



## Clinical trial results:

**A phase III, double-blind, randomised, placebo-controlled, multi-centre study to assess the efficacy, immunogenicity and safety of two doses of GSK Biologicals' oral live attenuated liquid human rotavirus (HRV) vaccine in healthy Chinese infants**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-005200-18 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 12 May 2012    |

### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 28 October 2022   |
| First version publication date | 11 June 2015  |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Correction of full data set and alignment between registries. |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 113808 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01171963 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

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

Notes:

### Paediatric regulatory details

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

Notes:

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**Results analysis stage**

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|  |             |
|--|-------------|
| Analysis stage                                       | Final       |
| Date of interim/final analysis                       | 12 May 2012 |
| Is this the analysis of the primary completion data? | Yes         |
| Primary completion date                              | 12 May 2012 |
| Global end of trial reached?                         | Yes         |
| Global end of trial date                             | 12 May 2012 |
| Was the trial ended prematurely?                     | No          |

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the efficacy of two doses of GSK Biologicals' liquid human rotavirus (HRV) vaccine against severe RV GE caused by the circulating wild-type RV strains during the efficacy follow-up period.  
Criteria: The primary objective will be reached if the lower limit of the 95 percent (%) Confidence Interval (CI) on vaccine efficacy is at least 10%.

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Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 29 August 2010 |
| Long term follow-up planned                               | No             |
| Independent data monitoring committee (IDMC) involvement? | No             |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | China: 3340 |
| Worldwide total number of subjects   | 3340        |
| EEA total number of subjects         | 0           |

Notes:

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**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)  | 3340 |
| 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:

Duration of the study was of a maximum of 21 months, with the enrolment of subjects starting in August 2010, and subjects being followed up to May 2012 (study Month 21 and Study End), end of the rotavirus season in China.

### Pre-assignment

Screening details:

Subjects were assigned to 2 sub-cohorts (1:1 ratio). Sub-cohort 1 and Sub-cohort 2 subjects received their OPV and Infanrix EPI vaccination respectively independently of, and concomitantly with their Rotarix/placebo vaccination. 3340 subjects were allocated study subject number allocated and 3333 subjects were vaccinated.

### Period 1

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

### Arms

|                              |               |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes           |
| <b>Arm title</b>             | Rotarix Group |

Arm description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Rotarix vaccine, liquid formulation, at Day 0 and at Month 1. As part of the routine childhood vaccination according to the Expanded Program of Immunization (EPI) recommendations in China, subjects in this group also received 3 doses of Infanrix vaccine and 3 doses of the oral poliovirus vaccine (OPV) manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences. The Infanrix and the OPV vaccines were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Rotarix vaccine. When administered concomitantly, subjects received the 3 doses of Infanrix vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Rotarix and OPV vaccines were administered orally; the Infanrix vaccine was administered intramuscularly in the left anterolateral thigh.

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Rotarix         |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Oral suspension |
| Routes of administration               | Oral use        |

Dosage and administration details:

2 doses of Rotarix administered orally at Day 0 and at Month 1.

|  |   |
|--|---|
| Investigational medicinal product name | Infanrix  |
| Investigational medicinal product code |   |
| Other name                             | Diphtheria, Tetanus, acellular Pertussis vaccine (DTPa) |
| Pharmaceutical forms                   | Suspension for injection                                |
| Routes of administration               | Intramuscular use                                       |

Dosage and administration details:

3 doses of Infanrix administered intramuscularly in the left anterolateral thigh at Months 1, 2 and 3.

|  |                               |
|--|-------------------------------|
| Investigational medicinal product name | Oral poliovirus vaccine (OPV) |
| Investigational medicinal product code |                               |
| Other name                             |                               |
| Pharmaceutical forms                   | Oral liquid                   |
| Routes of administration               | Oral use                      |

Dosage and administration details:

3 doses of OPV administered orally at Day 0, Month 1 and Month 2.

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Placebo Group |
|------------------|---------------|

Arm description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Placebo at Day 0 and at Month 1. As part of the routine childhood vaccination according to the EPI recommendations in China, subjects in this group also received 3 doses of Infanrix vaccine and 3 doses of the oral poliovirus vaccine manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences. The Infanrix and the OPV vaccine were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Placebo. When administered concomitantly, subjects received the 3 doses of Infanrix vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Placebo and the OPV vaccine were administered orally; the Infanrix vaccine was administered intramuscularly in the left anterolateral thigh.

|  |           |
|--|-----------|
| Arm type                               | Placebo   |
| Investigational medicinal product name | Placebo   |
| Investigational medicinal product code |           |
| Other name                             |           |
| Pharmaceutical forms                   | Injection |
| Routes of administration               | Oral use  |

Dosage and administration details:

2 doses of placebo administered orally at Day 0 and Month 1.

|  |   |
|--|---|
| Investigational medicinal product name | Infanrix  |
| Investigational medicinal product code |   |
| Other name                             | Diphtheria, Tetanus, acellular Pertussis vaccine (DTPa) |
| Pharmaceutical forms                   | Suspension for injection                                |
| Routes of administration               | Intramuscular use                                       |

Dosage and administration details:

3 doses of Infanrix administered intramuscularly in the left anterolateral thigh at Months 1, 2 and 3.

|  |                               |
|--|-------------------------------|
| Investigational medicinal product name | Oral poliovirus vaccine (OPV) |
| Investigational medicinal product code |                               |
| Other name                             |                               |
| Pharmaceutical forms                   | Oral liquid                   |
| Routes of administration               | Oral use                      |

Dosage and administration details:

3 doses of OPV administered orally at Day 0, Month 1 and Month 2.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Rotarix Group | Placebo Group |
|---|---------------|---------------|
| Started   | 1666          | 1667          |
| Completed   | 1518          | 1499          |
| Not completed                                       | 148           | 168           |
| Adverse event, serious fatal                        | 6             | 7             |
| Consent withdrawn by subject                        | 55            | 46            |
| Adverse event, non-fatal                            | 4             | 8             |
| Not willing to participate in the EFU-visit 7       | 59            | 83            |

|                                |    |    |
|--------------------------------|----|----|
| Migrated/moved from study area | 23 | 24 |
| Diarrhea                       | 1  | -  |

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Notes:

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

Justification: 3340 subjects were allocated study subject number allocated and 3333 subjects were vaccinated.

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Rotarix Group |
|-----------------------|---------------|

Reporting group description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Rotarix vaccine, liquid formulation, at Day 0 and at Month 1. As part of the routine childhood vaccination according to the Expanded Program of Immunization (EPI) recommendations in China, subjects in this group also received 3 doses of Infanrix vaccine and 3 doses of the oral poliovirus vaccine (OPV) manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences. The Infanrix and the OPV vaccines were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Rotarix vaccine. When administered concomitantly, subjects received the 3 doses of Infanrix vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Rotarix and OPV vaccines were administered orally; the Infanrix vaccine was administered intramuscularly in the left anterolateral thigh.

|                       |               |
|-----------------------|---------------|
| Reporting group title | Placebo Group |
|-----------------------|---------------|

Reporting group description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Placebo at Day 0 and at Month 1. As part of the routine childhood vaccination according to the EPI recommendations in China, subjects in this group also received 3 doses of Infanrix vaccine and 3 doses of the oral poliovirus vaccine manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences. The Infanrix and the OPV vaccine were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Placebo. When administered concomitantly, subjects received the 3 doses of Infanrix vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Placebo and the OPV vaccine were administered orally; the Infanrix vaccine was administered intramuscularly in the left anterolateral thigh.

| Reporting group values                                | Rotarix Group | Placebo Group | Total |
|---|---------------|---------------|-------|
| Number of subjects                                    | 1666          | 1667          | 3333  |
| Age categorical<br>Units: Subjects                    |               |               |       |
| In utero  |               |               | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) |               |               | 0     |
| Newborns (0-27 days)                                  |               |               | 0     |
| Infants and toddlers (28 days-23 months)              |               |               | 0     |
| Children (2-11 years)                                 |               |               | 0     |
| Adolescents (12-17 years)                             |               |               | 0     |
| Adults (18-64 years)                                  |               |               | 0     |
| From 65-84 years                                      |               |               | 0     |
| 85 years and over                                     |               |               | 0     |
| Age continuous<br>Units: weeks                        |               |               |       |
| arithmetic mean                                       | 9.5           | 9.7           |       |
| standard deviation                                    | ± 2.64        | ± 2.59        | -     |
| Gender categorical<br>Units: Subjects                 |               |               |       |
| Female  | 795           | 836           | 1631  |
| Male  | 871           | 831           | 1702  |

## End points

### End points reporting groups

|  |               |
|--|---------------|
| Reporting group title  | Rotarix Group |
| Reporting group description:   |               |
| Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Rotarix vaccine, liquid formulation, at Day 0 and at Month 1. As part of the routine childhood vaccination according to the Expanded Program of Immunization (EPI) recommendations in China, subjects in this group also received 3 doses of Infanrix vaccine and 3 doses of the oral poliovirus vaccine (OPV) manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences. The Infanrix and the OPV vaccines were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Rotarix vaccine. When administered concomitantly, subjects received the 3 doses of Infanrix vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Rotarix and OPV vaccines were administered orally; the Infanrix vaccine was administered intramuscularly in the left anterolateral thigh. |               |
| Reporting group title  | Placebo Group |
| Reporting group description:   |               |
| Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Placebo at Day 0 and at Month 1. As part of the routine childhood vaccination according to the EPI recommendations in China, subjects in this group also received 3 doses of Infanrix vaccine and 3 doses of the oral poliovirus vaccine manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences. The Infanrix and the OPV vaccine were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Placebo. When administered concomitantly, subjects received the 3 doses of Infanrix vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Placebo and the OPV vaccine were administered orally; the Infanrix vaccine was administered intramuscularly in the left anterolateral thigh.   |               |

### Primary: Number of subjects with severe episode(s) of rotavirus gastroenteritis (RVGE) caused by the circulating wild type (WT) strains

|  |   |
|--|---|
| End point title  | Number of subjects with severe episode(s) of rotavirus gastroenteritis (RVGE) caused by the circulating wild type (WT) strains <sup>[1]</sup> |
| End point description:   |   |
| A gastroenteritis episode was classified positive for rotavirus (RV) and caused by the circulating wild-type (WT) RV strains if RV other than the vaccine strain was identified in a stool sample collected during the episode. Severe RVGE was defined as an episode of RV GE with score equal to or higher than ( $\geq$ ) 11 on a 20-point Vesikari scoring system. |   |
| End point type   | Primary   |
| End point timeframe:   |   |
| From Month 1 ½ to Month 21   |   |

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values             | Rotarix Group   | Placebo Group   |  |  |
|------------------------------|-----------------|-----------------|--|--|
| Subject group type           | Reporting group | Reporting group |  |  |
| Number of subjects analysed  | 1575            | 1573            |  |  |
| Units: Subjects              |                 |                 |  |  |
| Subjects with severe WT RVGE | 21              | 75              |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any episode(s) of rotavirus gastroenteritis (RVGE) caused by the circulating wild-type strains

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any episode(s) of rotavirus gastroenteritis (RVGE) caused by the circulating wild-type strains |
|-----------------|--|

End point description:

A gastroenteritis episode was classified positive for rotavirus (RV) and caused by the circulating wild-type (WT) RV strains if RV other than the vaccine strain was identified in a stool sample collected during the episode.

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

End point timeframe:

From Month 1 ½ to Month 21

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1575            | 1573            |  |  |
| Units: Subjects             |                 |                 |  |  |
| Subjects with WT RVGE       | 70              | 167             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any episode(s) of rotavirus gastroenteritis (RVGE) of any type

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any episode(s) of rotavirus gastroenteritis (RVGE) of any type |
|-----------------|--|

End point description:

A gastroenteritis episode was classified positive for rotavirus (RV) if RV was identified in a stool sample collected during the episode. RV types assessed were G1 Wild Type (G1WT), G2, G3, G9, GX (G type unknown, but not vaccine strain), P4, P8 Wild Type (P8WT), P9, PX (P type unknown, but not vaccine strain) and Pooled Non-G1WT.

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

End point timeframe:

From Month 1 ½ to Month 21

| End point values                   | Rotarix Group   | Placebo Group   |  |  |
|------------------------------------|-----------------|-----------------|--|--|
| Subject group type                 | Reporting group | Reporting group |  |  |
| Number of subjects analysed        | 1575            | 1573            |  |  |
| Units: Subjects                    |                 |                 |  |  |
| Subjects with G1WT RVGE            | 22              | 46              |  |  |
| Subjects with G2 RVGE              | 42              | 105             |  |  |
| Subjects with G3 RVGE              | 1               | 12              |  |  |
| Subjects with G9 RVGE              | 1               | 5               |  |  |
| Subjects with GX RVGE              | 6               | 8               |  |  |
| Subjects with P4 RVGE              | 43              | 107             |  |  |
| Subjects with P8WT RVGE            | 25              | 59              |  |  |
| Subjects with P9 RVGE              | 0               | 1               |  |  |
| Subjects with PX RVGE              | 4               | 1               |  |  |
| Subjects with Pooled Non-G1WT RVGE | 49              | 129             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with severe episode(s) of rotavirus gastroenteritis (RVGE) of any type

|  |   |
|--|---|
| End point title  | Number of subjects with severe episode(s) of rotavirus gastroenteritis (RVGE) of any type |
| End point description:   |   |
| A gastroenteritis episode was classified positive for rotavirus (RV) if RV was identified in a stool sample collected during the episode. Severe RVGE was defined as an episode of RVGE with score equal to or higher than ( $\geq$ ) 11 on a 20-point Vesikari scoring system. RV types assessed were G1 Wild Type (G1WT), G2, G3, G9, GX (G type unknown, but not vaccine strain), P4, P8 Wild Type (P8WT), P9, PX (P type unknown, but not vaccine strain) and Pooled Non-G1WT. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| From Month 1 ½ to Month 21   |   |

| End point values                          | Rotarix Group   | Placebo Group   |  |  |
|---|-----------------|-----------------|--|--|
| Subject group type                        | Reporting group | Reporting group |  |  |
| Number of subjects analysed               | 1575            | 1573            |  |  |
| Units: Subjects                           |                 |                 |  |  |
| Subjects with severe G1WT RVGE            | 9               | 25              |  |  |
| Subjects with severe G2 RVGE              | 11              | 43              |  |  |
| Subjects with severe G3 RVGE              | 0               | 3               |  |  |
| Subjects with severe G9 RVGE              | 0               | 3               |  |  |
| Subjects with severe GX RVGE              | 1               | 6               |  |  |
| Subjects with severe P4 RVGE              | 12              | 43              |  |  |
| Subjects with severe P8WT RVGE            | 9               | 31              |  |  |
| Subjects with severe PX RVGE              | 1               | 1               |  |  |
| Subjects with severe Pooled Non-G1WT RVGE | 12              | 54              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with episodes of rotavirus gastroenteritis (RVGE) caused by the circulating wild type (WT) strains requiring hospitalization

|                 |   |
|-----------------|---|
| End point title | Number of subjects with episodes of rotavirus gastroenteritis (RVGE) caused by the circulating wild type (WT) strains requiring hospitalization |
|-----------------|---|

End point description:

A gastroenteritis episode was classified positive for rotavirus (RV) and caused by the circulating WT RV strains if RV other than the vaccine strain was identified in a stool sample collected during the episode.

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

End point timeframe:

From Month 1 ½ to Month 21

| End point values                             | Rotarix Group   | Placebo Group   |  |  |
|--|-----------------|-----------------|--|--|
| Subject group type                           | Reporting group | Reporting group |  |  |
| Number of subjects analysed                  | 1575            | 1573            |  |  |
| Units: Subjects                              |                 |                 |  |  |
| Subjects with RVGE requiring hospitalization | 4               | 21              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any and severe gastroenteritis (GE) due to any cause

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any and severe gastroenteritis (GE) due to any cause |
|-----------------|--|

End point description:

Severe GE was defined as an episode of GE with score equal to or higher than ( $\geq$ ) 11 on a 20-point Vesikari scoring system. This outcome measure concerns results for GE episodes due to any cause.

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

End point timeframe:

From Month 1 ½ to Month 21

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1575            | 1573            |  |  |
| Units: Subjects             |                 |                 |  |  |
| Subjects with any GE        | 728             | 759             |  |  |
| Subjects with any severe GE | 187             | 206             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any solicited general symptoms following vaccination with the Rotarix vaccine/placebo

|                 |   |
|-----------------|---|
| End point title | Number of subjects with any solicited general symptoms following vaccination with the Rotarix vaccine/placebo |
|-----------------|---|

End point description:

Assessed solicited general symptoms were fever, defined as axillary temperature (T) above or equal to ( $\geq$ ) 37.5 degrees Celsius [ $^{\circ}\text{C}$ ] or  $\geq 37.1^{\circ}\text{C}$ , fussiness/irritability, loss of appetite, cough/runny nose, diarrhea and vomiting. Any = any occurrence of the specified solicited general symptom regardless of the intensity grade or relationship to vaccination. This outcome measure was only assessed in subjects from Sub-cohort 1, who received the EPI vaccination independently of study vaccination with the Rotarix vaccine/placebo.

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

End point timeframe:

Within the 8-day (Days 0–7) follow-up periods after any dose of Rotarix vaccine/placebo

| End point values  | Rotarix Group   | Placebo Group   |  |  |
|---|-----------------|-----------------|--|--|
| Subject group type  | Reporting group | Reporting group |  |  |
| Number of subjects analysed                                       | 1513            | 1514            |  |  |
| Units: Subjects   |                 |                 |  |  |
| Any cough/runny nose  | 313             | 366             |  |  |
| Any diarrhoea   | 127             | 123             |  |  |
| Any Irritability/Fussiness  | 415             | 448             |  |  |
| Any Loss of appetite  | 253             | 250             |  |  |
| Any Fever – Chinese scale: Axillary T $\geq 37.1^{\circ}\text{C}$ | 302             | 313             |  |  |
| Any Fever – GSK scale: Axillary T $\geq 37.5^{\circ}\text{C}$     | 83              | 104             |  |  |
| Any Vomiting  | 213             | 232             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any solicited general symptoms following administration of the co-administered EPI vaccines

|   |   |
|---|---|
| End point title   | Number of subjects with any solicited general symptoms following administration of the co-administered EPI vaccines |
| End point description:<br>Solicited general symptoms assessed following administration of the co-administered EPI vaccines were drowsiness, gastrointestinal symptoms, fussiness/irritability, loss of appetite, and fever, defined as axillary temperature (T) above or equal to ( $\geq$ ) 37.5 degrees Celsius [ $^{\circ}\text{C}$ ] or $\geq 37.1^{\circ}\text{C}$ . Any = any occurrence of the specified solicited general symptom regardless of the intensity grade or relationship to vaccination. This outcome measure was only assessed in subjects from Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix vaccine/placebo. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Within the 8-day (Days 0–7) follow-up periods following Doses 1 and 2 of the OPV vaccine and Dose 1 of the Infanrix vaccine   |   |

| End point values  | Rotarix Group   | Placebo Group   |  |  |
|---|-----------------|-----------------|--|--|
| Subject group type  | Reporting group | Reporting group |  |  |
| Number of subjects analysed                                       | 153             | 153             |  |  |
| Units: Subjects   |                 |                 |  |  |
| Any Drowsiness  | 44              | 38              |  |  |
| Any Gastrointestinal  | 43              | 38              |  |  |
| Any Irritability/Fussiness  | 56              | 52              |  |  |
| Any Loss of appetite  | 43              | 32              |  |  |
| Any Fever – Chinese scale: Axillary T $\geq 37.1^{\circ}\text{C}$ | 18              | 20              |  |  |
| Any Fever – GSK scale: Axillary T $\geq 37.5^{\circ}\text{C}$     | 6               | 7               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any solicited local symptoms following Dose 2 of the Rotarix vaccine/placebo

|   |  |
|---|--|
| End point title   | Number of subjects with any solicited local symptoms following Dose 2 of the Rotarix vaccine/placebo |
| End point description:<br>Solicited local symptoms assessed following administration of the co-administered EPI vaccines were pain, swelling, and redness. Any = any occurrence of the specified solicited local symptom regardless of the intensity grade. This outcome measure was only assessed in subjects from Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix vaccine/placebo. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Within the 8-day (Days 0–7) follow-up periods following Dose 2 of the Rotarix vaccine/placebo   |  |

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 150             | 151             |  |  |
| Units: Subjects             |                 |                 |  |  |
| Any Pain                    | 14              | 9               |  |  |
| Any Redness                 | 20              | 13              |  |  |
| Any Swelling                | 13              | 6               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any unsolicited adverse events (AEs)

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any unsolicited adverse events (AEs) |
|-----------------|--|

End point description:

An unsolicited AE is any adverse event (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any = occurrence of an unsolicited AE regardless of the intensity grade or relationship to vaccination.

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

End point timeframe:

Within the 31-day (Days 0–30) follow-up periods following any dose of the Rotarix vaccine or placebo

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1666            | 1667            |  |  |
| Units: Subjects             |                 |                 |  |  |
| Any unsolicited AE(s)       | 310             | 368             |  |  |

## Statistical analyses

No statistical analyses for this end point

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

|                 |   |
|-----------------|---|
| End point title | Number of subjects with any serious adverse events (SAEs) |
|-----------------|---|

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, or result in disability/incapacity. Any = occurrence of an SAE regardless of the intensity grade or relationship to vaccination.

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

End point timeframe:

Throughout the entire study period (from Day 0 to Study End at Month 21)

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1666            | 1667            |  |  |
| Units: Subjects             |                 |                 |  |  |
| Any SAE(s)                  | 183             | 246             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Seroconverted Subjects for Anti-rotavirus (Anti-RV) Immunoglobulin A (IgA) Antibodies

|                 |   |
|-----------------|---|
| End point title | Number of Seroconverted Subjects for Anti-rotavirus (Anti-RV) Immunoglobulin A (IgA) Antibodies |
|-----------------|---|

End point description:

A seroconverted subject was defined as a subject seronegative at baseline (Day 0) with the appearance of anti-RV IgA antibody concentration greater than or equal to ( $\geq$ ) 20 units per milliliter (U/mL) at the time point assessed. A seronegative subject was defined as a subject with anti-RV IgA antibody concentration lower than ( $<$ ) 20 U/mL.

Analysis was performed on the According-to-Protocol (ATP) cohort for immunogenicity Sub-cohort 1, which included subjects vaccinated with at least 1 dose of HRV vaccine/Placebo, complying with protocol, with EPI childhood vaccinations completed according to Chinese recommendations and available immunogenicity data at post sampling time-point.

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

End point timeframe:

At Month 2 and at 12 months of age

| End point values                           | Rotarix Group   | Placebo Group   |  |  |
|--|-----------------|-----------------|--|--|
| Subject group type                         | Reporting group | Reporting group |  |  |
| Number of subjects analysed                | 257             | 254             |  |  |
| Units: Subjects                            |                 |                 |  |  |
| Anti-RV IgA - Month 2 [N=257;254]          | 192             | 9               |  |  |
| Anti-RV IgA - 12 months of age [N=246;252] | 176             | 118             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seroconverted subjects for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies

|                 |   |
|-----------------|---|
| End point title | Number of seroconverted subjects for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies |
|-----------------|---|

---

**End point description:**

A seroconverted subject was defined as a subject seronegative at baseline (Day 0) with the appearance of anti-RV IgA antibody concentration greater than or equal to ( $\geq$ ) 20 units per milliliter (U/mL) at the time point assessed. A seronegative subject was defined as a subject with anti-RV IgA antibody concentration lower than ( $<$ ) 20 U/mL.

Analysis was performed on the ATP cohort for immunogenicity Sub-cohort 2, which included subjects with OPV and Infanrix vaccines co-administered with the study vaccine, complying with protocol, with EPI childhood vaccinations completed according to Chinese recommendations and available immunogenicity data at post sampling time-point.

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

---

End point timeframe:

At Month 2 and at 12 months of age

---

| End point values                           | Rotarix Group   | Placebo Group   |  |  |
|--|-----------------|-----------------|--|--|
| Subject group type                         | Reporting group | Reporting group |  |  |
| Number of subjects analysed                | 134             | 139             |  |  |
| Units: Subjects                            |                 |                 |  |  |
| Anti-RV IgA - Month 2 [N=134;139]          | 86              | 13              |  |  |
| Anti-RV IgA - 12 months of age [N=124;133] | 62              | 29              |  |  |

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Number of seroconverted subjects for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies**

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|                 |   |
|-----------------|---|
| End point title | Number of seroconverted subjects for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies |
|-----------------|---|

---

End point description:

A seroconverted subject was defined as a subject seronegative at baseline (Day 0) with the appearance of anti-RV IgA antibody concentration greater than or equal to ( $\geq$ ) 20 units per milliliter (U/mL) at the time point assessed. A seronegative subject was defined as a subject with anti-RV IgA antibody concentration lower than ( $<$ ) 20 U/mL.

Analysis was performed on the ATP cohort for immunogenicity, which included eligible subjects in the ATP cohorts for immunogenicity sub-cohorts 1 and 2 seronegative for serum anti-rotavirus immunoglobulin A (IgA) antibodies at Day 0 and with availability immunogenicity data at pre and post sampling time-points.

---

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

---

End point timeframe:

At Month 2 and at 12 months of age

---



| End point values                              | Rotarix Group   | Placebo Group   |  |  |
|---|-----------------|-----------------|--|--|
| Subject group type                            | Reporting group | Reporting group |  |  |
| Number of subjects analysed                   | 391             | 393             |  |  |
| Units: Subjects                               |                 |                 |  |  |
| Anti-RV IgA - Month 2 [N=391;393]             | 278             | 22              |  |  |
| Anti-RV IgA – 12 months of age<br>[N=370;385] | 238             | 147             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies

|                 |  |
|-----------------|--|
| End point title | Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies |
|-----------------|--|

End point description:

A subject seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies was defined as a subject anti-RV IgA antibody concentration greater than or equal to ( $\geq$ ) the seropositivity cut-off of 20 units per milliliter (U/mL).

Analysis was performed on the According-to-Protocol (ATP) cohort for immunogenicity Sub-cohort 1, which included subjects vaccinated with at least 1 dose of HRV vaccine/Placebo, complying with protocol, with EPI childhood vaccinations completed according to Chinese recommendations and available immunogenicity data at post sampling time-point.

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

End point timeframe:

At Day 0, Month 2 and at 12 months of age

| End point values                              | Rotarix Group   | Placebo Group   |  |  |
|---|-----------------|-----------------|--|--|
| Subject group type                            | Reporting group | Reporting group |  |  |
| Number of subjects analysed                   | 257             | 254             |  |  |
| Units: Subjects                               |                 |                 |  |  |
| Anti-RV IgA – Day 0 [N=257;254]               | 0               | 0               |  |  |
| Anti-RV IgA - Month 2 [N=257;254]             | 192             | 9               |  |  |
| Anti-RV IgA – 12 months of age<br>[N=246;252] | 176             | 118             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies

|                 |  |
|-----------------|--|
| End point title | Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies |
|-----------------|--|

**End point description:**

A subject seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies was defined as a subject anti-RV IgA antibody concentration greater than or equal to ( $\geq$ ) the seropositivity cut-off of 20 units per milliliter (U/mL).

Analysis was performed on the ATP cohort for immunogenicity Sub-cohort 2, which included subjects with OPV and Infanrix vaccines co-administered with the study vaccine, complying with protocol, with EPI childhood vaccinations completed according to Chinese recommendations and available immunogenicity data at post sampling time-point.

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

**End point timeframe:**

At Day 0, Month 2 and at 12 months of age

| End point values                           | Rotarix Group   | Placebo Group   |  |  |
|--|-----------------|-----------------|--|--|
| Subject group type                         | Reporting group | Reporting group |  |  |
| Number of subjects analysed                | 134             | 139             |  |  |
| Units: Subjects                            |                 |                 |  |  |
| Anti-RV IgA – Day 0 [N=134;139]            | 0               | 0               |  |  |
| Anti-RV IgA - Month 2 [N=134;139]          | 86              | 13              |  |  |
| Anti-RV IgA – 12 months of age [N=124;133] | 62              | 29              |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies**

|                 |  |
|-----------------|--|
| End point title | Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies |
|-----------------|--|

**End point description:**

A subject seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies was defined as a subject anti-RV IgA antibody concentration greater than or equal to ( $\geq$ ) the seropositivity cut-off of 20 units per milliliter (U/mL).

Analysis was performed on the ATP cohort for immunogenicity, which included eligible subjects in the ATP cohorts for immunogenicity sub-cohorts 1 and 2 seronegative for serum anti-rotavirus immunoglobulin A (IgA) antibodies at Day 0 and with availability immunogenicity data at pre and post sampling time-points.

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

**End point timeframe:**

At Day 0, Month 2 and at 12 months of age

| End point values                  | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 391             | 393             |  |  |
| Units: Subjects                   |                 |                 |  |  |
| Anti-RV IgA – Day 0 [N=391;393]   | 0               | 0               |  |  |
| Anti-RV IgA - Month 2 [N=391;393] | 278             | 22              |  |  |

|   |     |     |  |  |
|---|-----|-----|--|--|
| Anti-RV IgA – 12 months of age<br>[N=370;385] | 238 | 147 |  |  |
|---|-----|-----|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations

|                 |   |
|-----------------|---|
| End point title | Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations |
|-----------------|---|

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs), in units per milliliter (U/mL). The cut-off of the assay was the seropositivity cut-off ( $\geq 20$  U/mL).

Analysis was performed on the According-to-Protocol (ATP) cohort for immunogenicity Sub-cohort 1, which included subjects vaccinated with at least 1 dose of HRV vaccine/Placebo, complying with protocol, with EPI childhood vaccinations completed according to Chinese recommendations and available immunogenicity data at post sampling time-point.

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

End point timeframe:

At Day 0, Month 2 and at 12 months of age

| End point values                           | Rotarix Group        | Placebo Group       |  |  |
|--|----------------------|---------------------|--|--|
| Subject group type                         | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed                | 257                  | 254                 |  |  |
| Units: U/mL                                |                      |                     |  |  |
| geometric mean (confidence interval 95%)   |                      |                     |  |  |
| Anti-RV IgA – Day 0 [N=257;254]            | 0 (0 to 0)           | 0 (0 to 0)          |  |  |
| Anti-RV IgA - Month 2 [N=257;254]          | 90.2 (73.3 to 111.1) | 0 (0 to 0)          |  |  |
| Anti-RV IgA – 12 months of age [N=246;252] | 66.5 (54.6 to 81)    | 35.3 (29.3 to 42.5) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations

|                 |   |
|-----------------|---|
| End point title | Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations |
|-----------------|---|

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs), in units per milliliter (U/mL). The cut-off of the assay was the seropositivity cut-off ( $\geq 20$  U/mL).

Analysis was performed on the ATP cohort for immunogenicity Sub-cohort 2, which included subjects with OPV and Infanrix vaccines co-administered with the study vaccine, complying with protocol, with

EPI childhood vaccinations completed according to Chinese recommendations and available immunogenicity data at post sampling time-point.

|  |           |
|--|-----------|
| End point type                             | Secondary |
| End point timeframe:                       |           |
| At Day 0, Month 2 and at 12 months of age. |           |

| End point values                           | Rotarix Group       | Placebo Group   |  |  |
|--|---------------------|-----------------|--|--|
| Subject group type                         | Reporting group     | Reporting group |  |  |
| Number of subjects analysed                | 134                 | 139             |  |  |
| Units: U/mL                                |                     |                 |  |  |
| geometric mean (confidence interval 95%)   |                     |                 |  |  |
| Anti-RV IgA – Day 0 [N=134;139]            | 0 (0 to 0)          | 0 (0 to 0)      |  |  |
| Anti-RV IgA - Month 2 [N=134;139]          | 84 (58.9 to 119.8)  | 0 (0 to 0)      |  |  |
| Anti-RV IgA – 12 months of age [N=124;133] | 31.3 (24.6 to 39.8) | 0 (0 to 0)      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations

|                 |   |
|-----------------|---|
| End point title | Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations |
|-----------------|---|

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs), in units per milliliter (U/mL). The cut-off of the assay was the seropositivity cut-off ( $\geq 20$  U/mL). Analysis was performed on the ATP cohort for immunogenicity, which included eligible subjects in the ATP cohorts for immunogenicity sub-cohorts 1 and 2 seronegative for serum anti-rotavirus immunoglobulin A (IgA) antibodies at Day 0 and with availability immunogenicity data at pre and post sampling time-points.

|   |           |
|---|-----------|
| End point type                            | Secondary |
| End point timeframe:                      |           |
| At Day 0, Month 2 and at 12 months of age |           |

| End point values                         | Rotarix Group      | Placebo Group   |  |  |
|--|--------------------|-----------------|--|--|
| Subject group type                       | Reporting group    | Reporting group |  |  |
| Number of subjects analysed              | 391                | 393             |  |  |
| Units: U/mL                              |                    |                 |  |  |
| geometric mean (confidence interval 95%) |                    |                 |  |  |
| Anti-RV IgA – Day 0 [N=391;393]          | 0 (0 to 0)         | 0 (0 to 0)      |  |  |
| Anti-RV IgA - Month 2 [N=391;393]        | 88 (73.4 to 105.6) | 0 (0 to 0)      |  |  |

|   |                        |                        |  |  |
|---|------------------------|------------------------|--|--|
| Anti-RV IgA – 12 months of age<br>[N=370;385] | 51.6 (44.1 to<br>60.5) | 27.4 (23.7 to<br>31.7) |  |  |
|---|------------------------|------------------------|--|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects seroprotected against diphtheria and tetanus

|   |   |
|---|---|
| End point title   | Number of subjects seroprotected against diphtheria and tetanus |
| End point description:<br>A subject seroprotected against diphtheria/tetanus was defined as a subject with an anti-diphtheria (anti-D)/anti-tetanus (anti-T) antibody concentrations greater than or equal to ( $\geq$ ) 0.1 international units per milliliter (IU/mL). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix vaccine/placebo. |   |
| End point type  | Secondary   |
| End point timeframe:<br>At Day 0 and at Month 4   |   |

| End point values              | Rotarix Group   | Placebo Group   |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 133             | 139             |  |  |
| Units: Subjects               |                 |                 |  |  |
| Anti-D at Day 0 [N=133;138]   | 1               | 1               |  |  |
| Anti-D at Month 4 [N=133;139] | 133             | 139             |  |  |
| Anti-T at Day 0 [N=133;138]   | 0               | 1               |  |  |
| Anti-T at Month 4 [N=133;139] | 133             | 139             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-Diphtheria (Anti-D) and anti-tetanus (anti-T) antibody concentrations

|   |  |
|---|--|
| End point title   | Anti-Diphtheria (Anti-D) and anti-tetanus (anti-T) antibody concentrations |
| End point description:<br>Concentrations were expressed as geometric mean concentrations (GMCs) in international unit per milliliter (IU/mL). The cut-off of the assay was the seroprotection cut-off assay ( $\geq$ 0.1 IU/mL). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix vaccine/placebo. |  |
| End point type  | Secondary  |
| End point timeframe:<br>At Day 0 and at Month 4   |  |

| End point values                         | Rotarix Group          | Placebo Group          |  |  |
|--|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed              | 133                    | 139                    |  |  |
| Units: IU/mL                             |                        |                        |  |  |
| geometric mean (confidence interval 95%) |                        |                        |  |  |
| Anti-D at Day 0 [N=133;138]              | 0.051 (0.049 to 0.052) | 0.05 (0.05 to 0.051)   |  |  |
| Anti-D at Month 4 [N=133;139]            | 0.375 (0.326 to 0.432) | 0.334 (0.308 to 0.363) |  |  |
| Anti-T at Day 0 [N=133;138]              | 0.05 (0.05 to 0.05)    | 0.05 (0.05 to 0.051)   |  |  |
| Anti-T at Month 4 [N=133;139]            | 1.281 (1.253 to 1.309) | 1.343 (1.215 to 1.486) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects seroprotected against poliovirus types 1, 2 and 3

|                 |  |
|-----------------|--|
| End point title | Number of subjects seroprotected against poliovirus types 1, 2 and 3 |
|-----------------|--|

End point description:

A subject seroprotected against poliovirus types 1, 2 and 3 was defined as a subject with anti-poliovirus type 1 (anti-polio 1)/anti-polio 2/anti-polio 3 antibody titer greater than or equal to ( $\geq$ ) 8 estimated doses 50 percent (%) (ED50). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix vaccine/placebo.

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

End point timeframe:

At Day 0 and at Month 4

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 136             | 139             |  |  |
| Units: Subjects             |                 |                 |  |  |
| Anti-polio 1 at Day 0       | 63              | 62              |  |  |
| Anti-polio 1 at Month 4     | 136             | 139             |  |  |
| Anti-polio 2 at Day 0       | 52              | 39              |  |  |
| Anti-polio 2 at Month 4     | 136             | 139             |  |  |
| Anti-polio 3 at Day 0       | 32              | 29              |  |  |
| Anti-polio 3 at Month 4     | 135             | 138             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Titers for anti-poliovirus type 1 (anti-polio 1), anti-polio 2 and anti-polio 3 antibodies

|                 |  |
|-----------------|--|
| End point title | Titers for anti-poliovirus type 1 (anti-polio 1), anti-polio 2 and anti-polio 3 antibodies |
|-----------------|--|

End point description:

Titers were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seroprotection cut-off ( $\geq 8$  ED50 for anti-poliovirus type 1 [anti-polio 1]/anti-polio 2/anti-polio 3 antibodies). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix vaccine/placebo.

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

End point timeframe:

At Day 0 and at Month 4

| End point values                         | Rotarix Group             | Placebo Group             |  |  |
|--|---------------------------|---------------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed              | 136                       | 139                       |  |  |
| Units: Titers                            |                           |                           |  |  |
| geometric mean (confidence interval 95%) |                           |                           |  |  |
| Anti-polio 1 at Day 0                    | 8.9 (7.5 to 10.5)         | 9.1 (7.6 to 11)           |  |  |
| Anti-polio 1 at Month 4                  | 2101.1 (1734.8 to 2544.8) | 2259.4 (1844.4 to 2767.9) |  |  |
| Anti-polio 2 at Day 0                    | 7.6 (6.5 to 9)            | 6.2 (5.4 to 7.1)          |  |  |
| Anti-polio 2 at Month 4                  | 402.5 (334.8 to 483.9)    | 425.1 (371 to 487.1)      |  |  |
| Anti-polio 3 at Day 0                    | 5.6 (4.9 to 6.3)          | 5.7 (4.9 to 6.6)          |  |  |
| Anti-polio 3 at Month 4                  | 426.6 (342.7 to 531)      | 360.3 (303 to 428.3)      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects seropositive for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibodies

|                 |  |
|-----------------|--|
| End point title | Number of subjects seropositive for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibodies |
|-----------------|--|

End point description:

Antibody assessment was performed by enzyme-linked immunosorbent assay (ELISA). A subject seropositive for anti-PT/anti-FHA/anti-PRN antibodies was defined as a subject with an anti-PT/anti-FHA/anti-PRN antibody concentrations greater than or equal to ( $\geq$ ) 5 ELISA units per milliliter (EL.U/mL). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix vaccine/placebo.

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

End point timeframe:  
At Day 0 and at Month 4

| End point values                | Rotarix Group   | Placebo Group   |  |  |
|---------------------------------|-----------------|-----------------|--|--|
| Subject group type              | Reporting group | Reporting group |  |  |
| Number of subjects analysed     | 133             | 139             |  |  |
| Units: Subjects                 |                 |                 |  |  |
| Anti-PT at Day 0 [N=131;139]    | 43              | 34              |  |  |
| Anti-PT at Month 4 [N=133;139]  | 133             | 139             |  |  |
| Anti-FHA at Day 0 [N=131;139]   | 31              | 47              |  |  |
| Anti-FHA at Month 4 [N=133;139] | 133             | 139             |  |  |
| Anti-PRN at Day 0 [N=131;139]   | 3               | 5               |  |  |
| Anti-PRN at Month 4 [N=133;139] | 133             | 139             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentrations of Anti-pertussis Toxoid (Anti-PT), Anti-filamentous Haemagglutinin (Anti-FHA) and Anti-pertactin (Anti-PRN) Antibodies

|                 |  |
|-----------------|--|
| End point title | Concentrations of Anti-pertussis Toxoid (Anti-PT), Anti-filamentous Haemagglutinin (Anti-FHA) and Anti-pertactin (Anti-PRN) Antibodies |
|-----------------|--|

End point description:

Antibody assessment was performed by enzyme-linked immunosorbent assay (ELISA). Concentrations were expressed as geometric mean concentrations (GMCs) in EL.U/mL. The cut-off of the assay was the seropositivity cut-off ( $\geq 5$  EL.U/mL) for all antibodies assessed (anti-PT, anti-FHA and anti-PRN). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix vaccine/placebo.

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

End point timeframe:

At Day 0 and Month 4

| End point values                         | Rotarix Group       | Placebo Group       |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 133                 | 139                 |  |  |
| Units: EL.U/mL                           |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| Anti-PT at Day 0 [N=131;139]             | 3.4 (3.1 to 3.7)    | 3.2 (3 to 3.4)      |  |  |
| Anti-PT at Month 4 [N=133;139]           | 88.9 (84.9 to 93.2) | 90.5 (86.4 to 94.8) |  |  |
| Anti-FHA at Day 0 [N=131;139]            | 3.1 (2.9 to 3.3)    | 3.5 (3.2 to 3.8)    |  |  |
| Anti-FHA at Month 4 [N=133;139]          | 59.5 (55.8 to 63.5) | 65.8 (61.3 to 70.5) |  |  |
| Anti-PRN at Day 0 [N=131;139]            | 2.6 (2.5 to 2.6)    | 2.6 (2.5 to 2.7)    |  |  |



|                                 |                     |                     |  |  |
|---------------------------------|---------------------|---------------------|--|--|
| Anti-PRN at Month 4 [N=133;139] | 41.9 (37.6 to 46.5) | 50.8 (44.3 to 58.1) |  |  |
|---------------------------------|---------------------|---------------------|--|--|

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms were collected during the 8-day (Days 0-7) post vaccination period. Unsolicited AEs were collected during the 31 day (Days 0-30) post vaccination. SAEs were collected throughout the entire study period (Months 0 to 21).

Adverse event reporting additional description:

1 subject in the Placebo Group experienced an SAE assessed by the investigators as causally related to study vaccination (Diarrhoea).

The number of occurrences reported for solicited symptoms, adverse events & SAEs were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 14.1   |

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Placebo Group |
|-----------------------|---------------|

Reporting group description: -

|                       |               |
|-----------------------|---------------|
| Reporting group title | Rotarix Group |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events  | Placebo Group          | Rotarix Group          |  |
|---|------------------------|------------------------|--|
| Total subjects affected by serious adverse events                   |                        |                        |  |
| subjects affected / exposed   | 246 / 1667<br>(14.76%) | 183 / 1666<br>(10.98%) |  |
| number of deaths (all causes)                                       | 7                      | 6                      |  |
| number of deaths resulting from adverse events                      | 0                      | 0                      |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                        |                        |  |
| Acute lymphocytic leukaemia   |                        |                        |  |
| subjects affected / exposed   | 1 / 1667 (0.06%)       | 0 / 1666 (0.00%)       |  |
| occurrences causally related to treatment / all                     | 0 / 1                  | 0 / 0                  |  |
| deaths causally related to treatment / all                          | 0 / 1                  | 0 / 0                  |  |
| Histiocytosis haematophagic   |                        |                        |  |
| subjects affected / exposed   | 1 / 1667 (0.06%)       | 0 / 1666 (0.00%)       |  |
| occurrences causally related to treatment / all                     | 0 / 1                  | 0 / 0                  |  |
| deaths causally related to treatment / all                          | 0 / 1                  | 0 / 0                  |  |
| General disorders and administration site conditions                |                        |                        |  |
| Multi-organ failure   |                        |                        |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1667 (0.12%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            |  |
| Death   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Drowning  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hernia  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (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 |                  |                  |  |
| Asphyxia  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 2 / 1666 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Respiratory failure                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Asthma  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 3 / 1666 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injury, poisoning and procedural complications  |                  |                  |  |
| Brain contusion                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Brain herniation                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Skull fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Liver function test abnormal                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Congenital, familial and genetic disorders      |                  |                  |  |
| Glucose-6-phosphate dehydrogenase deficiency    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 3 / 1666 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Heart disease congenital                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 1667 (0.12%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Thalassaemia beta                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 2 / 1666 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ventricular septal defect                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 1667 (0.12%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atrial septal defect                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Cortical dysplasia                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hydrocele                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Patent ductus arteriosus                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thalassaemia                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac disorders                               |                  |                  |  |
| Myocarditis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nervous system disorders                        |                  |                  |  |
| Convulsion                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Febrile convulsion                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 1667 (0.12%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral haematoma                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Epilepsy  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Extrapyramidal disorder                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhage intracranial                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hydrocephalus                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subarachnoid haemorrhage                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Ureteric stenosis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blood and lymphatic system disorders            |                  |                  |  |
| Deficiency anaemia                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphadenitis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaemia   |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 1667 (0.18%)  | 2 / 1666 (0.12%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Gastrointestinal disorders</b>               |                   |                   |  |
| <b>Enteritis</b>                                |                   |                   |  |
| subjects affected / exposed                     | 73 / 1667 (4.38%) | 44 / 1666 (2.64%) |  |
| occurrences causally related to treatment / all | 0 / 73            | 0 / 44            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Diarrhoea</b>                                |                   |                   |  |
| subjects affected / exposed                     | 11 / 1667 (0.66%) | 4 / 1666 (0.24%)  |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| <b>Gastrointestinal disorder</b>                |                   |                   |  |
| subjects affected / exposed                     | 3 / 1667 (0.18%)  | 1 / 1666 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Inguinal hernia, obstructive</b>             |                   |                   |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%)  | 1 / 1666 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Intestinal obstruction</b>                   |                   |                   |  |
| subjects affected / exposed                     | 2 / 1667 (0.12%)  | 0 / 1666 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Intussusception</b>                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%)  | 1 / 1666 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Dyspepsia</b>                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%)  | 0 / 1666 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Food poisoning</b>                           |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroesophageal reflux disease                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inguinal hernia                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatobiliary disorders                         |                  |                  |  |
| Hepatic function abnormal                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin and subcutaneous tissue disorders          |                  |                  |  |
| Dermatitis diaper                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urticaria                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal and urinary disorders                     |                  |                  |  |
| Hydronephrosis                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infections and infestations                     |                  |                  |  |
| Bronchitis                                      |                  |                  |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 98 / 1667 (5.88%) | 74 / 1666 (4.44%) |  |
| occurrences causally related to treatment / all | 0 / 98            | 0 / 74            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchopneumonia                                |                   |                   |  |
| subjects affected / exposed                     | 61 / 1667 (3.66%) | 58 / 1666 (3.48%) |  |
| occurrences causally related to treatment / all | 0 / 61            | 0 / 58            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Pneumonia                                       |                   |                   |  |
| subjects affected / exposed                     | 14 / 1667 (0.84%) | 14 / 1666 (0.84%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pharyngitis                                     |                   |                   |  |
| subjects affected / exposed                     | 8 / 1667 (0.48%)  | 2 / 1666 (0.12%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hand-foot-and-mouth disease                     |                   |                   |  |
| subjects affected / exposed                     | 4 / 1667 (0.24%)  | 5 / 1666 (0.30%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tracheitis                                      |                   |                   |  |
| subjects affected / exposed                     | 4 / 1667 (0.24%)  | 4 / 1666 (0.24%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Acute tonsillitis                               |                   |                   |  |
| subjects affected / exposed                     | 2 / 1667 (0.12%)  | 5 / 1666 (0.30%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Candidiasis                                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%)  | 3 / 1666 (0.18%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroenteritis                                 |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1667 (0.12%) | 2 / 1666 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngitis                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 1667 (0.12%) | 2 / 1666 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diarrhoea infectious                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 1667 (0.12%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cytomegalovirus infection                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 2 / 1666 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis bacterial                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 1667 (0.12%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpangina                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia klebsiella                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 2 / 1666 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Varicella                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 2 / 1666 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial diarrhoea                             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Central nervous system infection                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Infectious mononucleosis                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lobar pneumonia                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meningitis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Otitis media                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia staphylococcal                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%) | 1 / 1666 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Shigella infection                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%) | 0 / 1666 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tracheobronchitis                               |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 1667 (0.00%)  | 1 / 1666 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Upper respiratory tract infection               |                   |                   |  |
| subjects affected / exposed                     | 26 / 1667 (1.56%) | 16 / 1666 (0.96%) |  |
| occurrences causally related to treatment / all | 0 / 26            | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchiolitis                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%)  | 1 / 1666 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Metabolism and nutrition disorders              |                   |                   |  |
| Hypokalaemia                                    |                   |                   |  |
| subjects affected / exposed                     | 3 / 1667 (0.18%)  | 1 / 1666 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Acidosis  |                   |                   |  |
| subjects affected / exposed                     | 2 / 1667 (0.12%)  | 0 / 1666 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hyponatraemia                                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 1667 (0.00%)  | 1 / 1666 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Malnutrition                                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 1667 (0.06%)  | 0 / 1666 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Dehydration                                     |                   |                   |  |
| subjects affected / exposed                     | 3 / 1667 (0.18%)  | 1 / 1666 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

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

| <b>Non-serious adverse events</b>                     | Placebo Group          | Rotarix Group          |  |
|---|------------------------|------------------------|--|
| Total subjects affected by non-serious adverse events |                        |                        |  |
| subjects affected / exposed                           | 880 / 1667<br>(52.79%) | 838 / 1666<br>(50.30%) |  |
| General disorders and administration site conditions  |                        |                        |  |
| Cough/runny nose                                      |                        |                        |  |
| alternative assessment type:<br>Systematic            |                        |                        |  |
| subjects affected / exposed <sup>[1]</sup>            | 366 / 1514<br>(24.17%) | 313 / 1513<br>(20.69%) |  |
| occurrences (all)                                     | 366                    | 313                    |  |
| Diarrhoea   |                        |                        |  |
| alternative assessment type:<br>Systematic            |                        |                        |  |
| subjects affected / exposed <sup>[2]</sup>            | 123 / 1514 (8.12%)     | 127 / 1513 (8.39%)     |  |
| occurrences (all)                                     | 123                    | 127                    |  |
| Irritability/Fussiness                                |                        |                        |  |
| alternative assessment type:<br>Systematic            |                        |                        |  |
| subjects affected / exposed <sup>[3]</sup>            | 448 / 1514<br>(29.59%) | 415 / 1513<br>(27.43%) |  |
| occurrences (all)                                     | 448                    | 415                    |  |
| Loss of appetite                                      |                        |                        |  |
| alternative assessment type:<br>Systematic            |                        |                        |  |
| subjects affected / exposed <sup>[4]</sup>            | 250 / 1514<br>(16.51%) | 253 / 1513<br>(16.72%) |  |
| occurrences (all)                                     | 250                    | 253                    |  |
| Fever (GSK scale) (Axillary T >= 37.5°C)              |                        |                        |  |
| alternative assessment type:<br>Systematic            |                        |                        |  |
| subjects affected / exposed <sup>[5]</sup>            | 104 / 1514 (6.87%)     | 83 / 1513 (5.49%)      |  |
| occurrences (all)                                     | 104                    | 83                     |  |
| Vomiting  |                        |                        |  |
| alternative assessment type:<br>Systematic            |                        |                        |  |
| subjects affected / exposed <sup>[6]</sup>            | 232 / 1514<br>(15.32%) | 213 / 1513<br>(14.08%) |  |
| occurrences (all)                                     | 232                    | 213                    |  |
| Pain  |                        |                        |  |
| alternative assessment type:<br>Systematic            |                        |                        |  |

|  |                     |                     |
|--|---------------------|---------------------|
| subjects affected / exposed <sup>[7]</sup>                         | 9 / 151 (5.96%)     | 14 / 150 (9.33%)    |
| occurrences (all)  | 9                   | 14                  |
| Redness  |                     |                     |
| alternative assessment type:<br>Systematic                         |                     |                     |
| subjects affected / exposed <sup>[8]</sup>                         | 13 / 151 (8.61%)    | 20 / 150 (13.33%)   |
| occurrences (all)  | 13                  | 20                  |
| Swelling   |                     |                     |
| alternative assessment type:<br>Systematic                         |                     |                     |
| subjects affected / exposed <sup>[9]</sup>                         | 6 / 151 (3.97%)     | 13 / 150 (8.67%)    |
| occurrences (all)  | 6                   | 13                  |
| Drowsiness   |                     |                     |
| alternative assessment type:<br>Systematic                         |                     |                     |
| subjects affected / exposed <sup>[10]</sup>                        | 38 / 153 (24.84%)   | 44 / 153 (28.76%)   |
| occurrences (all)  | 38                  | 44                  |
| Irritability/Fussiness (OPV and DTPa vaccine)                      |                     |                     |
| alternative assessment type:<br>Systematic                         |                     |                     |
| subjects affected / exposed <sup>[11]</sup>                        | 52 / 153 (33.99%)   | 56 / 153 (36.60%)   |
| occurrences (all)  | 52                  | 56                  |
| Loss of appetite (OPV and DTPa vaccine)                            |                     |                     |
| alternative assessment type:<br>Systematic                         |                     |                     |
| subjects affected / exposed <sup>[12]</sup>                        | 32 / 153 (20.92%)   | 43 / 153 (28.10%)   |
| occurrences (all)  | 32                  | 43                  |
| Fever – Chinese scale: Axillary T >= 37.1°C                        |                     |                     |
| alternative assessment type:<br>Systematic                         |                     |                     |
| subjects affected / exposed <sup>[13]</sup>                        | 313 / 1514 (20.67%) | 302 / 1513 (19.96%) |
| occurrences (all)  | 313                 | 302                 |
| Gastrointestinal symptoms  |                     |                     |
| alternative assessment type:<br>Systematic                         |                     |                     |
| subjects affected / exposed <sup>[14]</sup>                        | 38 / 153 (24.84%)   | 43 / 153 (28.10%)   |
| occurrences (all)  | 38                  | 43                  |
| Fever – Chinese scale: Axillary T >= 37.1°C (OPV and DTPa vaccine) |                     |                     |
| alternative assessment type:<br>Systematic                         |                     |                     |

|   |                    |                    |  |
|---|--------------------|--------------------|--|
| subjects affected / exposed <sup>[15]</sup> | 20 / 153 (13.07%)  | 18 / 153 (11.76%)  |  |
| occurrences (all)                           | 20                 | 18                 |  |
| Infections and infestations                 |                    |                    |  |
| Upper respiratory tract infection           |                    |                    |  |
| subjects affected / exposed                 | 124 / 1667 (7.44%) | 119 / 1666 (7.14%) |  |
| occurrences (all)                           | 124                | 119                |  |
| Nasopharyngitis                             |                    |                    |  |
| subjects affected / exposed                 | 123 / 1667 (7.38%) | 103 / 1666 (6.18%) |  |
| occurrences (all)                           | 123                | 103                |  |

Notes:

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications, respectively).

medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date           | Amendment  |
|----------------|--|
| 05 August 2011 | Based on the preliminary review of GE episodes reported to date prior to unblinding and complete cleaning of the database, the rotavirus (RV) attack rate seems lower than what was anticipated in the protocol. In order to have the acceptable statistical power for the primary endpoint, the efficacy follow-up was extended till April 2012 (i.e. end of RV season in China). |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported