigational medicinal product code |               |
| Other name                             | V260          |
| Pharmaceutical forms                   | Oral solution |
| Routes of administration               | Oral use      |

---

**Dosage and administration details:**

Live, oral, pentavalent vaccine containing 5 human-bovine reassortant rotavirus strains. 2 mL oral administration at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

|  |                  |
|--|------------------|
| Investigational medicinal product name | DTP-IPV          |
| Investigational medicinal product code |                  |
| Other name                             | TetrabikTM       |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

**Dosage and administration details:**

Diphtheria, tetanus, pertussis, inactivated polio vaccine used as part of the Japanese vaccination schedule. 0.5 mL subcutaneous injection at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

| <b>Number of subjects in period 1</b> | Concomitant<br>RotaTeqTM + DTP-<br>IPV | Staggered<br>RotaTeqTM + DTP-<br>IPV |
|---------------------------------------|--|--------------------------------------|
| Started                               | 96                                     | 96                                   |
| Received $\geq 1$ Vaccination         | 94                                     | 96                                   |
| Completed                             | 94                                     | 95                                   |
| Not completed                         | 2                                      | 1                                    |
| Withdrawal By Parent/Guardian         | -                                      | 1                                    |
| Randomised Not Treated                | 2                                      | -                                    |

## Baseline characteristics

### Reporting groups

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Concomitant RotaTeq™ + DTP-IPV |
|-----------------------|--------------------------------|

Reporting group description:

RotaTeq™ (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Staggered RotaTeq™ + DTP-IPV |
|-----------------------|------------------------------|

Reporting group description:

RotaTeq™ (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

| Reporting group values   | Concomitant<br>RotaTeq™ + DTP-<br>IPV | Staggered<br>RotaTeq™ + DTP-<br>IPV | Total |
|--|---------------------------------------|-------------------------------------|-------|
| Number of subjects   | 96                                    | 96                                  | 192   |
| Age Categorical<br>Units: Subjects                               |                                       |                                     |       |
| Age Continuous<br>Units: weeks<br>median<br>full range (min-max) | 8<br>6 to 10                          | 9<br>6 to 10                        | -     |
| Gender Categorical<br>Units: Subjects                            |                                       |                                     |       |
| Female   | 47                                    | 41                                  | 88    |
| Male   | 49                                    | 55                                  | 104   |

### Subject analysis sets

|                            |                                |
|----------------------------|--------------------------------|
| Subject analysis set title | Concomitant RotaTeq™ + DTP-IPV |
|----------------------------|--------------------------------|

|                           |              |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

RotaTeq™ (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

|                            |                              |
|----------------------------|------------------------------|
| Subject analysis set title | Staggered RotaTeq™ + DTP-IPV |
|----------------------------|------------------------------|

|                           |              |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

RotaTeq™ (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

| Reporting group values             | Concomitant<br>RotaTeq™ + DTP-<br>IPV | Staggered<br>RotaTeq™ + DTP-<br>IPV |  |
|------------------------------------|---------------------------------------|-------------------------------------|--|
| Number of subjects                 | 93                                    | 94                                  |  |
| Age Categorical<br>Units: Subjects |                                       |                                     |  |

|                      |         |         |  |
|----------------------|---------|---------|--|
| Age Continuous       |         |         |  |
| Units: weeks         |         |         |  |
| median               | 8       | 9       |  |
| full range (min-max) | 6 to 10 | 6 to 10 |  |
| Gender Categorical   |         |         |  |
| Units: Subjects      |         |         |  |
| Female               |         |         |  |
| Male                 |         |         |  |

---

## End points

### End points reporting groups

|  |                                |
|--|--------------------------------|
| Reporting group title  | Concomitant RotaTeq™ + DTP-IPV |
| Reporting group description:<br>RotaTeq™ (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 ( $\geq 4$ weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)  |                                |
| Reporting group title  | Staggered RotaTeq™ + DTP-IPV   |
| Reporting group description:<br>RotaTeq™ (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 ( $\geq 4$ weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)      |                                |
| Subject analysis set title   | Concomitant RotaTeq™ + DTP-IPV |
| Subject analysis set type  | Per protocol                   |
| Subject analysis set description:<br>RotaTeq™ (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 ( $\geq 4$ weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)   |                                |
| Subject analysis set title   | Staggered RotaTeq™ + DTP-IPV   |
| Subject analysis set type  | Per protocol                   |
| Subject analysis set description:<br>RotaTeq™ (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 ( $\geq 4$ weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4) |                                |

### Primary: Percentage of Participants Who Achieved a Serologic Response for Diphtheria Toxin, Tetanus Toxin, Pertussis Toxin, Pertussis Filamentous Hemagglutinin (FHA) and Poliovirus (PV) Type 1/2/3

|   |   |
|---|---|
| End point title   | Percentage of Participants Who Achieved a Serologic Response for Diphtheria Toxin, Tetanus Toxin, Pertussis Toxin, Pertussis Filamentous Hemagglutinin (FHA) and Poliovirus (PV) Type 1/2/3 |
| End point description:<br>Participant serum was collected for determination of antibody responses. Threshold levels for serologic response were the following: Diphtheria Toxin, $\geq 0.1$ International Units (IU)/mL; Tetanus Toxin, $\geq 0.01$ IU/mL; Pertussis Toxin and Pertussis FHA, $\geq 10$ Enzyme Units (EU)/mL; Poliovirus Types 1, 2, and 3, neutralising antibody (NA) titer $\geq 8$ . |   |
| End point type  | Primary   |
| End point timeframe:<br>4 to 6 weeks after the third dose of DTP-IPV  |   |

| End point values                  | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|-----------------------------------|--------------------------------|------------------------------|--|--|
| Subject group type                | Subject analysis set           | Subject analysis set         |  |  |
| Number of subjects analysed       | 93                             | 94                           |  |  |
| Units: Percentage of participants |                                |                              |  |  |
| number (not applicable)           |                                |                              |  |  |
| Diphtheria Toxin $\geq 0.1$ IU/mL | 100                            | 100                          |  |  |
| Tetanus Toxin $\geq 0.01$ IU/mL   | 100                            | 100                          |  |  |
| Pertussis Toxin $\geq 10$ EU/mL   | 100                            | 100                          |  |  |
| Pertussis FHA $\geq 10$ EU/mL     | 100                            | 100                          |  |  |
| Poliovirus Type 1 NA $\geq 8$     | 100                            | 100                          |  |  |

|                               |     |     |  |  |
|-------------------------------|-----|-----|--|--|
| Poliovirus Type 2 NA $\geq 8$ | 100 | 100 |  |  |
| Poliovirus Type 3 NA $\geq 8$ | 100 | 100 |  |  |

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Compared Seroprotection Against Diphtheria Toxin              |
| Comparison groups                       | Staggered RotaTeq™ + DTP-IPV v Concomitant RotaTeq™ + DTP-IPV |
| Number of subjects included in analysis | 187   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority <sup>[1]</sup>                                |
| P-value                                 | < 0.001   |
| Method                                  | Miettinen and Nurminen  |
| Parameter estimate                      | Difference in Serologic Response Rates                        |
| Point estimate                          | 0   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -3.99   |
| upper limit                             | 3.95  |

Notes:

[1] - The infection control threshold level for seroprotection against Diphtheria Toxin is  $\geq 0.1$  IU/mL. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference  $\geq 10\%$ , is  $\geq -0.10$ .

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Compared Seroprotection Against Diphtheria Toxin              |
| Comparison groups                       | Concomitant RotaTeq™ + DTP-IPV v Staggered RotaTeq™ + DTP-IPV |
| Number of subjects included in analysis | 187   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority <sup>[2]</sup>                                |
| P-value                                 | < 0.001   |
| Method                                  | Miettinen and Nurminen  |
| Parameter estimate                      | Difference in Serologic Response Rates                        |
| Point estimate                          | 0   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -3.99   |
| upper limit                             | 3.95  |

Notes:

[2] - The infection control threshold level for seroprotection against Tetanus Toxin is  $\geq 0.01$  IU/mL. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference  $\geq 10\%$ , is  $\geq -0.10$ .

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Compared Seroprotection Against Pertussis Toxin               |
| Comparison groups                 | Concomitant RotaTeq™ + DTP-IPV v Staggered RotaTeq™ + DTP-IPV |



|   |  |
|---|--|
| Number of subjects included in analysis | 187                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | non-inferiority <sup>[3]</sup>         |
| P-value                                 | < 0.001                                |
| Method                                  | Miettinen and Nurminen                 |
| Parameter estimate                      | Difference in Serologic Response Rates |
| Point estimate                          | 0                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -3.99                                  |
| upper limit                             | 3.95                                   |

Notes:

[3] - The infection control threshold level for seroprotection against Pertussis Toxin is  $\geq 10$  EU/mL. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference  $\geq 10\%$ , is  $\geq -0.10$ .

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Compared Seroprotection Against Pertussis FHA                 |
| Comparison groups                       | Concomitant RotaTeq™ + DTP-IPV v Staggered RotaTeq™ + DTP-IPV |
| Number of subjects included in analysis | 187   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority <sup>[4]</sup>                                |
| P-value                                 | < 0.001   |
| Method                                  | Miettinen and Nurminen  |
| Parameter estimate                      | Difference in Serologic Response Rates                        |
| Point estimate                          | 0   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -3.99   |
| upper limit                             | 3.95  |

Notes:

[4] - The infection control threshold level for seroprotection against Pertussis FHA is  $\geq 10$  EU/mL. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference  $\geq 10\%$ , is  $\geq -0.10$ .

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Compared Seroprotection Against PV Type 1                     |
| Comparison groups                       | Concomitant RotaTeq™ + DTP-IPV v Staggered RotaTeq™ + DTP-IPV |
| Number of subjects included in analysis | 187   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority <sup>[5]</sup>                                |
| P-value                                 | < 0.001   |
| Method                                  | Miettinen and Nurminen  |
| Parameter estimate                      | Difference in Serologic Response Rates                        |
| Point estimate                          | 0   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -3.99   |
| upper limit                             | 3.95  |

Notes:

[5] - The infection control threshold level for seroprotection against PV Type 1 is neutralising antibody titer (NA)  $\geq 8$ . Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference  $\geq 10\%$ , is  $\geq -0.10$ .

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Compared Seroprotection Against PV Type 2                     |
| Comparison groups                       | Concomitant RotaTeq™ + DTP-IPV v Staggered RotaTeq™ + DTP-IPV |
| Number of subjects included in analysis | 187   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority <sup>[6]</sup>                                |
| P-value                                 | $< 0.001$   |
| Method                                  | Miettinen and Nurminen  |
| Parameter estimate                      | Difference in Serologic Response Rates                        |
| Point estimate                          | 0   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -3.99   |
| upper limit                             | 3.95  |

Notes:

[6] - The infection control threshold level for seroprotection against PV Type 2 is NA  $\geq 8$ . Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference  $\geq 10\%$ , is  $\geq -0.10$ .

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Compared Seroprotection Against PV Type 3                     |
| Comparison groups                       | Concomitant RotaTeq™ + DTP-IPV v Staggered RotaTeq™ + DTP-IPV |
| Number of subjects included in analysis | 187   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority <sup>[7]</sup>                                |
| P-value                                 | $< 0.001$   |
| Method                                  | Miettinen and Nurminen  |
| Parameter estimate                      | Difference in Serologic Response Rates                        |
| Point estimate                          | 0   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -3.99   |
| upper limit                             | 3.95  |

Notes:

[7] - The infection control threshold level for seroprotection against PV Type 3 is NA  $\geq 8$ . Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference  $\geq 10\%$ , is  $\geq -0.10$ .

## **Secondary: Percentage of Participants Reporting an Adverse Event With Incidence $\geq 1\%$**

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Reporting an Adverse Event With Incidence $\geq 1\%$ |
|-----------------|---|

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events with an incidence  $\geq 1\%$  in either treatment group were recorded. Each participant was counted only once within a study Period and only once Overall.

|   |           |
|---|-----------|
| End point type                                | Secondary |
| End point timeframe:                          |           |
| Up to 14 days after any of the 6 study visits |           |

| End point values                  | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|-----------------------------------|--------------------------------|------------------------------|--|--|
| Subject group type                | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed       | 94                             | 96                           |  |  |
| Units: Percentage of participants |                                |                              |  |  |
| number (not applicable)           | 68.1                           | 86.5                         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Reporting an Adverse Event of Special Interest: Fever

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Reporting an Adverse Event of Special Interest: Fever |
|-----------------|--|

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events of special interest included fever, diarrhoea, vomiting, and injection-site adverse events. The safety population included randomised participants who received  $\geq 1$  dose of study vaccine and had safety follow-up. Each participant was counted only once within a study Period and only once Overall.

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

End point timeframe:

Period 1 (up to 14 days after Visit 1 [V1] or V2), Period 2 (up to 14 days after V3 or V4), Period 3 (up to 14 days after V5 or V6), and Overall (up to 14 days after any visit)

| End point values                                      | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|---|--------------------------------|------------------------------|--|--|
| Subject group type                                    | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed                           | 94                             | 96                           |  |  |
| Units: Percentage of participants                     |                                |                              |  |  |
| number (not applicable)                               |                                |                              |  |  |
| Period 1 (up to 14 days after V1 or V2)<br>(n=94, 96) | 5.3                            | 6.3                          |  |  |
| Period 2 (up to 14 days after V3 or V4)<br>(n=94, 96) | 1.1                            | 12.5                         |  |  |
| Period 3 (up to 14 days after V5 or V6)(n=94, 95)     | 4.3                            | 6.3                          |  |  |
| Overall (up to 14 days after any visit)(n=94, 96)     | 10.6                           | 22.9                         |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Reporting an Adverse Event of Special Interest: Diarrhoea

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Reporting an Adverse Event of Special Interest: Diarrhoea |
|-----------------|--|

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events of special interest included fever, diarrhea, vomiting, and injection-site adverse events. The safety population included randomized participants who received  $\geq 1$  dose of study vaccine and had safety follow-up. Each participant was counted only once within a study Period and only once Overall.

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

End point timeframe:

Period 1 (up to 14 days after Visit 1 [V1] or V2), Period 2 (up to 14 days after V3 or V4), Period 3 (up to 14 days after V5 or V6), and Overall (up to 14 days after any visit)

| End point values                                      | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|---|--------------------------------|------------------------------|--|--|
| Subject group type                                    | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed                           | 94                             | 96                           |  |  |
| Units: Percentage of participants                     |                                |                              |  |  |
| number (not applicable)                               |                                |                              |  |  |
| Period 1 (up to 14 days after V1 or V2)<br>(n=94, 96) | 17                             | 31.3                         |  |  |
| Period 2 (up to 14 days after V3 or V4)<br>(n=94, 96) | 10.6                           | 20.8                         |  |  |
| Period 3 (up to 14 days after V5 or V6)<br>(n=94, 95) | 7.4                            | 18.9                         |  |  |
| Overall (up to 14 days after any visit)(n=94, 96)     | 25.5                           | 46.9                         |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Reporting an Adverse Event of Special Interest: Vomiting

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Reporting an Adverse Event of Special Interest: Vomiting |
|-----------------|---|

**End point description:**

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events of special interest included fever, diarrhoea, vomiting, and injection-site adverse events. The safety population included randomized participants who received  $\geq 1$  dose of study vaccine and had safety follow-up. Each participant was counted only once within a study Period and only once Overall.

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

**End point timeframe:**

Period 1 (up to 14 days after Visit 1 [V1] or V2), Period 2 (up to 14 days after V3 or V4), Period 3 (up to 14 days after V5 or V6), and Overall (up to 14 days after any visit)

| <b>End point values</b>                               | Concomitant RotaTeq <sup>TM</sup> + DTP-IPV | Staggered RotaTeq <sup>TM</sup> + DTP-IPV |  |  |
|---|---|---|--|--|
| Subject group type                                    | Reporting group                             | Reporting group                           |  |  |
| Number of subjects analysed                           | 94  | 96  |  |  |
| Units: Percentage of participants                     |   |   |  |  |
| number (not applicable)                               |   |   |  |  |
| Period 1 (up to 14 days after V1 or V2)<br>(n=94, 96) | 5.3   | 9.4                                       |  |  |
| Period 2 (up to 14 days after V3 or V4)<br>(n=94, 96) | 3.2   | 6.3                                       |  |  |
| Period 3 (up to 14 days after V5 or V6)<br>(n=94, 95) | 1.1   | 4.2                                       |  |  |
| Overall (up to 14 days after any visit)<br>(n=94, 96) | 8.5   | 16.7                                      |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of Participants Reporting an Adverse Event of Special Interest: Injection-site Adverse Events**

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Reporting an Adverse Event of Special Interest: Injection-site Adverse Events |
|-----------------|--|

**End point description:**

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events of special interest included fever, diarrhoea, vomiting, and injection-site adverse events. The safety population included randomized participants who received  $\geq 1$  dose of study vaccine and had safety follow-up. Each participant was counted only once within a study Period and only once Overall.

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

**End point timeframe:**

Period 1 (up to 14 days after Visit 1 [V1] or V2), Period 2 (up to 14 days after V3 or V4), Period 3 (up to 14 days after V5 or V6), and Overall (up to 14 days after any visit)

| End point values                                      | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|---|--------------------------------|------------------------------|--|--|
| Subject group type                                    | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed                           | 94                             | 96                           |  |  |
| Units: Percentage of participants                     |                                |                              |  |  |
| number (not applicable)                               |                                |                              |  |  |
| Period 1 (up to 14 days after V1 or V2)<br>(n=94, 96) | 2.1                            | 4.2                          |  |  |
| Period 2 (up to 14 days after V3 or V4)<br>(n=94, 96) | 0                              | 8.3                          |  |  |
| Period 3 (up to 14 days after V5 or V6)<br>(n=94, 95) | 0                              | 2.1                          |  |  |
| Overall (up to 14 days after any visit)<br>(n=94, 96) | 2.1                            | 10.4                         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers for Diphtheria Toxin Antibody

|                 |   |
|-----------------|---|
| End point title | Geometric Mean Titers for Diphtheria Toxin Antibody |
|-----------------|---|

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

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

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

| End point values                             | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|--|--------------------------------|------------------------------|--|--|
| Subject group type                           | Subject analysis set           | Subject analysis set         |  |  |
| Number of subjects analysed                  | 93                             | 94                           |  |  |
| Units: IU/mL                                 |                                |                              |  |  |
| geometric mean (confidence interval 95%)     |                                |                              |  |  |
| Baseline                                     | 0.025 (0.018 to 0.034)         | 0.019 (0.014 to 0.026)       |  |  |
| 4 to 6 weeks after the third dose of DTP-IPV | 2.377 (2.032 to 2.78)          | 2.493 (2.165 to 2.871)       |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Geometric Mean Titers for Tetanus Toxin Antibody**

|                 |  |
|-----------------|--|
| End point title | Geometric Mean Titers for Tetanus Toxin Antibody |
|-----------------|--|

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

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

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

| End point values                             | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|--|--------------------------------|------------------------------|--|--|
| Subject group type                           | Subject analysis set           | Subject analysis set         |  |  |
| Number of subjects analysed                  | 93                             | 94                           |  |  |
| Units: IU/mL                                 |                                |                              |  |  |
| geometric mean (confidence interval 95%)     |                                |                              |  |  |
| Baseline                                     | 0.082 (0.059 to 0.114)         | 0.093 (0.067 to 0.128)       |  |  |
| 4 to 6 weeks after the third dose of DTP-IPV | 1.001 (0.702 to 1.428)         | 1.338 (1.009 to 1.774)       |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Geometric Mean Titers for Pertussis Toxin Antibody**

|                 |  |
|-----------------|--|
| End point title | Geometric Mean Titers for Pertussis Toxin Antibody |
|-----------------|--|

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

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

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

| End point values                         | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|--|--------------------------------|------------------------------|--|--|
| Subject group type                       | Subject analysis set           | Subject analysis set         |  |  |
| Number of subjects analysed              | 93                             | 94                           |  |  |
| Units: EU/mL                             |                                |                              |  |  |
| geometric mean (confidence interval 95%) |                                |                              |  |  |

|  |                             |                              |  |  |
|--|-----------------------------|------------------------------|--|--|
| Baseline                                     | 2.67 (2.143 to 3.328)       | 2.757 (2.278 to 3.338)       |  |  |
| 4 to 6 weeks after the third dose of DTP-IPV | 198.811 (177.43 to 222.768) | 241.857 (218.225 to 268.049) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers for Pertussis FHA Antibody

|   |  |
|---|--|
| End point title   | Geometric Mean Titers for Pertussis FHA Antibody |
| End point description:  |  |
| Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV   |  |

| End point values                             | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|--|--------------------------------|------------------------------|--|--|
| Subject group type                           | Subject analysis set           | Subject analysis set         |  |  |
| Number of subjects analysed                  | 93 <sup>[8]</sup>              | 94                           |  |  |
| Units: EU/mL                                 |                                |                              |  |  |
| geometric mean (confidence interval 95%)     |                                |                              |  |  |
| Baseline                                     | 7.513 (6.285 to 8.98)          | 6.951 (5.703 to 8.472)       |  |  |
| 4 to 6 weeks after the third dose of DTP-IPV | 77.386 (67.959 to 88.119)      | 88.275 (76.065 to 102.445)   |  |  |

Notes:

[8] - 6.951

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers for Poliovirus Type 1 Antibody

|   |  |
|---|--|
| End point title   | Geometric Mean Titers for Poliovirus Type 1 Antibody |
| End point description:  |  |
| Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. Poliovirus antibodies are expressed as neutralising antibody (NA) titers. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint. |  |
| End point type  | Secondary  |



End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

| End point values                             | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|--|--------------------------------|------------------------------|--|--|
| Subject group type                           | Subject analysis set           | Subject analysis set         |  |  |
| Number of subjects analysed                  | 93                             | 94                           |  |  |
| Units: NA titer                              |                                |                              |  |  |
| geometric mean (confidence interval 95%)     |                                |                              |  |  |
| Baseline                                     | 23.5 (17.21 to 32.05)          | 21.1 (15.47 to 28.76)        |  |  |
| 4 to 6 weeks after the third dose of DTP-IPV | 1578 (1237.3 to 2012)          | 1703 (1314.4 to 2207)        |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers for Poliovirus Type 2 Antibody

|                 |  |
|-----------------|--|
| End point title | Geometric Mean Titers for Poliovirus Type 2 Antibody |
|-----------------|--|

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. Poliovirus antibodies are expressed as neutralising antibody (NA) titers. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

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

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

| End point values                             | Concomitant RotaTeq™ + DTP-IPV | Staggered RotaTeq™ + DTP-IPV |  |  |
|--|--------------------------------|------------------------------|--|--|
| Subject group type                           | Subject analysis set           | Subject analysis set         |  |  |
| Number of subjects analysed                  | 93                             | 94                           |  |  |
| Units: NA titer                              |                                |                              |  |  |
| geometric mean (confidence interval 95%)     |                                |                              |  |  |
| Baseline                                     | 32 (23.97 to 42.72)            | 27.8 (20.64 to 37.49)        |  |  |
| 4 to 6 weeks after the third dose of DTP-IPV | 2886 (2346.9 to 3547.8)        | 3259 (2678.2 to 3965.8)      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Titers for Poliovirus Type 3 Antibody

|                 |  |
|-----------------|--|
| End point title | Geometric Mean Titers for Poliovirus Type 3 Antibody |
|-----------------|--|

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. Poliovirus antibodies are expressed as neutralising (NA) titers. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

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

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

| End point values                                | Concomitant<br>RotaTeq™ +<br>DTP-IPV | Staggered<br>RotaTeq™ +<br>DTP-IPV |  |  |
|---|--------------------------------------|------------------------------------|--|--|
| Subject group type                              | Subject analysis set                 | Subject analysis set               |  |  |
| Number of subjects analysed                     | 93                                   | 94                                 |  |  |
| Units: NA titer                                 |                                      |                                    |  |  |
| geometric mean (confidence interval<br>95%)     |                                      |                                    |  |  |
| Baseline  | 3.9 (3.43 to<br>4.43)                | 4.8 (3.92 to<br>5.85)              |  |  |
| 4 to 6 weeks after the third dose of<br>DTP-IPV | 2377 (1973.1<br>to 2864)             | 2671 (2193.5<br>to 3251.5)         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All adverse events: up to 14 days after any study visit; all deaths, vaccine-related serious adverse events, overdoses, and intussusception: up to 26 weeks after Visit 1

Adverse event reporting additional description:

The safety population included randomised participants who received  $\geq 1$  dose of study vaccine and had safety follow-up.

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Staggered RotaTeq <sup>TM</sup> + DTP-IPV |
|-----------------------|---|

Reporting group description:

RotaTeq<sup>TM</sup> (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

|                       |   |
|-----------------------|---|
| Reporting group title | Concomitant RotaTeq <sup>TM</sup> + DTP-IPV |
|-----------------------|---|

Reporting group description:

RotaTeq<sup>TM</sup> (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 ( $\geq 4$  weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

| Serious adverse events                            | Staggered<br>RotaTeq <sup>TM</sup> + DTP-<br>IPV | Concomitant<br>RotaTeq <sup>TM</sup> + DTP-<br>IPV |  |
|---|--|--|--|
| Total subjects affected by serious adverse events |  |  |  |
| subjects affected / exposed                       | 2 / 96 (2.08%)                                   | 0 / 94 (0.00%)                                     |  |
| number of deaths (all causes)                     | 0  | 0  |  |
| number of deaths resulting from adverse events    | 0  | 0  |  |
| Respiratory, thoracic and mediastinal disorders   |  |  |  |
| Upper respiratory tract inflammation              |  |  |  |
| subjects affected / exposed                       | 1 / 96 (1.04%)                                   | 0 / 94 (0.00%)                                     |  |
| occurrences causally related to treatment / all   | 0 / 1  | 0 / 0  |  |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0  |  |
| Infections and infestations                       |  |  |  |
| Pneumonia respiratory syncytial viral             |  |  |  |
| subjects affected / exposed                       | 1 / 96 (1.04%)                                   | 0 / 94 (0.00%)                                     |  |
| occurrences causally related to treatment / all   | 0 / 1  | 0 / 0  |  |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0  |  |

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

| <b>Non-serious adverse events</b>                     | Staggered<br>RotaTeq™ + DTP-<br>IPV | Concomitant<br>RotaTeq™ + DTP-<br>IPV |  |
|---|-------------------------------------|---------------------------------------|--|
| Total subjects affected by non-serious adverse events |                                     |                                       |  |
| subjects affected / exposed                           | 79 / 96 (82.29%)                    | 57 / 94 (60.64%)                      |  |
| General disorders and administration site conditions  |                                     |                                       |  |
| Injection site erythema                               |                                     |                                       |  |
| subjects affected / exposed                           | 5 / 96 (5.21%)                      | 2 / 94 (2.13%)                        |  |
| occurrences (all)                                     | 7                                   | 2                                     |  |
| Pyrexia   |                                     |                                       |  |
| subjects affected / exposed                           | 22 / 96 (22.92%)                    | 10 / 94 (10.64%)                      |  |
| occurrences (all)                                     | 27                                  | 10                                    |  |
| Gastrointestinal disorders                            |                                     |                                       |  |
| Diarrhoea   |                                     |                                       |  |
| subjects affected / exposed                           | 45 / 96 (46.88%)                    | 24 / 94 (25.53%)                      |  |
| occurrences (all)                                     | 86                                  | 41                                    |  |
| Infantile spitting up                                 |                                     |                                       |  |
| subjects affected / exposed                           | 6 / 96 (6.25%)                      | 0 / 94 (0.00%)                        |  |
| occurrences (all)                                     | 7                                   | 0                                     |  |
| Vomiting  |                                     |                                       |  |
| subjects affected / exposed                           | 16 / 96 (16.67%)                    | 8 / 94 (8.51%)                        |  |
| occurrences (all)                                     | 23                                  | 15                                    |  |
| Respiratory, thoracic and mediastinal disorders       |                                     |                                       |  |
| Rhinorrhoea   |                                     |                                       |  |
| subjects affected / exposed                           | 7 / 96 (7.29%)                      | 7 / 94 (7.45%)                        |  |
| occurrences (all)                                     | 8                                   | 8                                     |  |
| Upper respiratory tract inflammation                  |                                     |                                       |  |
| subjects affected / exposed                           | 12 / 96 (12.50%)                    | 9 / 94 (9.57%)                        |  |
| occurrences (all)                                     | 18                                  | 10                                    |  |
| Skin and subcutaneous tissue disorders                |                                     |                                       |  |
| Dermatitis diaper                                     |                                     |                                       |  |
| subjects affected / exposed                           | 9 / 96 (9.38%)                      | 6 / 94 (6.38%)                        |  |
| occurrences (all)                                     | 9                                   | 6                                     |  |
| Eczema infantile                                      |                                     |                                       |  |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 7 / 96 (7.29%)<br>7 | 7 / 94 (7.45%)<br>7 |  |
| Infections and infestations                      |                     |                     |  |
| Bronchitis                                       |                     |                     |  |
| subjects affected / exposed                      | 4 / 96 (4.17%)      | 5 / 94 (5.32%)      |  |
| occurrences (all)                                | 5                   | 5                   |  |
| Conjunctivitis                                   |                     |                     |  |
| subjects affected / exposed                      | 6 / 96 (6.25%)      | 2 / 94 (2.13%)      |  |
| occurrences (all)                                | 6                   | 2                   |  |
| Nasopharyngitis                                  |                     |                     |  |
| subjects affected / exposed                      | 20 / 96 (20.83%)    | 7 / 94 (7.45%)      |  |
| occurrences (all)                                | 24                  | 7                   |  |
| Upper respiratory tract infection                |                     |                     |  |
| subjects affected / exposed                      | 12 / 96 (12.50%)    | 9 / 94 (9.57%)      |  |
| occurrences (all)                                | 15                  | 10                  |  |

## **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