



## Clinical trial results:

**A phase III, open, controlled study in South Africa to assess the immunogenicity, safety and reactogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine administered as a 3-dose (6, 10, 14 weeks) primary immunization course in HIV infected infants, HIV exposed uninfected infants and HIV unexposed uninfected infants followed by a booster vaccination at 9-10 months of age.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2011-002077-35 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 27 June 2012   |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1               |
| This version publication date  | 16 February 2016 |
| First version publication date | 11 June 2015     |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 111634 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00829010 |
| 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)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-000673-PIP01-09 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes                 |

Notes:

## Results analysis stage

|                                                      |               |
|------------------------------------------------------|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 02 April 2014 |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 27 June 2012  |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate and characterize the immune response to the Synflorix™ vaccine one month following a 3-dose (6, 10 and 14 weeks of age) primary vaccination course in HIV infected infants, HIV exposed uninfected infants and HIV unexposed uninfected infants.

Protection of trial subjects:

All subjects were supervised after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Only eligible subjects that had no contraindications to any components of the vaccines were vaccinated. Subjects were followed-up after each vaccination.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 17 February 2009 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | South Africa: 489 |
| Worldwide total number of subjects   | 489               |
| EEA total number of subjects         | 0                 |

Notes:

### Subjects enrolled per age group

|                                           |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 489 |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |

|                      |   |
|----------------------|---|
| Adults (18-64 years) | 0 |
| From 65 to 84 years  | 0 |
| 85 years and over    | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The oral poliovirus vaccine could be given at any time during the study (routinely given concurrently with Tritanrix™-HepB/Hib vaccine) but was not considered as study vaccine. Out of the 489 subjects enrolled in the study, only 484 subjects were assigned to a study group and received vaccination.

### Pre-assignment

Screening details:

The study included 3 populations defined based on the human immunodeficiency virus status of the mother and the infant. Infant born from: •a HIV positive mother and HIV infected at Month 0 = HIV+/+. •a HIV positive mother and HIV exposed uninfected at screening = HIV+/- . •a HIV negative mother and HIV unexposed uninfected at Month 0 = HIV-

### Pre-assignment period milestones

|                              |     |
|------------------------------|-----|
| Number of subjects started   | 489 |
| Number of subjects completed | 484 |

### Pre-assignment subject non-completion reasons

|                            |                                           |
|----------------------------|-------------------------------------------|
| Reason: Number of subjects | subjects non-assigned to a study group: 5 |
|----------------------------|-------------------------------------------|

### Period 1

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

### Arms

|                              |              |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes          |
| Arm title                    | HIV+/+ Group |

Arm description:

Infants born from a HIV positive mother and confirmed as HIV infected. Subjects received 3 primary doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 and 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age and 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered intramuscularly in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ given orally.

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Synflorix              |
| Investigational medicinal product code | GSK1024850A            |
| Other name                             | 10Pn-PD-DiT, 10Pn      |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8).

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Tritanrix™-HepB/Hib    |
| Investigational medicinal product code |                        |
| Other name                             | DTPW-HBV/Hib           |
| Pharmaceutical forms                   | Solution for injection |

|                                                                                                                                                                                              |                        |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|
| Routes of administration                                                                                                                                                                     | Intramuscular use      |
| Dosage and administration details:                                                                                                                                                           |                        |
| Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14). |                        |
| Investigational medicinal product name                                                                                                                                                       | Rotarix                |
| Investigational medicinal product code                                                                                                                                                       |                        |
| Other name                                                                                                                                                                                   | HRV                    |
| Pharmaceutical forms                                                                                                                                                                         | Oral solution          |
| Routes of administration                                                                                                                                                                     | Oral use               |
| Dosage and administration details:                                                                                                                                                           |                        |
| Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).                                                                                                        |                        |
| Investigational medicinal product name                                                                                                                                                       | Measles                |
| Investigational medicinal product code                                                                                                                                                       |                        |
| Other name                                                                                                                                                                                   |                        |
| Pharmaceutical forms                                                                                                                                                                         | Solution for injection |
| Routes of administration                                                                                                                                                                     | Intramuscular use      |
| Dosage and administration details:                                                                                                                                                           |                        |
| Subjects received 2 doses at 9-10 months and 15-18 months of age.                                                                                                                            |                        |
| <b>Arm title</b>                                                                                                                                                                             | HIV+/- Group           |

**Arm description:**

Infants born from a HIV positive mother and confirmed as HIV exposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                                                                                                                                                                             |                        |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|
| Arm type                                                                                                                                                                    | Experimental           |
| Investigational medicinal product name                                                                                                                                      | Synflorix              |
| Investigational medicinal product code                                                                                                                                      | GSK1024850A            |
| Other name                                                                                                                                                                  | 10Pn-PD-DiT, 10Pn      |
| Pharmaceutical forms                                                                                                                                                        | Solution for injection |
| Routes of administration                                                                                                                                                    | Intramuscular use      |
| Dosage and administration details:                                                                                                                                          |                        |
| Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). |                        |
| Investigational medicinal product name                                                                                                                                      | Tritanrix™-HepB/Hib    |
| Investigational medicinal product code                                                                                                                                      |                        |
| Other name                                                                                                                                                                  | DTPW-HBV/Hib           |
| Pharmaceutical forms                                                                                                                                                        | Solution for injection |
| Routes of administration                                                                                                                                                    | Intramuscular use      |

**Dosage and administration details:**

Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14).

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Rotarix       |
| Investigational medicinal product code |               |
| Other name                             | HRV           |
| Pharmaceutical forms                   | Oral solution |
| Routes of administration               | Oral use      |

**Dosage and administration details:**

Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).

|                                                                   |                        |
|-------------------------------------------------------------------|------------------------|
| Investigational medicinal product name                            | Measles                |
| Investigational medicinal product code                            |                        |
| Other name                                                        |                        |
| Pharmaceutical forms                                              | Solution for injection |
| Routes of administration                                          | Intramuscular use      |
| Dosage and administration details:                                |                        |
| Subjects received 2 doses at 9-10 months and 15-18 months of age. |                        |
| <b>Arm title</b>                                                  | HIV-(3+1) Group        |

**Arm description:**

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Synflorix              |
| Investigational medicinal product code | GSK1024850A            |
| Other name                             | 10Pn-PD-DiT, 10Pn      |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

**Dosage and administration details:**

Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8).

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Tritanrix™-HepB/Hib    |
| Investigational medicinal product code |                        |
| Other name                             | DTPW-HBV/Hib           |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

**Dosage and administration details:**

Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14).

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Rotarix       |
| Investigational medicinal product code |               |
| Other name                             | HRV           |
| Pharmaceutical forms                   | Oral solution |
| Routes of administration               | Oral use      |

**Dosage and administration details:**

Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Measles                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

**Dosage and administration details:**

Subjects received 2 doses at 9-10 months and 15-18 months of age.

|                  |                 |
|------------------|-----------------|
| <b>Arm title</b> | HIV-(EPI) Group |
|------------------|-----------------|

**Arm description:**

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses of Synflorix™ vaccine (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study

Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Synflorix              |
| Investigational medicinal product code | GSK1024850A            |
| Other name                             | 10Pn-PD-DiT, 10Pn      |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2).

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Tritanrix™-HepB/Hib    |
| Investigational medicinal product code |                        |
| Other name                             | DTPW-HBV/Hib           |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14).

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Rotarix       |
| Investigational medicinal product code |               |
| Other name                             | HRV           |
| Pharmaceutical forms                   | Oral solution |
| Routes of administration               | Oral use      |

Dosage and administration details:

Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Measles                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Subjects received 2 doses at 9-10 months and 15-18 months of age.

|                  |                 |
|------------------|-----------------|
| <b>Arm title</b> | HIV-(2+1) Group |
|------------------|-----------------|

Arm description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 2 primary doses (at 6 & 14 weeks of age at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Synflorix              |
| Investigational medicinal product code | GSK1024850A            |
| Other name                             | 10Pn-PD-DiT, 10Pn      |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Subjects received 2 primary doses (at 6 & 14 weeks of age, at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8).

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Tritanrix™-HepB/Hib    |
| Investigational medicinal product code |                        |
| Other name                             | DTPW-HBV/Hib           |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14).

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Rotarix       |
| Investigational medicinal product code |               |
| Other name                             | HRV           |
| Pharmaceutical forms                   | Oral solution |
| Routes of administration               | Oral use      |

Dosage and administration details:

Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Measles                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Subjects received 2 doses at 9-10 months and 15-18 months of age.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | HIV+/+ Group | HIV+/- Group | HIV-(3+1) Group |
|-----------------------------------------------------|--------------|--------------|-----------------|
| Started                                             | 87           | 97           | 100             |
| Completed up to Month 9                             | 81           | 92           | 98              |
| Completed                                           | 81           | 92           | 98              |
| Not completed                                       | 6            | 5            | 2               |
| Consent withdrawn by subject                        | -            | 1            | 1               |
| Adverse event, non-fatal                            | 6            | 3            | -               |
| Migrated /moved from study area                     | -            | 1            | -               |
| Lost to follow-up                                   | -            | -            | 1               |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | HIV-(EPI) Group | HIV-(2+1) Group |
|-----------------------------------------------------|-----------------|-----------------|
| Started                                             | 100             | 100             |
| Completed up to Month 9                             | 94              | 98              |
| Completed                                           | 94              | 98              |
| Not completed                                       | 6               | 2               |
| Consent withdrawn by subject                        | -               | 2               |
| Adverse event, non-fatal                            | 3               | -               |
| Migrated /moved from study area                     | 3               | -               |



|                   |   |   |
|-------------------|---|---|
| Lost to follow-up | - | - |
|-------------------|---|---|

---

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: 5 subjects enrolled, but not allocated to a group and did not receive a vaccine

## Baseline characteristics

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | HIV+/+ Group |
|-----------------------|--------------|

#### Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV infected. Subjects received 3 primary doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 and 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age and 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered intramuscularly in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ given orally.

|                       |              |
|-----------------------|--------------|
| Reporting group title | HIV+/- Group |
|-----------------------|--------------|

#### Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV exposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | HIV-(3+1) Group |
|-----------------------|-----------------|

#### Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | HIV-(EPI) Group |
|-----------------------|-----------------|

#### Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses of Synflorix™ vaccine (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | HIV-(2+1) Group |
|-----------------------|-----------------|

#### Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 2 primary doses (at 6 & 14 weeks of age at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

| <b>Reporting group values</b>                                                                                                                                                                                                                             | HIV+/+ Group | HIV+/- Group | HIV-(3+1) Group |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|--------------|-----------------|
| Number of subjects                                                                                                                                                                                                                                        | 87           | 97           | 100             |
| Age categorical<br>Units: Subjects                                                                                                                                                                                                                        |              |              |                 |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |              |              |                 |
| Age continuous<br>Units: weeks                                                                                                                                                                                                                            |              |              |                 |
| arithmetic mean                                                                                                                                                                                                                                           | 6.6          | 6.3          | 6.1             |
| standard deviation                                                                                                                                                                                                                                        | ± 0.92       | ± 0.64       | ± 0.41          |
| Gender categorical<br>Units: Subjects                                                                                                                                                                                                                     |              |              |                 |
| Female                                                                                                                                                                                                                                                    | 50           | 46           | 58              |
| Male                                                                                                                                                                                                                                                      | 37           | 51           | 42              |

| <b>Reporting group values</b>                                                                                                                                                                                                                             | HIV-(EPI) Group | HIV-(2+1) Group | Total                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|-----------------|--------------------------------------|
| Number of subjects                                                                                                                                                                                                                                        | 100             | 100             | 484                                  |
| Age categorical<br>Units: Subjects                                                                                                                                                                                                                        |                 |                 |                                      |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                 |                 | 0<br>0<br>0<br>0<br>0<br>0<br>0<br>0 |
| Age continuous<br>Units: weeks                                                                                                                                                                                                                            |                 |                 |                                      |
| arithmetic mean                                                                                                                                                                                                                                           | 6.1             | 6.1             | -                                    |
| standard deviation                                                                                                                                                                                                                                        | ± 0.35          | ± 0.29          |                                      |
| Gender categorical<br>Units: Subjects                                                                                                                                                                                                                     |                 |                 |                                      |
| Female                                                                                                                                                                                                                                                    | 50              | 47              | 251                                  |
| Male                                                                                                                                                                                                                                                      | 50              | 53              | 233                                  |

## End points

### End points reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | HIV+/+ Group |
|-----------------------|--------------|

#### Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV infected. Subjects received 3 primary doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 and 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age and 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered intramuscularly in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ given orally.

|                       |              |
|-----------------------|--------------|
| Reporting group title | HIV+/- Group |
|-----------------------|--------------|

#### Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV exposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | HIV-(3+1) Group |
|-----------------------|-----------------|

#### Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | HIV-(EPI) Group |
|-----------------------|-----------------|

#### Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses of Synflorix™ vaccine (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | HIV-(2+1) Group |
|-----------------------|-----------------|

#### Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 2 primary doses (at 6 & 14 weeks of age at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

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**Primary: Number of Subjects With Anti-pneumococcal Vaccine Serotype Antibody Concentrations Equal to or Above 0.20 Microgram Per Millilitre (µg/mL).**

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|                 |                                                                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Anti-pneumococcal Vaccine Serotype Antibody Concentrations Equal to or Above 0.20 Microgram Per Millilitre (µg/mL). <sup>[1]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|

**End point description:**

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration  $\geq 0.05$  µg/mL. Results were not available at the time of the posting and are entered as equal to "9"

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

**End point timeframe:**

1 month following primary immunization (post-Dose 3 at Month 3 for the HIV+/+ Group, HIV+/- Group, HIV- (3+1) Group, HIV- (EPI) Group and post-Dose 2 at Month 3 for the HIV- (2+1) Group)

**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 intent of this endpoint was descriptive, no comparison of groups was performed.

| End point values            | HIV+/+ Group    | HIV+/- Group    | HIV-(3+1) Group | HIV-(EPI) Group |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 87              | 97              | 100             | 100             |
| Units: Subject              |                 |                 |                 |                 |
| ANTI-1                      | 9               | 9               | 9               | 9               |

| End point values            | HIV-(2+1) Group |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 100             |  |  |  |
| Units: Subject              |                 |  |  |  |
| ANTI-1                      | 9               |  |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Number of Subjects With Any and Severe (Grade 3) Solicited Local Adverse Events (AEs).**

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|                 |                                                                                        |
|-----------------|----------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Any and Severe (Grade 3) Solicited Local Adverse Events (AEs). |
|-----------------|----------------------------------------------------------------------------------------|

**End point description:**

Solicited local AEs assessed were pain, redness and swelling. Any = incidence of any local symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling above 30 millimeter.

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

End point timeframe:

During the 4-day (Days 0-3) post-primary vaccination period across doses.

| End point values            | HIV+/+ Group    | HIV+/- Group    | HIV-(3+1) Group | HIV-(EPI) Group |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 87              | 97              | 98              | 98              |
| Units: Subjects             |                 |                 |                 |                 |
| Any pain                    | 76              | 90              | 92              | 95              |
| Grade 3 pain                | 19              | 17              | 28              | 42              |
| Any redness                 | 66              | 76              | 83              | 83              |
| Redness > 30 mm             | 14              | 10              | 17              | 20              |
| Any swelling                | 71              | 79              | 84              | 91              |
| Swelling > 30 mm            | 25              | 30              | 41              | 44              |

| End point values            | HIV-(2+1) Group |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 98              |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Any pain                    | 97              |  |  |  |
| Grade 3 pain                | 34              |  |  |  |
| Any redness                 | 84              |  |  |  |
| Redness > 30 mm             | 14              |  |  |  |
| Any swelling                | 84              |  |  |  |
| Swelling > 30 mm            | 31              |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects with Any, Severe (Grade 3) and Related Solicited General Adverse Events (AEs).

|                 |                                                                                                   |
|-----------------|---------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects with Any, Severe (Grade 3) and Related Solicited General Adverse Events (AEs). |
|-----------------|---------------------------------------------------------------------------------------------------|

End point description:

General AEs = diarrhoea, drowsiness, irritability, loss of appetite, vomiting and fever (axillary  $\geq 37.5$  degrees Celsius). Any= Incidence of any symptom regardless of intensity grade or relationship to vaccination. Grade 3: drowsiness = prevented normal activity. irritability = crying that could not be comforted/ prevented normal activity. loss of appetite = not eating at all. diarrhoea:  $\geq 6$  looser than normal stools/day. vomiting:  $\geq 3$  episodes of vomiting/day. Fever =  $> 39.5^{\circ}\text{C}$  Related = symptom assessed by the investigator as related to the vaccination.

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

End point timeframe:

During the 4-day (Days 0-3) post-primary vaccination period across doses.

| <b>End point values</b>                      | HIV+/+ Group    | HIV+/- Group    | HIV-(3+1) Group | HIV-(EPI) Group |
|----------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type                           | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed                  | 87              | 97              | 98              | 98              |
| Units: Subjects                              |                 |                 |                 |                 |
| Any diarrhoea                                | 8               | 5               | 12              | 10              |
| Grade 3 diarrhoea                            | 2               | 0               | 3               | 3               |
| Related diarrhoea                            | 8               | 5               | 11              | 9               |
| Any drowsiness                               | 50              | 61              | 70              | 70              |
| Grade 3 drowsiness                           | 1               | 6               | 5               | 7               |
| Related drowsiness                           | 48              | 57              | 67              | 66              |
| Fever (axillary) $\geq 37.5^{\circ}\text{C}$ | 40              | 34              | 41              | 28              |
| Fever (axillary) $> 39.5^{\circ}\text{C}$    | 0               | 0               | 2               | 0               |
| Related fever                                | 34              | 29              | 38              | 27              |
| Any irritability                             | 66              | 81              | 89              | 89              |
| Grade 3 irritability                         | 6               | 10              | 19              | 13              |
| Related irritability                         | 65              | 77              | 86              | 83              |
| Any loss of appetite                         | 37              | 52              | 56              | 57              |
| Grade 3 loss of appetite                     | 0               | 1               | 2               | 2               |
| Related loss of appetite                     | 36              | 46              | 53              | 53              |
| Any vomiting                                 | 17              | 19              | 15              | 18              |
| Grade 3 vomiting                             | 3               | 3               | 4               | 5               |
| Related vomiting                             | 16              | 16              | 14              | 13              |

| <b>End point values</b>                      | HIV-(2+1) Group |  |  |  |
|----------------------------------------------|-----------------|--|--|--|
| Subject group type                           | Reporting group |  |  |  |
| Number of subjects analysed                  | 98              |  |  |  |
| Units: Subjects                              |                 |  |  |  |
| Any diarrhoea                                | 5               |  |  |  |
| Grade 3 diarrhoea                            | 2               |  |  |  |
| Related diarrhoea                            | 5               |  |  |  |
| Any drowsiness                               | 68              |  |  |  |
| Grade 3 drowsiness                           | 8               |  |  |  |
| Related drowsiness                           | 63              |  |  |  |
| Fever (axillary) $\geq 37.5^{\circ}\text{C}$ | 28              |  |  |  |
| Fever (axillary) $> 39.5^{\circ}\text{C}$    | 0               |  |  |  |
| Related fever                                | 25              |  |  |  |
| Any irritability                             | 91              |  |  |  |
| Grade 3 irritability                         | 15              |  |  |  |
| Related irritability                         | 85              |  |  |  |
| Any loss of appetite                         | 62              |  |  |  |
| Grade 3 loss of appetite                     | 5               |  |  |  |
| Related loss of appetite                     | 58              |  |  |  |
| Any vomiting                                 | 23              |  |  |  |
| Grade 3 vomiting                             | 2               |  |  |  |

|                  |    |  |  |  |
|------------------|----|--|--|--|
| Related vomiting | 17 |  |  |  |
|------------------|----|--|--|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Any and Severe (Grade 3) Solicited Local Adverse Events (AEs).

|                 |                                                                                                       |
|-----------------|-------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Any and Severe (Grade 3) Solicited Local Adverse Events (AEs). <sup>[2]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------|

End point description:

Solicited local AEs assessed were pain, redness and swelling. Any = incidence of any local symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling above 30 millimeter.

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

End point timeframe:

During the 4-day (Days 0-3) period following booster vaccination with Synflorix vaccine

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: Since HIV - (EPI) Group didn't receive booster vaccination, there are no results to be analyzed for that timeframe.

| End point values            | HIV+/+ Group    | HIV+/- Group    | HIV-(3+1) Group | HIV-(2+1) Group |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 78              | 91              | 96              | 96              |
| Units: Subjects             |                 |                 |                 |                 |
| Any pain                    | 42              | 56              | 62              | 60              |
| Grade 3 pain                | 2               | 1               | 2               | 6               |
| Any redness                 | 27              | 29              | 39              | 45              |
| Redness > 30 mm             | 5               | 1               | 3               | 0               |
| Any swelling                | 30              | 37              | 38              | 53              |
| Swelling > 30 mm            | 5               | 4               | 8               | 10              |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Any, Severe (Grade 3) and Related Solicited General Adverse Events (AEs).

|                 |                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Any, Severe (Grade 3) and Related Solicited General Adverse Events (AEs). <sup>[3]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------------|

End point description:

Solicited general AEs = drowsiness, irritability, loss of appetite and fever (axillary  $\geq 37.5$  degrees Celsius). Any= Incidence of any symptom regardless of intensity grade or relationship to vaccination. Grade 3: drowsiness = prevented normal activity. irritability = crying that could not be comforted/prevented normal activity. loss of appetite = not eating at all. Fever = temperature > 39.5°C Related =



symptom assessed by the investigator as related to the vaccination.

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

End point timeframe:

During the 4-day (Days 0-3) period following booster vaccination with Synflorix vaccine.

Notes:

[3] - 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: Since HIV - (EPI) Group didn't receive booster vaccination, there are no results to be analyzed for that timeframe.

| End point values                  | HIV+/+ Group    | HIV+/- Group    | HIV-(3+1) Group | HIV-(2+1) Group |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type                | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed       | 78              | 91              | 96              | 96              |
| Units: Subjects                   |                 |                 |                 |                 |
| Any drowsiness                    | 19              | 26              | 34              | 33              |
| Grade 3 drowsiness                | 2               | 0               | 1               | 1               |
| Related drowsiness                | 18              | 25              | 31              | 32              |
| Fever $\geq 37.5^{\circ}\text{C}$ | 9               | 11              | 7               | 11              |
| Fever $> 39.5^{\circ}\text{C}$    | 0               | 0               | 0               | 0               |
| Related fever                     | 8               | 10              | 7               | 10              |
| Any irritability                  | 27              | 33              | 31              | 43              |
| Grade 3 irritability              | 4               | 1               | 1               | 1               |
| Related irritability              | 26              | 33              | 31              | 42              |
| Any loss of appetite              | 17              | 23              | 29              | 37              |
| Grade 3 loss of appetite          | 0               | 0               | 1               | 2               |
| Related loss of appetite          | 16              | 23              | 29              | 33              |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Unsolicited AEs.

|                 |                                          |
|-----------------|------------------------------------------|
| End point title | Number of Subjects With Unsolicited AEs. |
|-----------------|------------------------------------------|

End point description:

An unsolicited adverse event 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.

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

End point timeframe:

Within the 31-day (Days 0-30) post-primary vaccination period.

| End point values            | HIV+/+ Group    | HIV+/- Group    | HIV-(3+1) Group | HIV-(EPI) Group |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 87              | 97              | 100             | 100             |
| Units: Subjects             |                 |                 |                 |                 |
| Any AE                      | 76              | 89              | 93              | 90              |

| End point values            | HIV-(2+1) Group |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 100             |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Any AE                      | 97              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Unsolicited AEs.

|                 |                                                         |
|-----------------|---------------------------------------------------------|
| End point title | Number of Subjects With Unsolicited AEs. <sup>[4]</sup> |
|-----------------|---------------------------------------------------------|

End point description:

An unsolicited adverse event 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.

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

End point timeframe:

Within the 31-day (Days 0-30) post Synflorix booster vaccination period.

Notes:

[4] - 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: Since HIV - (EPI) Group didn't receive booster vaccination, there are no results to be analyzed for that timeframe.

| End point values            | HIV+/+ Group    | HIV+/- Group    | HIV-(3+1) Group | HIV-(2+1) Group |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 80              | 92              | 98              | 98              |
| Units: Subjects             |                 |                 |                 |                 |
| Any AEs                     | 38              | 44              | 50              | 44              |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Serious Adverse Events (SAEs).

|                                                                                                                                                                                                                                                                    |                                                        |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                    | Number of Subjects With Serious Adverse Events (SAEs). |
| End point description:                                                                                                                                                                                                                                             |                                                        |
| SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects. |                                                        |
| End point type                                                                                                                                                                                                                                                     | Secondary                                              |
| End point timeframe:                                                                                                                                                                                                                                               |                                                        |
| From study start at Month 0 (6 weeks of age and above) up to 1 month after Sinflorix booster vaccination (up to Month 9).                                                                                                                                          |                                                        |

| End point values            | HIV+/+ Group    | HIV+/- Group    | HIV-(3+1) Group | HIV-(EPI) Group |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 87              | 97              | 100             | 100             |
| Units: Subjects             |                 |                 |                 |                 |
| Any SAEs                    | 27              | 14              | 9               | 8               |

| End point values            | HIV-(2+1) Group |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 100             |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Any SAEs                    | 8               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAEs: from Month 0 up to Month 9. Unsolicited AEs: within the 31-day post-primary and post booster Synflorix vaccination period. Solicited AEs: During the 4-day period following the primary and booster Synflorix vaccination.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

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

### Dictionary used

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

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

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | HIV+/+ Group |
|-----------------------|--------------|

Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV infected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered intramuscularly in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |              |
|-----------------------|--------------|
| Reporting group title | HIV+/- Group |
|-----------------------|--------------|

Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV exposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | HIV- (3+1) Group |
|-----------------------|------------------|

Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | HIV- (EPI) Group |
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses of Synflorix™ vaccine (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered

IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | HIV- (2+1) Group |
|-----------------------|------------------|

Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 2 primary doses (at 6 & 14 weeks of age at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

| Serious adverse events                            | HIV+/+ Group     | HIV+/- Group     | HIV- (3+1) Group |
|---------------------------------------------------|------------------|------------------|------------------|
| Total subjects affected by serious adverse events |                  |                  |                  |
| subjects affected / exposed                       | 27 / 87 (31.03%) | 14 / 97 (14.43%) | 9 / 100 (9.00%)  |
| number of deaths (all causes)                     | 1                | 0                | 0                |
| number of deaths resulting from adverse events    | 0                | 0                | 0                |
| Injury, poisoning and procedural complications    |                  |                  |                  |
| Herbal toxicity                                   |                  |                  |                  |
| subjects affected / exposed                       | 0 / 87 (0.00%)   | 1 / 97 (1.03%)   | 0 / 100 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            | 0 / 0            |
| Near drowning                                     |                  |                  |                  |
| subjects affected / exposed                       | 0 / 87 (0.00%)   | 0 / 97 (0.00%)   | 0 / 100 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            | 0 / 0            |
| Thermal burn                                      |                  |                  |                  |
| subjects affected / exposed                       | 0 / 87 (0.00%)   | 0 / 97 (0.00%)   | 0 / 100 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            | 0 / 0            |
| Congenital, familial and genetic disorders        |                  |                  |                  |
| Cerebral palsy                                    |                  |                  |                  |
| subjects affected / exposed                       | 0 / 87 (0.00%)   | 1 / 97 (1.03%)   | 0 / 100 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            | 0 / 0            |
| Trisomy 21                                        |                  |                  |                  |

|                                                      |                |                |                 |
|------------------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 87 (0.00%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Ventricular septal defect                            |                |                |                 |
| subjects affected / exposed                          | 0 / 87 (0.00%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Nervous system disorders                             |                |                |                 |
| Convulsion                                           |                |                |                 |
| subjects affected / exposed                          | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0          | 0 / 0           |
| Febrile convulsion                                   |                |                |                 |
| subjects affected / exposed                          | 0 / 87 (0.00%) | 1 / 97 (1.03%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Blood and lymphatic system disorders                 |                |                |                 |
| Anaemia                                              |                |                |                 |
| subjects affected / exposed                          | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Iron deficiency anaemia                              |                |                |                 |
| subjects affected / exposed                          | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| General disorders and administration site conditions |                |                |                 |
| Death                                                |                |                |                 |
| subjects affected / exposed                          | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0          | 0 / 0           |
| Sudden death                                         |                |                |                 |
| subjects affected / exposed                          | 2 / 87 (2.30%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 2          | 0 / 0          | 0 / 0           |

|                                                             |                |                |                 |
|-------------------------------------------------------------|----------------|----------------|-----------------|
| Sudden infant death syndrome<br>subjects affected / exposed | 0 / 87 (0.00%) | 1 / 97 (1.03%) | 0 / 100 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 1 / 1          | 0 / 0           |
| deaths causally related to<br>treatment / all               | 0 / 0          | 1 / 1          | 0 / 0           |
| Gastrointestinal disorders                                  |                |                |                 |
| Diarrhoea                                                   |                |                |                 |
| subjects affected / exposed                                 | 0 / 87 (0.00%) | 1 / 97 (1.03%) | 1 / 100 (1.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 1          | 0 / 1           |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 1          | 0 / 1           |
| Vomiting                                                    |                |                |                 |
| subjects affected / exposed                                 | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 1          | 0 / 0          | 0 / 1           |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0           |
| Hepatobiliary disorders                                     |                |                |                 |
| Hepatitis neonatal                                          |                |                |                 |
| subjects affected / exposed                                 | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0           |
| Respiratory, thoracic and mediastinal<br>disorders          |                |                |                 |
| Atelectasis                                                 |                |                |                 |
| subjects affected / exposed                                 | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0           |
| Bronchospasm                                                |                |                |                 |
| subjects affected / exposed                                 | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0           |
| Pneumonia aspiration                                        |                |                |                 |
| subjects affected / exposed                                 | 0 / 87 (0.00%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0           |
| Renal and urinary disorders                                 |                |                |                 |
| Renal impairment                                            |                |                |                 |

|                                                 |                  |                |                 |
|-------------------------------------------------|------------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 87 (1.15%)   | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Infections and infestations                     |                  |                |                 |
| Aids encephalopathy                             |                  |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%)   | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Bronchitis                                      |                  |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%)   | 1 / 97 (1.03%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Bronchopneumonia                                |                  |                |                 |
| subjects affected / exposed                     | 12 / 87 (13.79%) | 3 / 97 (3.09%) | 3 / 100 (3.00%) |
| occurrences causally related to treatment / all | 0 / 12           | 0 / 3          | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1          | 0 / 0           |
| Croup infectious                                |                  |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%)   | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Cytomegalovirus infection                       |                  |                |                 |
| subjects affected / exposed                     | 2 / 87 (2.30%)   | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Gastroenteritis                                 |                  |                |                 |
| subjects affected / exposed                     | 7 / 87 (8.05%)   | 3 / 97 (3.09%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 1 / 7            | 0 / 3          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| H1n1 influenza                                  |                  |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%)   | 0 / 97 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Lower respiratory tract infection               |                  |                |                 |



|                                                 |                |                |                 |
|-------------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 87 (0.00%) | 1 / 97 (1.03%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Measles                                         |                |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%) | 2 / 97 (2.06%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 2          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0           |
| Meningitis meningococcal                        |                |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Meningitis tuberculous                          |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 97 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Oral candidiasis                                |                |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Pneumococcal sepsis                             |                |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Pneumocystis jiroveci pneumonia                 |                |                |                 |
| subjects affected / exposed                     | 4 / 87 (4.60%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Pneumonia                                       |                |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%) | 1 / 97 (1.03%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Pneumonia staphylococcal                        |                |                |                 |

|                                                 |                  |                |                 |
|-------------------------------------------------|------------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 87 (1.15%)   | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Pulmonary tuberculosis                          |                  |                |                 |
| subjects affected / exposed                     | 10 / 87 (11.49%) | 1 / 97 (1.03%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 10           | 0 / 1          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Rectal abscess                                  |                  |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%)   | 0 / 97 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Streptococcal sepsis                            |                  |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%)   | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Tuberculosis                                    |                  |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%)   | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Upper respiratory tract infection               |                  |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%)   | 0 / 97 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Urinary tract infection                         |                  |                |                 |
| subjects affected / exposed                     | 2 / 87 (2.30%)   | 2 / 97 (2.06%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Bronchiolitis                                   |                  |                |                 |
| subjects affected / exposed                     | 2 / 87 (2.30%)   | 1 / 97 (1.03%) | 2 / 100 (2.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Gastroenteritis rotavirus                       |                  |                |                 |

|                                                 |                |                |                 |
|-------------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 87 (0.00%) | 1 / 97 (1.03%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| <b>Metabolism and nutrition disorders</b>       |                |                |                 |
| Kwashiorkor                                     |                |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Marasmus                                        |                |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%) | 0 / 97 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |

| <b>Serious adverse events</b>                         | HIV- (EPI) Group | HIV- (2+1) Group |  |
|-------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by serious adverse events     |                  |                  |  |
| subjects affected / exposed                           | 8 / 100 (8.00%)  | 8 / 100 (8.00%)  |  |
| number of deaths (all causes)                         | 0                | 0                |  |
| number of deaths resulting from adverse events        | 0                | 0                |  |
| <b>Injury, poisoning and procedural complications</b> |                  |                  |  |
| Herbal toxicity                                       |                  |                  |  |
| subjects affected / exposed                           | 0 / 100 (0.00%)  | 0 / 100 (0.00%)  |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Near drowning                                         |                  |                  |  |
| subjects affected / exposed                           | 0 / 100 (0.00%)  | 1 / 100 (1.00%)  |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Thermal burn                                          |                  |                  |  |
| subjects affected / exposed                           | 1 / 100 (1.00%)  | 0 / 100 (0.00%)  |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| <b>Congenital, familial and genetic disorders</b>     |                  |                  |  |
| Cerebral palsy                                        |                  |                  |  |

|                                                      |                 |                 |  |
|------------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Trisomy 21                                           |                 |                 |  |
| subjects affected / exposed                          | 0 / 100 (0.00%) | 1 / 100 (1.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Ventricular septal defect                            |                 |                 |  |
| subjects affected / exposed                          | 0 / 100 (0.00%) | 1 / 100 (1.00%) |  |
| 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                          | 2 / 100 (2.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           |  |
| Febrile convulsion                                   |                 |                 |  |
| subjects affected / exposed                          | 0 / 100 (0.00%) | 1 / 100 (1.00%) |  |
| 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                 |                 |                 |  |
| Anaemia                                              |                 |                 |  |
| subjects affected / exposed                          | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Iron deficiency anaemia                              |                 |                 |  |
| subjects affected / exposed                          | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Death                                                |                 |                 |  |
| subjects affected / exposed                          | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Sudden death                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0           |  |
| Sudden infant death syndrome                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Diarrhoea                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vomiting                                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Hepatitis neonatal                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Atelectasis                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchospasm                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia aspiration                            |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 100 (0.00%) | 2 / 100 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Renal impairment                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Aids encephalopathy                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchitis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchopneumonia                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 2 / 100 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Croup infectious                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Cytomegalovirus infection                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| subjects affected / exposed                     | 2 / 100 (2.00%) | 1 / 100 (1.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| H1n1 influenza                                  |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lower respiratory tract infection               |                 |                 |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) | 1 / 100 (1.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Measles                                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) | 1 / 100 (1.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Meningitis meningococcal                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Meningitis tuberculous                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Oral candidiasis                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumococcal sepsis                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumocystis jiroveci pneumonia                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia staphylococcal                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pulmonary tuberculosis                          |                 |                 |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Rectal abscess                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Streptococcal sepsis                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tuberculosis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper respiratory tract infection               |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchiolitis                                   |                 |                 |  |



|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 100 (1.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis rotavirus                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Kwashiorkor                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Marasmus                                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 100 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | HIV+/+ Group     | HIV+/- Group     | HIV- (3+1) Group  |
|-------------------------------------------------------|------------------|------------------|-------------------|
| Total subjects affected by non-serious adverse events |                  |                  |                   |
| subjects affected / exposed                           | 76 / 87 (87.36%) | 90 / 97 (92.78%) | 93 / 100 (93.00%) |
| General disorders and administration site conditions  |                  |                  |                   |
| Diarrhoea (solicited post-primary)                    |                  |                  |                   |
| alternative assessment type: Systematic               |                  |                  |                   |
| subjects affected / exposed <sup>[1]</sup>            | 8 / 87 (9.20%)   | 5 / 97 (5.15%)   | 12 / 98 (12.24%)  |
| occurrences (all)                                     | 8                | 5                | 12                |
| Drowsiness (solicited post-primary)                   |                  |                  |                   |
| alternative assessment type: Systematic               |                  |                  |                   |
| subjects affected / exposed <sup>[2]</sup>            | 50 / 87 (57.47%) | 61 / 97 (62.89%) | 70 / 98 (71.43%)  |
| occurrences (all)                                     | 50               | 61               | 70                |
| Drowsiness (solicited post-booster)                   |                  |                  |                   |
| alternative assessment type: Systematic               |                  |                  |                   |

|                                             |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed <sup>[3]</sup>  | 19 / 78 (24.36%) | 26 / 91 (28.57%) | 34 / 96 (35.42%) |
| occurrences (all)                           | 19               | 26               | 34               |
| Fever (post-primary)                        |                  |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |                  |
| subjects affected / exposed <sup>[4]</sup>  | 40 / 87 (45.98%) | 34 / 97 (35.05%) | 41 / 98 (41.84%) |
| occurrences (all)                           | 40               | 34               | 41               |
| Fever (post-booster)                        |                  |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |                  |
| subjects affected / exposed <sup>[5]</sup>  | 9 / 78 (11.54%)  | 11 / 91 (12.09%) | 7 / 96 (7.29%)   |
| occurrences (all)                           | 9                | 11               | 7                |
| Irritability (post-primary)                 |                  |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |                  |
| subjects affected / exposed <sup>[6]</sup>  | 66 / 87 (75.86%) | 81 / 97 (83.51%) | 89 / 98 (90.82%) |
| occurrences (all)                           | 66               | 81               | 89               |
| Irritability (post-booster)                 |                  |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |                  |
| subjects affected / exposed <sup>[7]</sup>  | 27 / 78 (34.62%) | 33 / 91 (36.26%) | 31 / 96 (32.29%) |
| occurrences (all)                           | 27               | 33               | 31               |
| Loss of appetite (post-primary)             |                  |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |                  |
| subjects affected / exposed <sup>[8]</sup>  | 37 / 87 (42.53%) | 52 / 97 (53.61%) | 56 / 98 (57.14%) |
| occurrences (all)                           | 37               | 52               | 56               |
| Loss of appetite (post-booster)             |                  |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |                  |
| subjects affected / exposed <sup>[9]</sup>  | 17 / 78 (21.79%) | 23 / 91 (25.27%) | 29 / 96 (30.21%) |
| occurrences (all)                           | 17               | 23               | 29               |
| Pain (post-primary)                         |                  |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |                  |
| subjects affected / exposed <sup>[10]</sup> | 76 / 87 (87.36%) | 90 / 97 (92.78%) | 92 / 98 (93.88%) |
| occurrences (all)                           | 76               | 90               | 92               |
| Pain (post-booster)                         |                  |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |                  |
| subjects affected / exposed <sup>[11]</sup> | 42 / 78 (53.85%) | 56 / 91 (61.54%) | 62 / 96 (64.58%) |
| occurrences (all)                           | 42               | 56               | 62               |

|                                                                                                                                                     |                        |                        |                         |
|-----------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------------|-------------------------|
| Redness (post-primary)<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[12]</sup><br>occurrences (all)            | 66 / 87 (75.86%)<br>66 | 76 / 97 (78.35%)<br>76 | 83 / 98 (84.69%)<br>83  |
| Redness (post-booster)<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[13]</sup><br>occurrences (all)            | 27 / 78 (34.62%)<br>27 | 29 / 91 (31.87%)<br>29 | 39 / 96 (40.63%)<br>39  |
| Swelling (post-primary)<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[14]</sup><br>occurrences (all)           | 71 / 87 (81.61%)<br>71 | 79 / 97 (81.44%)<br>79 | 84 / 98 (85.71%)<br>84  |
| Swelling (post-booster)<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[15]</sup><br>occurrences (all)           | 30 / 78 (38.46%)<br>30 | 37 / 91 (40.66%)<br>37 | 38 / 96 (39.58%)<br>38  |
| Vomiting (solicited post-primary)<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[16]</sup><br>occurrences (all) | 17 / 87 (19.54%)<br>17 | 19 / 97 (19.59%)<br>19 | 15 / 98 (15.31%)<br>15  |
| Gastrointestinal disorders<br>Diarrhoea (unsol. primary)<br>subjects affected / exposed<br>occurrences (all)                                        | 13 / 87 (14.94%)<br>13 | 16 / 97 (16.49%)<br>16 | 18 / 100 (18.00%)<br>18 |
| Diarrhoea (unsol. post-booster)<br>subjects affected / exposed <sup>[17]</sup><br>occurrences (all)                                                 | 5 / 80 (6.25%)<br>5    | 10 / 92 (10.87%)<br>10 | 10 / 98 (10.20%)<br>10  |
| Vomiting (unsolicited post-primary)<br>subjects affected / exposed<br>occurrences (all)                                                             | 18 / 87 (20.69%)<br>18 | 16 / 97 (16.49%)<br>16 | 11 / 100 (11.00%)<br>11 |
| Vomiting (unsolicited post-booster)<br>subjects affected / exposed <sup>[18]</sup><br>occurrences (all)                                             | 1 / 80 (1.25%)<br>1    | 8 / 92 (8.70%)<br>8    | 7 / 98 (7.14%)<br>7     |
| Respiratory, thoracic and mediastinal disorders                                                                                                     |                        |                        |                         |

|                                                                                                                                        |                        |                        |                         |
|----------------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------------|-------------------------|
| Cough (post-primary)<br>subjects affected / exposed<br>occurrences (all)                                                               | 38 / 87 (43.68%)<br>38 | 69 / 97 (71.13%)<br>69 | 67 / 100 (67.00%)<br>67 |
| Cough (post-booster)<br>subjects affected / exposed <sup>[19]</sup><br>occurrences (all)                                               | 19 / 80 (23.75%)<br>19 | 21 / 92 (22.83%)<br>21 | 24 / 98 (24.49%)<br>24  |
| Nasal Obstruction (post-primary)<br>subjects affected / exposed<br>occurrences (all)                                                   | 29 / 87 (33.33%)<br>29 | 40 / 97 (41.24%)<br>40 | 50 / 100 (50.00%)<br>50 |
| Nasal Obstruction (post-booster)<br>subjects affected / exposed <sup>[20]</sup><br>occurrences (all)                                   | 7 / 80 (8.75%)<br>7    | 4 / 92 (4.35%)<br>4    | 6 / 98 (6.12%)<br>6     |
| Rhinorrhoea<br>subjects affected / exposed <sup>[21]</sup><br>occurrences (all)                                                        | 1 / 80 (1.25%)<br>1    | 5 / 92 (5.43%)<br>5    | 7 / 98 (7.14%)<br>7     |
| Skin and subcutaneous tissue disorders<br>Eczema<br>subjects affected / exposed<br>occurrences (all)                                   | 9 / 87 (10.34%)<br>9   | 12 / 97 (12.37%)<br>12 | 11 / 100 (11.00%)<br>11 |
| Rash (post-primary)<br>subjects affected / exposed<br>occurrences (all)                                                                | 27 / 87 (31.03%)<br>27 | 24 / 97 (24.74%)<br>24 | 16 / 100 (16.00%)<br>16 |
| Rash (post-booster)<br>subjects affected / exposed <sup>[22]</sup><br>occurrences (all)                                                | 4 / 80 (5.00%)<br>4    | 4 / 92 (4.35%)<br>4    | 3 / 98 (3.06%)<br>3     |
| Infections and infestations<br>Upper respiratory tract infection<br>(post-primary)<br>subjects affected / exposed<br>occurrences (all) | 4 / 87 (4.60%)<br>4    | 13 / 97 (13.40%)<br>13 | 13 / 100 (13.00%)<br>13 |
| Upper respiratory tract infection<br>(post-booster)<br>subjects affected / exposed <sup>[23]</sup><br>occurrences (all)                | 3 / 80 (3.75%)<br>3    | 4 / 92 (4.35%)<br>4    | 6 / 98 (6.12%)<br>6     |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed <sup>[24]</sup><br>occurrences (all)           | 4 / 80 (5.00%)<br>4    | 6 / 92 (6.52%)<br>6    | 4 / 98 (4.08%)<br>4     |

| <b>Non-serious adverse events</b>                     | HIV- (EPI) Group  | HIV- (2+1) Group  |  |
|-------------------------------------------------------|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                   |                   |  |
| subjects affected / exposed                           | 95 / 100 (95.00%) | 97 / 100 (97.00%) |  |
| General disorders and administration site conditions  |                   |                   |  |
| Diarrhoea (solicited post-primary)                    |                   |                   |  |
| alternative assessment type: Systematic               |                   |                   |  |
| subjects affected / exposed <sup>[1]</sup>            | 10 / 98 (10.20%)  | 5 / 98 (5.10%)    |  |
| occurrences (all)                                     | 10                | 5                 |  |
| Drowsiness (solicited post-primary)                   |                   |                   |  |
| alternative assessment type: Systematic               |                   |                   |  |
| subjects affected / exposed <sup>[2]</sup>            | 70 / 98 (71.43%)  | 68 / 98 (69.39%)  |  |
| occurrences (all)                                     | 70                | 68                |  |
| Drowsiness (solicited post-booster)                   |                   |                   |  |
| alternative assessment type: Systematic               |                   |                   |  |
| subjects affected / exposed <sup>[3]</sup>            | 0 / 100 (0.00%)   | 33 / 96 (34.38%)  |  |
| occurrences (all)                                     | 0                 | 33                |  |
| Fever (post-primary)                                  |                   |                   |  |
| alternative assessment type: Systematic               |                   |                   |  |
| subjects affected / exposed <sup>[4]</sup>            | 28 / 98 (28.57%)  | 28 / 98 (28.57%)  |  |
| occurrences (all)                                     | 28                | 28                |  |
| Fever (post-booster)                                  |                   |                   |  |
| alternative assessment type: Systematic               |                   |                   |  |
| subjects affected / exposed <sup>[5]</sup>            | 0 / 100 (0.00%)   | 11 / 96 (11.46%)  |  |
| occurrences (all)                                     | 0                 | 11                |  |
| Irritability (post-primary)                           |                   |                   |  |
| alternative assessment type: Systematic               |                   |                   |  |
| subjects affected / exposed <sup>[6]</sup>            | 89 / 98 (90.82%)  | 91 / 98 (92.86%)  |  |
| occurrences (all)                                     | 89                | 91                |  |
| Irritability (post-booster)                           |                   |                   |  |
| alternative assessment type: Systematic               |                   |                   |  |
| subjects affected / exposed <sup>[7]</sup>            | 0 / 100 (0.00%)   | 43 / 96 (44.79%)  |  |
| occurrences (all)                                     | 0                 | 43                |  |
| Loss of appetite (post-primary)                       |                   |                   |  |
| alternative assessment type: Systematic               |                   |                   |  |

|                                             |                  |                  |
|---------------------------------------------|------------------|------------------|
| subjects affected / exposed <sup>[8]</sup>  | 57 / 98 (58.16%) | 62 / 98 (63.27%) |
| occurrences (all)                           | 57               | 62               |
| Loss of appetite (post-booster)             |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |
| subjects affected / exposed <sup>[9]</sup>  | 0 / 100 (0.00%)  | 37 / 96 (38.54%) |
| occurrences (all)                           | 0                | 37               |
| Pain (post-primary)                         |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |
| subjects affected / exposed <sup>[10]</sup> | 95 / 98 (96.94%) | 97 / 98 (98.98%) |
| occurrences (all)                           | 95               | 97               |
| Pain (post-booster)                         |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |
| subjects affected / exposed <sup>[11]</sup> | 0 / 100 (0.00%)  | 60 / 96 (62.50%) |
| occurrences (all)                           | 0                | 60               |
| Redness (post-primary)                      |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |
| subjects affected / exposed <sup>[12]</sup> | 83 / 98 (84.69%) | 84 / 98 (85.71%) |
| occurrences (all)                           | 83               | 84               |
| Redness (post-booster)                      |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |
| subjects affected / exposed <sup>[13]</sup> | 0 / 100 (0.00%)  | 45 / 96 (46.88%) |
| occurrences (all)                           | 0                | 45               |
| Swelling (post-primary)                     |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |
| subjects affected / exposed <sup>[14]</sup> | 91 / 98 (92.86%) | 84 / 98 (85.71%) |
| occurrences (all)                           | 91               | 84               |
| Swelling (post-booster)                     |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |
| subjects affected / exposed <sup>[15]</sup> | 0 / 100 (0.00%)  | 53 / 96 (55.21%) |
| occurrences (all)                           | 0                | 53               |
| Vomiting (solicited post-primary)           |                  |                  |
| alternative assessment type:<br>Systematic  |                  |                  |
| subjects affected / exposed <sup>[16]</sup> | 18 / 98 (18.37%) | 23 / 98 (23.47%) |
| occurrences (all)                           | 18               | 23               |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| Gastrointestinal disorders                      |                   |                   |  |
| Diarrhoea (unsol. primary)                      |                   |                   |  |
| subjects affected / exposed                     | 13 / 100 (13.00%) | 7 / 100 (7.00%)   |  |
| occurrences (all)                               | 13                | 7                 |  |
| Diarrhoea (unsol. post-booster)                 |                   |                   |  |
| subjects affected / exposed <sup>[17]</sup>     | 0 / 100 (0.00%)   | 8 / 98 (8.16%)    |  |
| occurrences (all)                               | 0                 | 8                 |  |
| Vomiting (unsolicited post-primary)             |                   |                   |  |
| subjects affected / exposed                     | 15 / 100 (15.00%) | 12 / 100 (12.00%) |  |
| occurrences (all)                               | 15                | 12                |  |
| Vomiting (unsolicited post-booster)             |                   |                   |  |
| subjects affected / exposed <sup>[18]</sup>     | 0 / 100 (0.00%)   | 5 / 98 (5.10%)    |  |
| occurrences (all)                               | 0                 | 5                 |  |
| Respiratory, thoracic and mediastinal disorders |                   |                   |  |
| Cough (post-primary)                            |                   |                   |  |
| subjects affected / exposed                     | 58 / 100 (58.00%) | 66 / 100 (66.00%) |  |
| occurrences (all)                               | 58                | 66                |  |
| Cough (post-booster)                            |                   |                   |  |
| subjects affected / exposed <sup>[19]</sup>     | 0 / 100 (0.00%)   | 13 / 98 (13.27%)  |  |
| occurrences (all)                               | 0                 | 13                |  |
| Nasal Obstruction (post-primary)                |                   |                   |  |
| subjects affected / exposed                     | 49 / 100 (49.00%) | 51 / 100 (51.00%) |  |
| occurrences (all)                               | 49                | 51                |  |
| Nasal Obstruction (post-booster)                |                   |                   |  |
| subjects affected / exposed <sup>[20]</sup>     | 0 / 100 (0.00%)   | 6 / 98 (6.12%)    |  |
| occurrences (all)                               | 0                 | 6                 |  |
| Rhinorrhoea                                     |                   |                   |  |
| subjects affected / exposed <sup>[21]</sup>     | 0 / 100 (0.00%)   | 5 / 98 (5.10%)    |  |
| occurrences (all)                               | 0                 | 5                 |  |
| Skin and subcutaneous tissue disorders          |                   |                   |  |
| Eczema                                          |                   |                   |  |
| subjects affected / exposed                     | 12 / 100 (12.00%) | 14 / 100 (14.00%) |  |
| occurrences (all)                               | 12                | 14                |  |
| Rash (post-primary)                             |                   |                   |  |
| subjects affected / exposed                     | 28 / 100 (28.00%) | 21 / 100 (21.00%) |  |
| occurrences (all)                               | 28                | 21                |  |

|                                                                                                                                        |                         |                         |  |
|----------------------------------------------------------------------------------------------------------------------------------------|-------------------------|-------------------------|--|
| Rash (post-booster)<br>subjects affected / exposed <sup>[22]</sup><br>occurrences (all)                                                | 0 / 100 (0.00%)<br>0    | 5 / 98 (5.10%)<br>5     |  |
| Infections and infestations<br>Upper respiratory tract infection<br>(post-primary)<br>subjects affected / exposed<br>occurrences (all) | 11 / 100 (11.00%)<br>11 | 12 / 100 (12.00%)<br>12 |  |
| Upper respiratory tract infection<br>(post-booster)<br>subjects affected / exposed <sup>[23]</sup><br>occurrences (all)                | 0 / 100 (0.00%)<br>0    | 5 / 98 (5.10%)<br>5     |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed <sup>[24]</sup><br>occurrences (all)           | 0 / 100 (0.00%)<br>0    | 4 / 98 (4.08%)<br>4     |  |

Notes:

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

Justification: The analysis of the solicited symptom included only subjects with documented data.

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

Justification: The analysis of the solicited symptom included only subjects with documented data.

[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.

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

Justification: The analysis of the unsolicited symptom included only subjects with documented data.

[18] - 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.

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[22] - 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.

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

Justification: The analysis of the unsolicited symptom included only subjects with documented data.

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

Justification: The analysis of the unsolicited symptom included only subjects with documented data.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                             |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 09 December 2008 | <ul style="list-style-type: none"><li>• Introduction of Prevenar in the national recommended vaccination program of South Africa as from April 2009.</li><li>• Decision to consider rotavirus vaccine as study vaccine due to its anticipated introduction into the national vaccination program during 2009.</li><li>• Addition of a rationale for including HIV exposed uninfected children in the study.</li></ul> |
| 29 June 2009     | <ul style="list-style-type: none"><li>• Decision to test immunogenicity of the oral poliovirus vaccine (OPV) on request of local authorities.</li><li>• Permission for inclusion of HIV infected infants with weight for age &lt; 3rd percentile at Visit 1, using standard growth charts, at the discretion of the investigator.</li></ul>                                                                           |
| 24 February 2010 | As a slow enrolment rate of HIV+/+ subjects was observed, it was decided to extend the recruitment time by approximately 6 months in Amendment 3 in order to increase the chance to reach target enrolment in the HIV+/+ study group.                                                                                                                                                                                 |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported