



## Clinical trial results:

**A phase II, double-blind, randomized, placebo-controlled study to assess the safety, reactogenicity and immunogenicity of three doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine (RIX4414 at 10 Exp 6.5 CCID50) administered to human immunodeficiency virus (HIV) infected infants at 6, 10 and 14 weeks of age in South Africa.**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2015-001484-39   |
| Trial protocol           | Outside EU/EEA   |
| Global end of trial date | 13 February 2008 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1            |
| This version publication date  | 20 April 2016 |
| First version publication date | 19 July 2015  |

### Trial information

#### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | 444563/022 |
|-----------------------|------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00263666 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                                         |
|------------------------------|---------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | GlaxoSmithKline Biologicals                                                                             |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330                                                        |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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**

|                                                      |                  |
|------------------------------------------------------|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 24 June 2008     |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 07 February 2008 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 13 February 2008 |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

To assess the safety and reactogenicity of 3 doses of GSK Biologicals' HRV vaccine versus placebo in HIV infected infants.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|                                                           |               |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment                          | 16 March 2005 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | South Africa: 100 |
| Worldwide total number of subjects   | 100               |
| 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)  | 100 |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 0   |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

In case of discrepancy between the HIV results (DNA PCR positive, viral load negative), performed at the Screening

Visit (one week prior to first vaccination) the infants were not enrolled in the study.

### 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 received 3 doses of Rotarix vaccine co-administered with routine Tritanrix™ HepB Hib and Polio Sabin™ vaccines.

|                                        |                                        |
|----------------------------------------|----------------------------------------|
| Arm type                               | Experimental                           |
| Investigational medicinal product name | Rotarix™                               |
| Investigational medicinal product code |                                        |
| Other name                             |                                        |
| Pharmaceutical forms                   | Powder and solvent for oral suspension |
| Routes of administration               | Oral use                               |

Dosage and administration details:

Oral vaccination

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Tritanrix™-HB+Hib |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Concomitant routine vaccination, IM administration

|                                        |                                        |
|----------------------------------------|----------------------------------------|
| Investigational medicinal product name | PolioSabin™                            |
| Investigational medicinal product code |                                        |
| Other name                             |                                        |
| Pharmaceutical forms                   | Powder and solvent for oral suspension |
| Routes of administration               | Oral use                               |

Dosage and administration details:

Oral administration, concomitant routine vaccination.

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

Arm description:

Subjects received 3 dose of placebo co-administered with routine Tritanrix™ HepB Hib and Polio Sabin™ vaccines.

|          |         |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

|                                                       |                                        |
|-------------------------------------------------------|----------------------------------------|
| Investigational medicinal product name                | Placebo                                |
| Investigational medicinal product code                |                                        |
| Other name                                            |                                        |
| Pharmaceutical forms                                  | Powder and solvent for oral suspension |
| Routes of administration                              | Oral use                               |
| Dosage and administration details:                    |                                        |
| Oral administration.                                  |                                        |
| Investigational medicinal product name                | Tritanrix™-HB+Hib                      |
| Investigational medicinal product code                |                                        |
| Other name                                            |                                        |
| Pharmaceutical forms                                  | Injection                              |
| Routes of administration                              | Intramuscular use                      |
| Dosage and administration details:                    |                                        |
| Concomitant routine vaccination, IM administration.   |                                        |
| Investigational medicinal product name                | PolioSabin™                            |
| Investigational medicinal product code                |                                        |
| Other name                                            |                                        |
| Pharmaceutical forms                                  | Powder and solvent for oral suspension |
| Routes of administration                              | Oral use                               |
| Dosage and administration details:                    |                                        |
| Oral administration, concomitant routine vaccination. |                                        |

| Number of subjects in period 1 | Rotarix Group | Placebo Group |
|--------------------------------|---------------|---------------|
| Started                        | 50            | 50            |
| Completed                      | 43            | 39            |
| Not completed                  | 7             | 11            |
| Consent withdrawn by subject   | -             | 1             |
| Adverse event, non-fatal       | 6             | 8             |
| Lost to follow-up              | 1             | 2             |

## Baseline characteristics

### Reporting groups

|                                                                                                                          |               |
|--------------------------------------------------------------------------------------------------------------------------|---------------|
| Reporting group title                                                                                                    | Rotarix Group |
| Reporting group description:                                                                                             |               |
| Subjects received 3 doses of Rotarix vaccine co-administered with routine Tritanrix™ HepB Hib and Polio Sabin™ vaccines. |               |
| Reporting group title                                                                                                    | Placebo Group |
| Reporting group description:                                                                                             |               |
| Subjects received 3 dose of placebo co-administered with routine Tritanrix™ HepB Hib and Polio Sabin™ vaccines.          |               |

| Reporting group values                             | Rotarix Group | Placebo Group | Total |
|----------------------------------------------------|---------------|---------------|-------|
| Number of subjects                                 | 50            | 50            | 100   |
| Age categorical                                    |               |               |       |
| Units: Subjects                                    |               |               |       |
| In utero                                           |               |               | 0     |
| Preterm newborn infants (gestational age < 37 wks) |               |               | 0     |
| Newborns (0-27 days)                               |               |               | 0     |
| Infants and toddlers (28 days-23 months)           |               |               | 0     |
| Children (2-11 years)                              |               |               | 0     |
| Adolescents (12-17 years)                          |               |               | 0     |
| Adults (18-64 years)                               |               |               | 0     |
| From 65-84 years                                   |               |               | 0     |
| 85 years and over                                  |               |               | 0     |
| Age continuous                                     |               |               |       |
| Units: weeks                                       |               |               |       |
| arithmetic mean                                    | 7.1           | 6.9           |       |
| standard deviation                                 | ± 1.1         | ± 1.02        | -     |
| Gender categorical                                 |               |               |       |
| Units: Subjects                                    |               |               |       |
| Female                                             | 28            | 25            | 53    |
| Male                                               | 22            | 25            | 47    |

## End points

### End points reporting groups

|                                                                                                                                                          |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| Reporting group title                                                                                                                                    | Rotarix Group |
| Reporting group description:<br>Subjects received 3 doses of Rotarix vaccine co-administered with routine Tritanrix™ HepB Hib and Polio Sabin™ vaccines. |               |
| Reporting group title                                                                                                                                    | Placebo Group |
| Reporting group description:<br>Subjects received 3 dose of placebo co-administered with routine Tritanrix™ HepB Hib and Polio Sabin™ vaccines.          |               |

### Primary: Number of subjects reporting grade "2" or grade "3" fever, vomiting or diarrhea.

|                                                                                                                                                                                                                        |                                                                                                 |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                        | Number of subjects reporting grade "2" or grade "3" fever, vomiting or diarrhea. <sup>[1]</sup> |
| End point description:<br>Symptoms reported in the table include: Fever: temperature (axillary route) > 38.0 degree Celsius (°C); Diarrhea: ≥ 4 looser than normal stools/day; Vomiting: ≥ 2 episodes of vomiting/day. |                                                                                                 |
| End point type                                                                                                                                                                                                         | Primary                                                                                         |
| End point timeframe:<br>Within the 15-day solicited follow-up period after any dose.                                                                                                                                   |                                                                                                 |

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 | 50              | 50              |  |  |
| Units: Subjects             |                 |                 |  |  |
| Any symptom, Across Doses   | 26              | 28              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any unsolicited symptoms (AEs).

|                                                                                                                                                                                                                                                  |                                                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                  | Number of subjects reporting any unsolicited symptoms (AEs). |
| End point description:<br>An unsolicited symptom was any spontaneously reported untoward medical occurrence in a subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. |                                                              |
| End point type                                                                                                                                                                                                                                   | Secondary                                                    |
| End point timeframe:<br>Within 30 days after each dose.                                                                                                                                                                                          |                                                              |

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 50              | 50              |  |  |
| Units: Subjects             |                 |                 |  |  |
| Any AE(s)                   | 47              | 48              |  |  |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

A serious adverse event (SAE) is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

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

End point timeframe:

Until 2 months after dose 3 (for subjects RV negative at Day 42 post-dose 3) or until end of RV shedding (for subjects who shed RV at Day 42 post-dose 3).

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 50              | 50              |  |  |
| Units: Subjects             |                 |                 |  |  |
| Any SAE(s)                  | 17              | 12              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting each type of solicited symptom.

|                 |                                                              |
|-----------------|--------------------------------------------------------------|
| End point title | Number of subjects reporting each type of solicited symptom. |
|-----------------|--------------------------------------------------------------|

End point description:

Solicited symptoms included Cough, Diarrhea (3 or more looser than normal stools/day), Fever (axillary temperature  $\geq 37.5^{\circ}\text{C}$ ), Irritability, Loss of appetite, and Vomiting.

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

End point timeframe:

Within the 15-day solicited follow-up period after each dose.

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 50              | 50              |  |  |
| Units: Subjects             |                 |                 |  |  |
| Cough                       | 35              | 31              |  |  |
| Diarrhea                    | 16              | 16              |  |  |
| Fever                       | 30              | 28              |  |  |
| Irritability                | 31              | 28              |  |  |
| Loss of appetite            | 23              | 23              |  |  |
| Vomiting                    | 19              | 15              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: The number of subjects with no evidence of immunosuppression and moderate/severe suppression, based on CD4+ absolute cell count and CD4+ percent.

|                 |                                                                                                                                                   |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | The number of subjects with no evidence of immunosuppression and moderate/severe suppression, based on CD4+ absolute cell count and CD4+ percent. |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Severe suppression: CD4+ cells/microliter ( $\mu$ l) < 750 and CD4+ percent < 15 percent (%); No evidence of suppression: CD4+ cells/ $\mu$ l  $\geq$  1500 and CD4+ percent  $\geq$  25%; Moderate suppression = all other CD4+ cell count and CD4+ % combinations.

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

End point timeframe:

At the screening visit and 2 months after dose 3 (Visit 4).

| End point values                              | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                            | Reporting group | Reporting group |  |  |
| Number of subjects analysed                   | 50              | 50              |  |  |
| Units: Subjects                               |                 |                 |  |  |
| Severe suppression at screening (n= 50, 50)   | 1               | 2               |  |  |
| Moderate suppression at screening (n= 50, 50) | 12              | 15              |  |  |
| No suppression at screening (n= 50, 50)       | 37              | 33              |  |  |
| Severe suppression at Visit 4 (n= 43, 39)     | 11              | 7               |  |  |
| Moderate suppression at Visit 4 (n= 43, 39)   | 15              | 18              |  |  |
| No suppression at Visit 4 (n= 43, 39)         | 13              | 10              |  |  |
| Unknown at Visit 4 (n= 43, 39)                | 4               | 4               |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Human immunodeficiency virus (HIV) Viral load.

|                 |                                                |
|-----------------|------------------------------------------------|
| End point title | Human immunodeficiency virus (HIV) Viral load. |
|-----------------|------------------------------------------------|

End point description:

Mean and standard deviation of the base-10 logarithm of HIV-1 ribonucleic acid (RNA) copies per milliliter (mL).

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

End point timeframe:

At the screening visit and 2 months after dose 3.

| End point values                              | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                            | Reporting group | Reporting group |  |  |
| Number of subjects analysed                   | 50              | 50              |  |  |
| Units: base-10 logarithm of copies/milliliter |                 |                 |  |  |
| arithmetic mean (standard deviation)          |                 |                 |  |  |
| At screening (n= 50, 50)                      | 5.7 (± 0.52)    | 5.7 (± 0.51)    |  |  |
| Two months after dose 3 (n= 43, 36)           | 5.6 (± 0.77)    | 5.7 (± 0.51)    |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects who seroconverted against rotavirus.

|                 |                                                         |
|-----------------|---------------------------------------------------------|
| End point title | Number of subjects who seroconverted against rotavirus. |
|-----------------|---------------------------------------------------------|

End point description:

A subject with anti-rotavirus Immunoglobulin (IgA) antibody concentration < 20 units/milliliter (U/mL) before vaccination and ≥ 20 U/mL after vaccination is considered as seroconverted.

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

End point timeframe:

Two months after dose 3.

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 21              | 22              |  |  |
| Units: Subjects             | 12              | 4               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with vaccine take.

|                                                                                                                                                                                                                                                                        |                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|
| End point title                                                                                                                                                                                                                                                        | Number of subjects with vaccine take. |
| End point description:<br>Vaccine take: appearance of serum IgA to rotavirus at a concentration of $\geq 20$ U/ml or rotavirus shedding in any stool sample collected from the Screening Visit to 2 months after dose 3 for subjects initially negative for rotavirus. |                                       |
| End point type                                                                                                                                                                                                                                                         | Secondary                             |
| End point timeframe:<br>Two months after the dose 3.                                                                                                                                                                                                                   |                                       |

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 23              | 23              |  |  |
| Units: Subjects             | 15              | 7               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Serum rotavirus immunoglobulin A (IgA) antibody concentrations.

|                                                                                                                                                                                                |                                                                                |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                | Serum rotavirus immunoglobulin A (IgA) antibody concentrations. <sup>[2]</sup> |
| End point description:<br>Concentrations are given as geometric mean concentrations (GMC) for anti-rotavirus IgA antibodies. This outcome measure concerns subjects in the Rotarix Group only. |                                                                                |
| End point type                                                                                                                                                                                 | Secondary                                                                      |
| End point timeframe:<br>Two months after dose 3.                                                                                                                                               |                                                                                |

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome measure concerns subjects in the Rotarix Group only.

|                                          |                      |  |  |  |
|------------------------------------------|----------------------|--|--|--|
| <b>End point values</b>                  | Rotarix Group        |  |  |  |
| Subject group type                       | Reporting group      |  |  |  |
| Number of subjects analysed              | 21                   |  |  |  |
| Units: U/ml                              |                      |  |  |  |
| geometric mean (confidence interval 95%) | 75.5 (29.1 to 195.7) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-polyribosyl ribitol phosphate (PRP) antibody concentrations more than or equal to the cut-off value.

|                                                                                                                                |                                                                                                                                   |
|--------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                | Number of subjects with anti-polyribosyl ribitol phosphate (PRP) antibody concentrations more than or equal to the cut-off value. |
| End point description:                                                                                                         |                                                                                                                                   |
| Cut-off values for anti-PRP antibody concentrations were $\geq 0.15$ and $\geq 1.0$ microgram/milliliter ( $\mu\text{g/mL}$ ). |                                                                                                                                   |
| End point type                                                                                                                 | Secondary                                                                                                                         |
| End point timeframe:                                                                                                           |                                                                                                                                   |
| Two months after dose 3.                                                                                                       |                                                                                                                                   |

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>     | Rotarix Group   | Placebo Group   |  |  |
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 25              | 24              |  |  |
| Units: Subjects             |                 |                 |  |  |
| $\geq 0.15 \mu\text{g/mL}$  | 20              | 23              |  |  |
| $\geq 1 \mu\text{g/mL}$     | 20              | 22              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Concentration for anti-PRP antibodies.

|                          |                                                       |
|--------------------------|-------------------------------------------------------|
| End point title          | Geometric Mean Concentration for anti-PRP antibodies. |
| End point description:   |                                                       |
| End point type           | Secondary                                             |
| End point timeframe:     |                                                       |
| Two months after dose 3. |                                                       |

| End point values                         | Rotarix Group           | Placebo Group           |  |  |
|------------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                       | Reporting group         | Reporting group         |  |  |
| Number of subjects analysed              | 25                      | 24                      |  |  |
| Units: µg/mL                             |                         |                         |  |  |
| geometric mean (confidence interval 95%) | 4.641 (1.764 to 12.215) | 4.865 (2.322 to 10.192) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-diphtheria and anti-tetanus toxoids antibody concentrations more than or equal to the cut-off value.

|                                                                          |                                                                                                                                   |
|--------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                          | Number of subjects with anti-diphtheria and anti-tetanus toxoids antibody concentrations more than or equal to the cut-off value. |
| End point description:                                                   |                                                                                                                                   |
| The cut-off value was $\geq 0.1$ International Units/milliliter (IU/mL). |                                                                                                                                   |
| End point type                                                           | Secondary                                                                                                                         |
| End point timeframe:                                                     |                                                                                                                                   |
| Two months after dose 3.                                                 |                                                                                                                                   |

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 25              | 25              |  |  |
| Units: Subjects             |                 |                 |  |  |
| Anti-diphtheria             | 19              | 19              |  |  |
| Anti-tetanus                | 23              | 24              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Concentration for anti-diphtheria and anti-tetanus toxoids antibodies.

|                          |                                                                                       |
|--------------------------|---------------------------------------------------------------------------------------|
| End point title          | Geometric Mean Concentration for anti-diphtheria and anti-tetanus toxoids antibodies. |
| End point description:   |                                                                                       |
| End point type           | Secondary                                                                             |
| End point timeframe:     |                                                                                       |
| Two months after dose 3. |                                                                                       |

| End point values                         | Rotarix Group          | Placebo Group          |  |  |
|------------------------------------------|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed              | 25                     | 25                     |  |  |
| Units: IU/mL                             |                        |                        |  |  |
| geometric mean (confidence interval 95%) |                        |                        |  |  |
| Anti-tetanus                             | 1.457 (0.794 to 2.674) | 1.035 (0.647 to 1.656) |  |  |
| Anti-diphtheria                          | 0.283 (0.167 to 0.481) | 0.219 (0.143 to 0.337) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-hepatitis B (HBs) antibody concentrations more than or equal to the cut-off value.

|                                                                                |                                                                                                                 |
|--------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| End point title                                                                | Number of subjects with anti-hepatitis B (HBs) antibody concentrations more than or equal to the cut-off value. |
| End point description:                                                         |                                                                                                                 |
| The cut-off value was $\geq 10$ milli international units/milliliter (mIU/mL). |                                                                                                                 |
| End point type                                                                 | Secondary                                                                                                       |
| End point timeframe:                                                           |                                                                                                                 |
| Two months after dose 3.                                                       |                                                                                                                 |

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 23              | 20              |  |  |
| Units: Subjects             | 15              | 15              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Concentration for anti-HBs antibodies.

|                          |                                                       |
|--------------------------|-------------------------------------------------------|
| End point title          | Geometric Mean Concentration for anti-HBs antibodies. |
| End point description:   |                                                       |
| End point type           | Secondary                                             |
| End point timeframe:     |                                                       |
| Two months after dose 3. |                                                       |

| End point values                         | Rotarix Group       | Placebo Group      |  |  |
|------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed              | 23                  | 20                 |  |  |
| Units: mIU/mL                            |                     |                    |  |  |
| geometric mean (confidence interval 95%) | 25.6 (14.3 to 45.8) | 18.9 (9.9 to 36.1) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-Bordetella pertussis (BPT) antibody concentrations more than or equal to the cut-off value.

|                        |                                                                                                                          |
|------------------------|--------------------------------------------------------------------------------------------------------------------------|
| End point title        | Number of subjects with anti-Bordetella pertussis (BPT) antibody concentrations more than or equal to the cut-off value. |
| End point description: | The cut-off value was $\geq 15$ Enzyme Linked Immunosorbent Assay Unit/milliliter(EL.U/mL).                              |
| End point type         | Secondary                                                                                                                |
| End point timeframe:   | Two months after dose 3.                                                                                                 |

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 25              | 24              |  |  |
| Units: Subjects             | 19              | 14              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Concentration for anti-BPT antibodies.

|                        |                                                       |
|------------------------|-------------------------------------------------------|
| End point title        | Geometric Mean Concentration for anti-BPT antibodies. |
| End point description: |                                                       |
| End point type         | Secondary                                             |
| End point timeframe:   | Two months after dose 3.                              |

| End point values                         | Rotarix Group       | Placebo Group       |  |  |
|------------------------------------------|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 25                  | 24                  |  |  |
| Units: EL.U/mL                           |                     |                     |  |  |
| geometric mean (confidence interval 95%) | 28.8 (19.3 to 42.8) | 18.1 (12.8 to 25.6) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-polio types 1, 2 and 3 antibody titers more than or equal to the cut-off value.

|                                                                                                                                               |                                                                                                              |
|-----------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                               | Number of subjects with anti-polio types 1, 2 and 3 antibody titers more than or equal to the cut-off value. |
| End point description:                                                                                                                        |                                                                                                              |
| The cut-off value was $\geq 1:8$ . The lowest dilution at which serum samples were tested was 1:8, from which a test was considered positive. |                                                                                                              |
| End point type                                                                                                                                | Secondary                                                                                                    |
| End point timeframe:                                                                                                                          |                                                                                                              |
| Two months after dose 3.                                                                                                                      |                                                                                                              |

| End point values              | Rotarix Group   | Placebo Group   |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 25              | 24              |  |  |
| Units: Subjects               |                 |                 |  |  |
| Anti-polio type 1 (n= 25, 24) | 19              | 15              |  |  |
| Anti-polio type 2 (n= 25, 24) | 23              | 21              |  |  |
| Anti-polio type 3 (n= 25, 23) | 18              | 15              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Titer for anti-polio types 1, 2 and 3 antibodies.

|                        |                                                                  |
|------------------------|------------------------------------------------------------------|
| End point title        | Geometric Mean Titer for anti-polio types 1, 2 and 3 antibodies. |
| End point description: |                                                                  |
| End point type         | Secondary                                                        |

End point timeframe:

Two months after dose 3.

| End point values                         | Rotarix Group         | Placebo Group         |  |  |
|------------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                       | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed              | 25                    | 24                    |  |  |
| Units: Titers                            |                       |                       |  |  |
| geometric mean (confidence interval 95%) |                       |                       |  |  |
| Anti-polio 1 (n= 25, 24)                 | 90.5 (36.4 to 225.3)  | 53 (19.4 to 144.5)    |  |  |
| Anti-polio 2 (n= 25, 24)                 | 142.6 (60.8 to 334.2) | 252.4 (91.2 to 698.7) |  |  |
| Anti-polio 3 (n= 25, 23)                 | 44.7 (19.2 to 104.2)  | 66 (22.6 to 192.2)    |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Rotavirus antigen excretion in stool samples.

|                 |                                               |
|-----------------|-----------------------------------------------|
| End point title | Rotavirus antigen excretion in stool samples. |
|-----------------|-----------------------------------------------|

End point description:

Number of subjects with rotavirus detected by Enzyme Linked Immunosorbent Assay (ELISA) in stool samples collected from Dose 1 until study end.

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

End point timeframe:

At day of each vaccination and at planned days following each vaccine dose until 2 months after dose 3 or until end of RV shedding.

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 25              | 25              |  |  |
| Units: Subjects             | 11              | 5               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Rotavirus in diarrheal stool samples.

|                 |                                       |
|-----------------|---------------------------------------|
| End point title | Rotavirus in diarrheal stool samples. |
|-----------------|---------------------------------------|



End point description:

Number of subjects reporting at least one rotavirus (vaccine strain or wild type rotavirus) gastroenteritis episode.

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

End point timeframe:

From Dose 1 until 2 months after dose 3 or until end of RV shedding.

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 50              | 50              |  |  |
| Units: Subjects             |                 |                 |  |  |
| Number of episodes          | 4               | 4               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Enteric pathogens identification.

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Enteric pathogens identification. |
|-----------------|-----------------------------------|

End point description:

Number of gastroenteritis (GE) episodes classified by enteric pathogen tests results.

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

End point timeframe:

From Dose 1 until 2 months after dose 3 or until end of RV shedding.

| End point values            | Rotarix Group   | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 29              | 34              |  |  |
| Units: Subjects             |                 |                 |  |  |
| Campylobacter, negative     | 18              | 24              |  |  |
| Campylobacter, positive     | 0               | 0               |  |  |
| Campylobacter, unknown      | 11              | 10              |  |  |
| E. histolytica, negative    | 18              | 24              |  |  |
| E. histolytica, positive    | 0               | 0               |  |  |
| E. histolytica, unknown     | 11              | 10              |  |  |
| Salmonella, negative        | 17              | 24              |  |  |
| Salmonella, positive        | 1               | 0               |  |  |
| Salmonella, unknown         | 11              | 10              |  |  |
| Sto Epec, negative          | 3               | 5               |  |  |
| Sto Epec, positive          | 0               | 0               |  |  |
| Sto Epec, unknown           | 26              | 29              |  |  |
| Sto G.Lambliia, negative    | 18              | 24              |  |  |
| Sto G.Lambliia, positive    | 0               | 0               |  |  |

|                        |    |    |  |  |
|------------------------|----|----|--|--|
| Sto G.Lamblia, unknown | 11 | 10 |  |  |
| Sto Shigella, negative | 18 | 24 |  |  |
| Sto Shigella, positive | 0  | 0  |  |  |
| Sto Shigella, unknown  | 11 | 10 |  |  |
| Sto Yersinia, negative | 18 | 24 |  |  |
| Sto Yersinia, positive | 0  | 0  |  |  |
| Sto Yersinia, unknown  | 11 | 10 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with the RV in stool samples.

|                                                                                                                                                                             |                                                  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| End point title                                                                                                                                                             | Number of subjects with the RV in stool samples. |
| End point description:                                                                                                                                                      |                                                  |
| Number of subjects with presence of RV in stool samples (shedding) collected at pre-determined time points by RV type (Yes, No, Mixed type and results not available [NA]). |                                                  |
| End point type                                                                                                                                                              | Secondary                                        |
| End point timeframe:                                                                                                                                                        |                                                  |
| From Dose 1 until post Dose 3.                                                                                                                                              |                                                  |

| End point values               | Rotarix Group   | Placebo Group   |  |  |
|--------------------------------|-----------------|-----------------|--|--|
| Subject group type             | Reporting group | Reporting group |  |  |
| Number of subjects analysed    | 50              | 50              |  |  |
| Units: Subjects                |                 |                 |  |  |
| Dose 1 (Day 7; Yes ) (N=9, 1)  | 7               | 0               |  |  |
| Dose 1 (Day 7; No) (N=9,1)     | 0               | 0               |  |  |
| Dose 1 (Day 7; NA) (N=9,1)     | 2               | 1               |  |  |
| Dose 1 (Day 14; Yes) (N=4,2)   | 0               | 0               |  |  |
| Dose 1 (Day 14; No) (N=4,2)    | 0               | 1               |  |  |
| Dose 1 (Day 14; Mixed) (N=4,2) | 0               | 1               |  |  |
| Dose 1 (Day 14; NA) (N=4,2)    | 4               | 0               |  |  |
| Dose 1 (Day 21; Yes) (N=5,1)   | 1               | 0               |  |  |
| Dose 1 (Day 21; No) (N=5,1)    | 0               | 1               |  |  |
| Dose 1 (Day 21; NA) (N=5,1)    | 4               | 0               |  |  |
| Dose 2 (Day 7; Yes) (N=0,1)    | 0               | 0               |  |  |
| Dose 2 (Day 7; No) (N=0,1)     | 0               | 1               |  |  |
| Dose 2 (Day 7; NA) (N=0,1)     | 0               | 0               |  |  |
| Dose 2 (Day 14; Yes) (N=1,0)   | 0               | 0               |  |  |
| Dose 2 (Day 14; No) (N=1,0)    | 0               | 0               |  |  |
| Dose 2 (Day 14; NA) (N=1,0)    | 1               | 0               |  |  |
| Dose 2 (Day 21; Yes) (N=2,0)   | 0               | 0               |  |  |
| Dose 2 (Day 21; No) (N=2,0)    | 0               | 0               |  |  |
| Dose 2 (Day 21; NA) (N=2,0)    | 2               | 0               |  |  |
| Dose 3 (Day 7; Yes) (N=1,1)    | 0               | 0               |  |  |
| Dose 3 (Day 7; No) (N=1,1)     | 0               | 1               |  |  |

|                                  |   |   |  |  |
|----------------------------------|---|---|--|--|
| Dose 3 (Day 7; NA) (N=1,1)       | 1 | 0 |  |  |
| Dose 3 (Day 14; Yes) (N=2,0)     | 2 | 0 |  |  |
| Dose 3 (Day 14; No) (N=2,0)      | 0 | 0 |  |  |
| Dose 3 (Day 14; NA) (N=2,0)      | 0 | 0 |  |  |
| Dose 3 (Day 42; Yes) (N=1,1)     | 0 | 0 |  |  |
| Dose 3 (Day 42; No) (N=1,1)      | 0 | 0 |  |  |
| Dose 3 (Day 42; NA) (N=1,1)      | 1 | 1 |  |  |
| Post Dose 3 (Day 0; Yes) (N=1,0) | 0 | 0 |  |  |
| Post Dose 3 (Day 0; No) (N=1,0)  | 0 | 0 |  |  |
| Post Dose 3 (Day 0; NA) (N=1,0)  | 1 | 0 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited general symptoms during the 15-day (Days 0-14) post-vaccination period following each dose and across doses, unsolicited AEs within 31 days (Days 0-30) after any vaccination and SAEs throughout the study period.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 11.0   |

### Reporting groups

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

Reporting group description:

Subjects received 3 doses of Rotarix vaccine co-administered with routine Tritanrix™ HepB Hib and Polio Sabin™ vaccines.

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

Reporting group description:

Subjects received 3 doses of placebo co-administered with routine Tritanrix™ HepB Hib and Polio Sabin™ vaccines.

| Serious adverse events                               | Rotarix Group    | Placebo Group    |  |
|------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by serious adverse events    |                  |                  |  |
| subjects affected / exposed                          | 17 / 50 (34.00%) | 12 / 50 (24.00%) |  |
| number of deaths (all causes)                        | 0                | 0                |  |
| number of deaths resulting from adverse events       | 0                | 0                |  |
| Blood and lymphatic system disorders                 |                  |                  |  |
| Anemia                                               |                  |                  |  |
| subjects affected / exposed                          | 1 / 50 (2.00%)   | 1 / 50 (2.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| General disorders and administration site conditions |                  |                  |  |
| Sudden infant death syndrome                         |                  |                  |  |
| subjects affected / exposed                          | 0 / 50 (0.00%)   | 1 / 50 (2.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 1            |  |
| Eye disorders                                        |                  |                  |  |
| Conjunctivitis                                       |                  |                  |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 50 (2.00%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Ileus paralytic                                 |                |                |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| Hepatobiliary disorders                         |                |                |  |
| Jaundice                                        |                |                |  |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Epistaxis                                       |                |                |  |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Pneumonia aspiration                            |                |                |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| Respiratory failure                             |                |                |  |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Infections and infestations                     |                |                |  |
| Bronchiolitis                                   |                |                |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bronchopneumonia                                |                |                |  |

|                                                 |                 |                |  |
|-------------------------------------------------|-----------------|----------------|--|
| subjects affected / exposed                     | 7 / 50 (14.00%) | 4 / 50 (8.00%) |  |
| occurrences causally related to treatment / all | 0 / 7           | 0 / 4          |  |
| deaths causally related to treatment / all      | 0 / 2           | 0 / 4          |  |
| Lobar pneumonia                                 |                 |                |  |
| subjects affected / exposed                     | 0 / 50 (0.00%)  | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1          |  |
| Pneumocystis jiroveci pneumonia                 |                 |                |  |
| subjects affected / exposed                     | 2 / 50 (4.00%)  | 2 / 50 (4.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1          |  |
| Pneumonia                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 50 (2.00%)  | 3 / 50 (6.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 2          |  |
| Lymph node tuberculosis                         |                 |                |  |
| subjects affected / exposed                     | 0 / 50 (0.00%)  | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pulmonary tuberculosis                          |                 |                |  |
| subjects affected / exposed                     | 0 / 50 (0.00%)  | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Tuberculosis                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 50 (2.00%)  | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Dysentery                                       |                 |                |  |
| subjects affected / exposed                     | 0 / 50 (0.00%)  | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastroenteritis                                 |                 |                |  |

|                                                 |                 |                |  |
|-------------------------------------------------|-----------------|----------------|--|
| subjects affected / exposed                     | 6 / 50 (12.00%) | 3 / 50 (6.00%) |  |
| occurrences causally related to treatment / all | 0 / 6           | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| HIV infection                                   |                 |                |  |
| subjects affected / exposed                     | 1 / 50 (2.00%)  | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Meningitis                                      |                 |                |  |
| subjects affected / exposed                     | 1 / 50 (2.00%)  | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Oral candidiasis                                |                 |                |  |
| subjects affected / exposed                     | 1 / 50 (2.00%)  | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Otitis media                                    |                 |                |  |
| subjects affected / exposed                     | 2 / 50 (4.00%)  | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Sepsis                                          |                 |                |  |
| subjects affected / exposed                     | 3 / 50 (6.00%)  | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 2           | 0 / 0          |  |
| Metabolism and nutrition disorders              |                 |                |  |
| Dehydration                                     |                 |                |  |
| subjects affected / exposed                     | 2 / 50 (4.00%)  | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1          |  |
| Electrolyte imbalance                           |                 |                |  |
| subjects affected / exposed                     | 0 / 50 (0.00%)  | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1          |  |
| Marasmus                                        |                 |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |

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

| <b>Non-serious adverse events</b>                     | Rotarix Group    | Placebo Group    |  |
|-------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 47 / 50 (94.00%) | 48 / 50 (96.00%) |  |
| Investigations                                        |                  |                  |  |
| Weight decreased                                      |                  |                  |  |
| subjects affected / exposed                           | 1 / 50 (2.00%)   | 4 / 50 (8.00%)   |  |
| occurrences (all)                                     | 1                | 4                |  |
| Blood and lymphatic system disorders                  |                  |                  |  |
| Lymphadenopathy                                       |                  |                  |  |
| subjects affected / exposed                           | 5 / 50 (10.00%)  | 3 / 50 (6.00%)   |  |
| occurrences (all)                                     | 5                | 3                |  |
| Splenomegaly                                          |                  |                  |  |
| subjects affected / exposed                           | 2 / 50 (4.00%)   | 4 / 50 (8.00%)   |  |
| occurrences (all)                                     | 2                | 4                |  |
| General disorders and administration site conditions  |                  |                  |  |
| Pyrexia                                               |                  |                  |  |
| subjects affected / exposed                           | 3 / 50 (6.00%)   | 6 / 50 (12.00%)  |  |
| occurrences (all)                                     | 3                | 6                |  |
| Cough (solicited)                                     |                  |                  |  |
| alternative assessment type: Systematic               |                  |                  |  |
| subjects affected / exposed                           | 35 / 50 (70.00%) | 31 / 50 (62.00%) |  |
| occurrences (all)                                     | 35               | 31               |  |
| Diarrhoea                                             |                  |                  |  |
| alternative assessment type: Systematic               |                  |                  |  |
| subjects affected / exposed                           | 16 / 50 (32.00%) | 16 / 50 (32.00%) |  |
| occurrences (all)                                     | 16               | 16               |  |
| Fever                                                 |                  |                  |  |
| alternative assessment type: Systematic               |                  |                  |  |



|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                         |                                                                                                                                         |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Irritability</p> <p>alternative assessment type:<br/>Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Loss of appetite</p> <p>alternative assessment type:<br/>Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting (solicited)</p> <p>alternative assessment type:<br/>Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>30 / 50 (60.00%)</p> <p>30</p> <p>31 / 50 (62.00%)</p> <p>31</p> <p>23 / 50 (46.00%)</p> <p>23</p> <p>19 / 50 (38.00%)</p> <p>19</p> | <p>28 / 50 (56.00%)</p> <p>28</p> <p>28 / 50 (56.00%)</p> <p>28</p> <p>23 / 50 (46.00%)</p> <p>23</p> <p>15 / 50 (30.00%)</p> <p>15</p> |  |
| <p>Gastrointestinal disorders</p> <p>Constipation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Abdominal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                  | <p>1 / 50 (2.00%)</p> <p>1</p> <p>1 / 50 (2.00%)</p> <p>1</p> <p>2 / 50 (4.00%)</p> <p>2</p>                                            | <p>3 / 50 (6.00%)</p> <p>3</p> <p>5 / 50 (10.00%)</p> <p>5</p> <p>3 / 50 (6.00%)</p> <p>3</p>                                           |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasal congestion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                              | <p>1 / 50 (2.00%)</p> <p>1</p> <p>4 / 50 (8.00%)</p> <p>4</p>                                                                           | <p>5 / 50 (10.00%)</p> <p>5</p> <p>4 / 50 (8.00%)</p> <p>4</p>                                                                          |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>Dermatitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dermatitis diaper</p>                                                                                                                                                                                                                                                                                                                             | <p>4 / 50 (8.00%)</p> <p>4</p>                                                                                                          | <p>4 / 50 (8.00%)</p> <p>4</p>                                                                                                          |  |

|                                                                                                                      |                        |                        |  |
|----------------------------------------------------------------------------------------------------------------------|------------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                     | 5 / 50 (10.00%)<br>5   | 4 / 50 (8.00%)<br>4    |  |
| Eczema<br>subjects affected / exposed<br>occurrences (all)                                                           | 2 / 50 (4.00%)<br>2    | 8 / 50 (16.00%)<br>8   |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                                                             | 4 / 50 (8.00%)<br>4    | 2 / 50 (4.00%)<br>2    |  |
| Rash papular<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 50 (0.00%)<br>0    | 3 / 50 (6.00%)<br>3    |  |
| Infections and infestations<br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 18 / 50 (36.00%)<br>18 | 14 / 50 (28.00%)<br>14 |  |
| Pulmonary tuberculosis<br>subjects affected / exposed<br>occurrences (all)                                           | 2 / 50 (4.00%)<br>2    | 3 / 50 (6.00%)<br>3    |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                                                        | 6 / 50 (12.00%)<br>6   | 0 / 50 (0.00%)<br>0    |  |
| Pharyngitis<br>subjects affected / exposed<br>occurrences (all)                                                      | 1 / 50 (2.00%)<br>1    | 3 / 50 (6.00%)<br>3    |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 05 November 2004 | <p>In response to comments from the Ethical committee of the WHO (SCRIHS), the following implementations were performed:</p> <ul style="list-style-type: none"><li>- The study sites were described. Information on the pool from which subjects will be recruited as well as on the screening process was added.</li><li>- The diagnostic plans for fatalities and their follow-up were described.</li><li>• An Independent Data Monitoring Committee (IDMC) who is monitoring the safety aspects of GSK Biologicals HRV vaccine clinical development, will review each SAE/IS case and may recommend a clinical study hold in case of safety concern.</li><li>• Since the study sites have different recommendations for the mother with regard to feeding the subjects, it was decided to record information on feeding practices. This will allow to explore any influence of feeding practice on vaccine take.</li><li>• The safety data obtained with GSK Biologicals HRV vaccine since the finalization of the original protocol (dated 29 July 2003) were updated.</li><li>• Other minor modifications (e.g. update of laboratory names and commercial kit versions for HIV testing; update to reflect the current processes to be followed for surgical specimens in case of IS) and administrative changes were made.</li></ul> |
| 19 August 2005   | <p>To update the safety data obtained with GSK Biologicals' HRV vaccine since the finalization of the original protocol and amendment 1 (dated 5 November 2004)</p> <p>To update the Regulatory reporting requirements for serious adverse events according to latest version of GSK Biologicals' standard protocol.</p> <p>Describe that GSK facilitate access to anti retroviral (ARV) treatment centers for subjects who develop clinical symptoms or have CD4 count below 20%.</p> <p>To add the more recent description of immunologic and clinical categories of HIV disease: according to the WHO and Republic of South Africa (RSA) National guidelines.</p> <p>To reflect other minor modifications (e.g. update of some laboratory tests and names of lab).</p> <p>To reflect the IDMC's request to evaluate the presence of persistent or recurrent shedding of rotavirus at the final visit.</p>                                                                                                                                                                                                                                                                                                                                                                                                                              |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported