



## Clinical trial results:

**A phase III, open, controlled study to evaluate the immunogenicity, safety and reactogenicity of GSK Biologicals' 10- valent pneumococcal conjugate vaccine administered to children with sickle cell disease between 8 weeks and 2 years of age, as compared to healthy children.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-000254-64 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 23 May 2013    |

### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v3 (current)  |
| This version publication date  | 31 March 2023   |
| First version publication date | 25 July 2015  |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Correction of full data set and alignment between registries. |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 114056 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01175083 |
| 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, 44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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                       | 04 August 2015 |
| Is this the analysis of the primary completion data? | No             |

|                                  |             |
|----------------------------------|-------------|
| Global end of trial reached?     | Yes         |
| Global end of trial date         | 23 May 2013 |
| Was the trial ended prematurely? | No          |

Notes:

## General information about the trial

Main objective of the trial:

To assess the immunogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine when co-administered with DTPw-HBV/Hib and OPV vaccines in children with sickle cell disease, one month after completion of the 3-dose primary vaccination course before 6 months of age

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 01 June 2011 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Burkina Faso: 300 |
| Worldwide total number of subjects   | 300               |
| 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)  | 300 |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 0   |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

### Period 1

|                              |                             |
|------------------------------|-----------------------------|
| Period 1 title               | Primary Epoch               |
| Is this the baseline period? | Yes                         |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes                                      |
| <b>Arm title</b>             | Tritanrix-HepB/Hib+Polio Sabin <6S Group |

Arm description:

Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | GSK1024850A (Synflorix)  |
| Investigational medicinal product code |  |
| Other name                             | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms                   | Suspension for injection   |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Tritanrix-HB             |
| Investigational medicinal product code |                          |
| Other name                             | DTPw-HBV                 |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

Intramuscular injection, 4 doses in the left thigh.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Polio Sabin     |
| Investigational medicinal product code |                 |
| Other name                             | OPV             |
| Pharmaceutical forms                   | Oral suspension |
| Routes of administration               | Oral use        |

Dosage and administration details:

4 doses administered orally.

|  |   |
|--|---|
| Investigational medicinal product name | Hiberix                                       |
| Investigational medicinal product code |   |
| Other name                             | Hib   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intramuscular use                             |

**Dosage and administration details:**

White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |
|------------------|---|

**Arm description:**

Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.

|  |  |
|--|--|
| Arm type                               | Active comparator  |
| Investigational medicinal product name | GSK1024850A (Synflorix)  |
| Investigational medicinal product code |  |
| Other name                             | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms                   | Suspension for injection   |
| Routes of administration               | Intramuscular use  |

**Dosage and administration details:**

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Tritanrix-HB             |
| Investigational medicinal product code |                          |
| Other name                             | DTPw-HB                  |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

**Dosage and administration details:**

Intramuscular injection, 4 doses in the left thigh.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Polio Sabin     |
| Investigational medicinal product code |                 |
| Other name                             | OPV             |
| Pharmaceutical forms                   | Oral suspension |
| Routes of administration               | Oral use        |

**Dosage and administration details:**

4 doses administered orally.

|  |   |
|--|---|
| Investigational medicinal product name | Hiberix                                       |
| Investigational medicinal product code |   |
| Other name                             | Hib   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intramuscular use                             |

**Dosage and administration details:**

White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Synflorix 7-11S Group |
|------------------|-----------------------|

**Arm description:**

Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|   |  |
|---|--|
| Investigational medicinal product name  | GSK1024850A (Synflorix)  |
| Investigational medicinal product code  |  |
| Other name  | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms  | Suspension for injection   |
| Routes of administration  | Intramuscular use  |
| Dosage and administration details:  |  |
| 2 intramuscular vaccine doses were administered intramuscularly into the right thigh.   |  |
| <b>Arm title</b>  | Synflorix 7-11NS Group   |
| Arm description:  |  |
| Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3. |  |
| Arm type  | Active comparator  |
| Investigational medicinal product name  | GSK1024850A (Synflorix)  |
| Investigational medicinal product code  |  |
| Other name  | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms  | Suspension for injection   |
| Routes of administration  | Intramuscular use  |
| Dosage and administration details:  |  |
| 2 intramuscular vaccine doses were administered intramuscularly into the right thigh.   |  |
| <b>Arm title</b>  | Synflorix 12-23S Group   |
| Arm description:  |  |
| Children between 12-23 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.                           |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | GSK1024850A (Synflorix)  |
| Investigational medicinal product code  |  |
| Other name  | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms  | Suspension for injection   |
| Routes of administration  | Intramuscular use  |
| Dosage and administration details:  |  |
| 2 intramuscular vaccine doses were administered intramuscularly into the right thigh.   |  |
| <b>Arm title</b>  | Synflorix 12-23NS Group  |
| Arm description:  |  |
| Healthy children between 12-23 months of age at time of enrolment, who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.   |  |
| Arm type  | Active comparator  |
| Investigational medicinal product name  | GSK1024850A (Synflorix)  |
| Investigational medicinal product code  |  |
| Other name  | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms  | Suspension for injection   |
| Routes of administration  | Intramuscular use  |
| Dosage and administration details:  |  |
| 2 intramuscular vaccine doses were administered intramuscularly into the right thigh.   |  |

| Number of subjects in period 1 | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group |
|--------------------------------|--|---|-----------------------|
| Started                        | 50                                       | 50  | 50                    |
| Completed                      | 50                                       | 50  | 50                    |
| Not completed                  | 0  | 0   | 0                     |
| Consent withdrawn by subject   | -  | -   | -                     |
| Lost to follow-up              | -  | -   | -                     |

| Number of subjects in period 1 | Synflorix 7-11NS Group | Synflorix 12-23S Group | Synflorix 12-23NS Group |
|--------------------------------|------------------------|------------------------|-------------------------|
| Started                        | 50                     | 50                     | 50                      |
| Completed                      | 50                     | 50                     | 47                      |
| Not completed                  | 0                      | 0                      | 3                       |
| Consent withdrawn by subject   | -                      | -                      | 2                       |
| Lost to follow-up              | -                      | -                      | 1                       |

## Period 2

|                              |                             |
|------------------------------|-----------------------------|
| Period 2 title               | Booster Epoch               |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

## Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes                                      |
| Arm title                    | Tritanrix-HepB/Hib+Polio Sabin <6S Group |

### Arm description:

Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | GSK1024850A (Synflorix)  |
| Investigational medicinal product code |  |
| Other name                             | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms                   | Suspension for injection   |
| Routes of administration               | Intramuscular use  |

### Dosage and administration details:

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Tritanrix-HB             |
| Investigational medicinal product code |                          |
| Other name                             | DTPw-HBV                 |
| Pharmaceutical forms                   | Suspension for injection |

|   |  |
|---|--|
| Routes of administration  | Intramuscular use  |
| Dosage and administration details:  |  |
| Intramuscular injection, 4 doses in the left thigh.   |  |
| Investigational medicinal product name  | Polio Sabin  |
| Investigational medicinal product code  |  |
| Other name  | OPV  |
| Pharmaceutical forms  | Oral suspension  |
| Routes of administration  | Oral use   |
| Dosage and administration details:  |  |
| 4 doses administered orally.  |  |
| Investigational medicinal product name  | Hiberix  |
| Investigational medicinal product code  |  |
| Other name  | Hib  |
| Pharmaceutical forms  | Powder and solvent for solution for injection  |
| Routes of administration  | Intramuscular use  |
| Dosage and administration details:  |  |
| White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.  |  |
| <b>Arm title</b>  | Tritanrix-HepB/Hib+Polio Sabin <6NS Group  |
| Arm description:  |  |
| Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8. |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | GSK1024850A (Synflorix)  |
| Investigational medicinal product code  |  |
| Other name  | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms  | Suspension for injection   |
| Routes of administration  | Intramuscular use  |
| Dosage and administration details:  |  |
| 3 intramuscular vaccine doses were administered intramuscularly into the right thigh.   |  |
| Investigational medicinal product name  | Tritanrix-HB   |
| Investigational medicinal product code  |  |
| Other name  | DTPw-HBV   |
| Pharmaceutical forms  | Suspension for injection   |
| Routes of administration  | Intramuscular use  |
| Dosage and administration details:  |  |
| Intramuscular injection, 4 doses in the left thigh.   |  |
| Investigational medicinal product name  | Polio Sabin  |
| Investigational medicinal product code  |  |
| Other name  | OPV  |
| Pharmaceutical forms  | Oral suspension  |
| Routes of administration  | Oral use   |
| Dosage and administration details:  |  |
| 4 doses administered orally.  |  |
| Investigational medicinal product name  | Hiberix  |
| Investigational medicinal product code  |  |
| Other name  | Hib  |
| Pharmaceutical forms  | Powder and solvent for solution for injection  |
| Routes of administration  | Intramuscular use  |

**Dosage and administration details:**

White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.

|   |  |
|---|--|
| <b>Arm title</b>  | Synflorix 7-11S Group  |
| Arm description:  |  |
| Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3. |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | GSK1024850A (Synflorix)  |
| Investigational medicinal product code  |  |
| Other name  | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms  | Suspension for injection   |
| Routes of administration  | Intramuscular use  |

**Dosage and administration details:**

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

|   |  |
|---|--|
| <b>Arm title</b>  | Synflorix 7-11NS Group   |
| Arm description:  |  |
| Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3. |  |
| Arm type  | Active comparator  |
| Investigational medicinal product name  | GSK1024850A (Synflorix)  |
| Investigational medicinal product code  |  |
| Other name  | GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine |
| Pharmaceutical forms  | Suspension for injection   |
| Routes of administration  | Intramuscular use  |

**Dosage and administration details:**

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group |
|---|--|---|-----------------------|
| Started   | 49                                       | 49  | 50                    |
| Completed   | 49                                       | 49  | 49                    |
| Not completed                                       | 0  | 0   | 1                     |
| Consent withdrawn by subject                        | -  | -   | -                     |
| Death   | -  | -   | 1                     |

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Synflorix 7-11NS Group |
|---|------------------------|
| Started   | 50                     |
| Completed   | 49                     |
| Not completed                                       | 1                      |



|                              |   |
|------------------------------|---|
| Consent withdrawn by subject | 1 |
| Death                        | - |

---

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One subject died between both Epochs and hence did not participate in the Booster Epoch.

## Baseline characteristics

### Reporting groups

|  |   |
|--|---|
| Reporting group title  | Tritanrix-HepB/Hib+Polio Sabin <6S Group  |
| Reporting group description:<br>Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8. |   |
| Reporting group title  | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |
| Reporting group description:<br>Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.                                |   |
| Reporting group title  | Synflorix 7-11S Group                     |
| Reporting group description:<br>Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.  |   |
| Reporting group title  | Synflorix 7-11NS Group                    |
| Reporting group description:<br>Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.  |   |
| Reporting group title  | Synflorix 12-23S Group                    |
| Reporting group description:<br>Children between 12-23 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.  |   |
| Reporting group title  | Synflorix 12-23NS Group                   |
| Reporting group description:<br>Healthy children between 12-23 months of age at time of enrolment, who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.  |   |

| Reporting group values                             | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group |
|--|--|---|-----------------------|
| Number of subjects                                 | 50                                       | 50  | 50                    |
| Age categorical<br>Units: Subjects                 |  |   |                       |
| In utero   | 0  | 0   | 0                     |
| Preterm newborn infants (gestational age < 37 wks) | 0  | 0   | 0                     |
| Newborns (0-27 days)                               | 0  | 0   | 0                     |
| Infants and toddlers (28 days-23 months)           | 50                                       | 50  | 50                    |
| Children (2-11 years)                              | 0  | 0   | 0                     |
| Adolescents (12-17 years)                          | 0  | 0   | 0                     |
| Adults (18-64 years)                               | 0  | 0   | 0                     |
| From 65-84 years                                   | 0  | 0   | 0                     |
| 85 years and over                                  | 0  | 0   | 0                     |
| Gender categorical<br>Units: Subjects              |  |   |                       |
| Female   | 21                                       | 29  | 26                    |
| Male   | 29                                       | 21  | 24                    |

| <b>Reporting group values</b>                         | Synflorix 7-11NS<br>Group | Synflorix 12-23S<br>Group | Synflorix 12-23NS<br>Group |
|---|---------------------------|---------------------------|----------------------------|
| Number of subjects                                    | 50                        | 50                        | 50                         |
| Age categorical<br>Units: Subjects                    |                           |                           |                            |
| In utero  | 0                         | 0                         | 0                          |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                         | 0                         | 0                          |
| Newborns (0-27 days)                                  | 0                         | 0                         | 0                          |
| Infants and toddlers (28 days-23<br>months)           | 50                        | 50                        | 50                         |
| Children (2-11 years)                                 | 0                         | 0                         | 0                          |
| Adolescents (12-17 years)                             | 0                         | 0                         | 0                          |
| Adults (18-64 years)                                  | 0                         | 0                         | 0                          |
| From 65-84 years                                      | 0                         | 0                         | 0                          |
| 85 years and over                                     | 0                         | 0                         | 0                          |
| Gender categorical<br>Units: Subjects                 |                           |                           |                            |
| Female  | 32                        | 15                        | 24                         |
| Male  | 18                        | 35                        | 26                         |

| <b>Reporting group values</b>                         | Total |  |  |
|---|-------|--|--|
| Number of subjects                                    | 300   |  |  |
| Age categorical<br>Units: Subjects                    |       |  |  |
| In utero  | 0     |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0     |  |  |
| Newborns (0-27 days)                                  | 0     |  |  |
| Infants and toddlers (28 days-23<br>months)           | 300   |  |  |
| Children (2-11 years)                                 | 0     |  |  |
| Adolescents (12-17 years)                             | 0     |  |  |
| Adults (18-64 years)                                  | 0     |  |  |
| From 65-84 years                                      | 0     |  |  |
| 85 years and over                                     | 0     |  |  |
| Gender categorical<br>Units: Subjects                 |       |  |  |
| Female  | 147   |  |  |
| Male  | 153   |  |  |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Tritanrix-HepB/Hib+Polio Sabin <6S Group  |
| Reporting group description:<br>Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8. |   |
| Reporting group title  | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |
| Reporting group description:<br>Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.                                |   |
| Reporting group title  | Synflorix 7-11S Group                     |
| Reporting group description:<br>Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.  |   |
| Reporting group title  | Synflorix 7-11NS Group                    |
| Reporting group description:<br>Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.  |   |
| Reporting group title  | Synflorix 12-23S Group                    |
| Reporting group description:<br>Children between 12-23 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.  |   |
| Reporting group title  | Synflorix 12-23NS Group                   |
| Reporting group description:<br>Healthy children between 12-23 months of age at time of enrolment, who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.  |   |
| Reporting group title  | Tritanrix-HepB/Hib+Polio Sabin <6S Group  |
| Reporting group description:<br>Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8. |   |
| Reporting group title  | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |
| Reporting group description:<br>Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.                                |   |
| Reporting group title  | Synflorix 7-11S Group                     |
| Reporting group description:<br>Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.  |   |
| Reporting group title  | Synflorix 7-11NS Group                    |
| Reporting group description:<br>Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.  |   |

**Primary: Concentrations of antibodies against vaccine pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines**

|                 |   |
|-----------------|---|
| End point title | Concentrations of antibodies against vaccine pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines <sup>[1][2]</sup> |
|-----------------|---|

End point description:

Antibodies have been assessed against the following 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), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration greater than or equal to (≥) 0.05 micrograms per milliliter (µg/mL). Antibody concentrations below than (<) 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

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

End point timeframe:

One month after primary vaccination (Month 3)

Notes:

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

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

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

| End point values                         | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |  |  |
|--|--|---|--|--|
| Subject group type                       | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed              | 48                                       | 46  |  |  |
| Units: µg/mL                             |  |   |  |  |
| geometric mean (confidence interval 95%) |  |   |  |  |
| Anti-1 [Month 3] (N=48,46)               | 3.51 (2.77 to 4.44)                      | 3.63 (2.91 to 4.53)                       |  |  |
| Anti-4 [Month 3] (N=47,46)               | 4.25 (3.18 to 5.67)                      | 3.51 (2.73 to 4.51)                       |  |  |
| Anti-5 [Month 3] (N=47,46)               | 5.15 (4.07 to 6.51)                      | 5.94 (4.91 to 7.18)                       |  |  |
| Anti-6B [Month 3] (N=48,46)              | 1.29 (0.83 to 1.99)                      | 1.13 (0.74 to 1.72)                       |  |  |
| Anti-7F [Month 3] (N=48,46)              | 4.91 (3.84 to 6.28)                      | 4.28 (3.49 to 5.26)                       |  |  |
| Anti-9V [Month 3] (N=47,46)              | 4.56 (3.51 to 5.92)                      | 4.59 (3.7 to 5.7)                         |  |  |
| Anti-14 [Month 3] (N=46,46)              | 4.3 (3.08 to 6)                          | 5.95 (4.27 to 8.29)                       |  |  |
| Anti-18C [Month 3] (N=47,45)             | 14.6 (11.01 to 19.36)                    | 11.33 (8.47 to 15.17)                     |  |  |
| Anti-19F [Month 3] (N=47,46)             | 11.87 (9.05 to 15.57)                    | 9.78 (7.01 to 13.64)                      |  |  |
| Anti-23F [Month 3] (N=48,46)             | 1.32 (0.9 to 1.93)                       | 1.41 (0.95 to 2.11)                       |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Concentrations of antibodies against protein D (PD) for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines

|                 |   |
|-----------------|---|
| End point title | Concentrations of antibodies against protein D (PD) for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines <sup>[3][4]</sup> |
|-----------------|---|

End point description:

Anti-PD antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was an antibody concentration  $\geq 100$  EL.U/mL. Antibody concentrations  $< 100$  EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

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

End point timeframe:

One month after the primary vaccination (Month 3)

Notes:

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

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

[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: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

| End point values                         | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |  |  |
|--|--|---|--|--|
| Subject group type                       | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed              | 47                                       | 46  |  |  |
| Units: EL.U/mL                           |  |   |  |  |
| geometric mean (confidence interval 95%) |  |   |  |  |
| Anti-PD [Month 3] (N=47,46)              | 2789.09<br>(2313.89 to 3361.87)          | 3065.4<br>(2530.54 to 3713.31)            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any and Grade 3 solicited local symptoms during the primary vaccination phase

|                 |   |
|-----------------|---|
| End point title | Number of subjects with any and Grade 3 solicited local symptoms during the primary vaccination phase |
|-----------------|---|

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

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

End point timeframe:

During the 4-day (Days 0-3) post-primary vaccination period following each dose and across doses

| <b>End point values</b>     | Tritanrix-<br>HepB/Hib+Poli<br>o Sabin <6S<br>Group | Tritanrix-<br>HepB/Hib+Poli<br>o Sabin <6NS<br>Group | Synflorix 7-11S<br>Group | Synflorix 7-<br>11NS Group |
|-----------------------------|---|--|--------------------------|----------------------------|
| Subject group type          | Reporting group                                     | Reporting group                                      | Reporting group          | Reporting group            |
| Number of subjects analysed | 50  | 50   | 50                       | 50                         |
| Units: Subjects             |   |  |                          |                            |
| Any Pain, Dose 1            | 8   | 12   | 7                        | 10                         |
| Grade 3 Pain, Dose 1        | 0   | 0  | 0                        | 0                          |
| Any Redness, Dose 1         | 0   | 0  | 0                        | 0                          |
| Grade 3 Redness, Dose 1     | 0   | 0  | 0                        | 0                          |
| Any Swelling, Dose 1        | 0   | 0  | 0                        | 0                          |
| Grade 3 Swelling, Dose 1    | 0   | 0  | 0                        | 0                          |
| Any Pain, Dose 2            | 7   | 7  | 5                        | 7                          |
| Grade 3 Pain, Dose 2        | 0   | 0  | 0                        | 0                          |
| Any Redness, Dose 2         | 0   | 0  | 0                        | 0                          |
| Grade 3 Redness, Dose 2     | 0   | 0  | 0                        | 0                          |
| Any Swelling, Dose 2        | 0   | 1  | 0                        | 1                          |
| Grade 3 Swelling, Dose 2    | 0   | 0  | 0                        | 0                          |
| Any Pain, Dose 3            | 4   | 6  | 0                        | 0                          |
| Grade 3 Pain, Dose 3        | 0   | 0  | 0                        | 0                          |
| Any Redness, Dose 3         | 0   | 0  | 0                        | 0                          |
| Grade 3 Redness, Dose 3     | 0   | 0  | 0                        | 0                          |
| Any Swelling, Dose 3        | 0   | 0  | 0                        | 0                          |
| Grade 3 Swelling, Dose 3    | 0   | 0  | 0                        | 0                          |
| Any Pain, Across            | 17  | 23   | 12                       | 15                         |
| Grade 3 Pain, Across        | 0   | 0  | 0                        | 0                          |
| Any Redness, Across         | 0   | 0  | 0                        | 0                          |
| Grade 3 Redness, Across     | 0   | 0  | 0                        | 0                          |
| Any Swelling, Across        | 0   | 1  | 0                        | 1                          |
| Grade 3 Swelling, Across    | 0   | 0  | 0                        | 0                          |

| <b>End point values</b>     | Synflorix 12-<br>23S Group | Synflorix 12-<br>23NS Group |  |  |
|-----------------------------|----------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group            | Reporting group             |  |  |
| Number of subjects analysed | 50                         | 50                          |  |  |
| Units: Subjects             |                            |                             |  |  |
| Any Pain, Dose 1            | 9                          | 6                           |  |  |
| Grade 3 Pain, Dose 1        | 0                          | 0                           |  |  |
| Any Redness, Dose 1         | 0                          | 0                           |  |  |
| Grade 3 Redness, Dose 1     | 0                          | 0                           |  |  |
| Any Swelling, Dose 1        | 1                          | 1                           |  |  |
| Grade 3 Swelling, Dose 1    | 0                          | 0                           |  |  |
| Any Pain, Dose 2            | 5                          | 3                           |  |  |
| Grade 3 Pain, Dose 2        | 0                          | 0                           |  |  |
| Any Redness, Dose 2         | 0                          | 0                           |  |  |

|                          |    |   |  |  |
|--------------------------|----|---|--|--|
| Grade 3 Redness, Dose 2  | 0  | 0 |  |  |
| Any Swelling, Dose 2     | 0  | 0 |  |  |
| Grade 3 Swelling, Dose 2 | 0  | 0 |  |  |
| Any Pain, Dose 3         | 0  | 0 |  |  |
| Grade 3 Pain, Dose 3     | 0  | 0 |  |  |
| Any Redness, Dose 3      | 0  | 0 |  |  |
| Grade 3 Redness, Dose 3  | 0  | 0 |  |  |
| Any Swelling, Dose 3     | 0  | 0 |  |  |
| Grade 3 Swelling, Dose 3 | 0  | 0 |  |  |
| Any Pain, Across         | 13 | 9 |  |  |
| Grade 3 Pain, Across     | 0  | 0 |  |  |
| Any Redness, Across      | 0  | 0 |  |  |
| Grade 3 Redness, Across  | 0  | 0 |  |  |
| Any Swelling, Across     | 1  | 1 |  |  |
| Grade 3 Swelling, Across | 0  | 0 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any, grade 3 and related solicited general symptoms during the primary vaccination phase

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any, grade 3 and related solicited general symptoms during the primary vaccination phase |
|-----------------|--|

End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as rectal temperature equal to or above ( $\geq$ ) 38 degrees Celsius ( $^{\circ}$ C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever  $> 40.0^{\circ}$ 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 following each dose and across doses

| End point values                 | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group | Synflorix 7-11NS Group |
|----------------------------------|--|---|-----------------------|------------------------|
| Subject group type               | Reporting group                          | Reporting group                           | Reporting group       | Reporting group        |
| Number of subjects analysed      | 50                                       | 50  | 50                    | 50                     |
| Units: Subjects                  |  |   |                       |                        |
| Any Drowsiness, Dose 1           | 0  | 0   | 0                     | 1                      |
| Grade 3 Drowsiness, Dose 1       | 0  | 0   | 0                     | 0                      |
| Related Drowsiness, Dose 1       | 0  | 0   | 0                     | 1                      |
| Any Irritability, Dose 1         | 0  | 2   | 0                     | 0                      |
| Grade 3 Irritability, Dose 1     | 0  | 0   | 0                     | 0                      |
| Related Irritability, Dose 1     | 0  | 0   | 0                     | 0                      |
| Any Loss of appetite, Dose 1     | 0  | 0   | 0                     | 0                      |
| Grade 3 Loss of appetite, Dose 1 | 0  | 0   | 0                     | 0                      |
| Related Loss of appetite, Dose 1 | 0  | 0   | 0                     | 0                      |



|  |    |    |    |    |
|--|----|----|----|----|
| Any Fever, Dose 1                      | 34 | 31 | 22 | 26 |
| Grade 3 Fever, Dose 1                  | 0  | 0  | 0  | 0  |
| Related Fever, Dose 1                  | 31 | 29 | 19 | 22 |
| Any Drowsiness, Dose 2                 | 0  | 0  | 0  | 0  |
| Grade 2 Drowsiness, Dose 2             | 0  | 0  | 0  | 0  |
| Related Drowsiness, Dose 2             | 0  | 0  | 0  | 0  |
| Any Irritability, Dose 2               | 0  | 0  | 0  | 0  |
| Grade 3 Irritability, Dose 2           | 0  | 0  | 0  | 0  |
| Related Irritability, Dose 2           | 0  | 0  | 0  | 0  |
| Any Loss of appetite, Dose 2           | 0  | 0  | 0  | 0  |
| Grade 3 Loss of appetite, Dose 2       | 0  | 0  | 0  | 0  |
| Related Loss of appetite, Dose 2       | 0  | 0  | 0  | 0  |
| Any Fever, Dose 2                      | 40 | 30 | 22 | 11 |
| Grade 3 Fever, Dose 2                  | 0  | 0  | 0  | 0  |
| Related Fever, Dose 2                  | 38 | 28 | 20 | 9  |
| Any Drowsiness, Dose 3                 | 0  | 0  | 0  | 0  |
| Grade 3 Drowsiness, Dose 3             | 0  | 0  | 0  | 0  |
| Related Drowsiness, Dose 3             | 0  | 0  | 0  | 0  |
| Any Irritability, Dose 3               | 3  | 4  | 0  | 0  |
| Grade 3 Irritability, Dose 3           | 0  | 0  | 0  | 0  |
| Related Irritability, Dose 3           | 3  | 3  | 0  | 0  |
| Any Loss of appetite, Dose 3           | 0  | 1  | 0  | 0  |
| Grade 3 Loss of appetite, Dose 3       | 0  | 0  | 0  | 0  |
| Related Loss of appetite, Dose 3       | 0  | 0  | 0  | 0  |
| Any Fever, Dose 3                      | 30 | 30 | 0  | 0  |
| Grade 3 Fever, Dose 3                  | 0  | 0  | 0  | 0  |
| Related Fever, Dose 3                  | 26 | 28 | 0  | 0  |
| Any Drowsiness, Across Doses           | 0  | 0  | 0  | 1  |
| Grade 3 Drowsiness, Across Doses       | 0  | 0  | 0  | 0  |
| Related Drowsiness, Across Doses       | 0  | 0  | 0  | 1  |
| Any Irritability, Across Doses         | 3  | 6  | 0  | 0  |
| Grade 3 Irritability, Across Doses     | 0  | 0  | 0  | 0  |
| Related Irritability, Across Doses     | 3  | 3  | 0  | 0  |
| Any Loss of appetite, Across Doses     | 0  | 1  | 0  | 0  |
| Grade 3 Loss of appetite, Across Doses | 0  | 0  | 0  | 0  |
| Related Loss of appetite, Across Doses | 0  | 0  | 0  | 0  |
| Any Fever, Across Doses                | 48 | 43 | 31 | 29 |
| Grade 3 Fever, Across Doses            | 0  | 0  | 0  | 0  |
| Related Fever, Across Doses            | 46 | 43 | 29 | 25 |

| End point values            | Synflorix 12-23S Group | Synflorix 12-23NS Group |  |  |
|-----------------------------|------------------------|-------------------------|--|--|
| Subject group type          | Reporting group        | Reporting group         |  |  |
| Number of subjects analysed | 50                     | 50                      |  |  |
| Units: Subjects             |                        |                         |  |  |
| Any Drowsiness, Dose 1      | 0                      | 0                       |  |  |
| Grade 3 Drowsiness, Dose 1  | 0                      | 0                       |  |  |
| Related Drowsiness, Dose 1  | 0                      | 0                       |  |  |
| Any Irritability, Dose 1    | 1                      | 0                       |  |  |

|  |    |    |  |  |
|--|----|----|--|--|
| Grade 3 Irritability, Dose 1           | 0  | 0  |  |  |
| Related Irritability, Dose 1           | 1  | 0  |  |  |
| Any Loss of appetite, Dose 1           | 0  | 1  |  |  |
| Grade 3 Loss of appetite, Dose 1       | 0  | 0  |  |  |
| Related Loss of appetite, Dose 1       | 0  | 1  |  |  |
| Any Fever, Dose 1                      | 21 | 15 |  |  |
| Grade 3 Fever, Dose 1                  | 0  | 0  |  |  |
| Related Fever, Dose 1                  | 21 | 13 |  |  |
| Any Drowsiness, Dose 2                 | 0  | 0  |  |  |
| Grade 2 Drowsiness, Dose 2             | 0  | 0  |  |  |
| Related Drowsiness, Dose 2             | 0  | 0  |  |  |
| Any Irritability, Dose 2               | 1  | 0  |  |  |
| Grade 3 Irritability, Dose 2           | 0  | 0  |  |  |
| Related Irritability, Dose 2           | 1  | 0  |  |  |
| Any Loss of appetite, Dose 2           | 0  | 0  |  |  |
| Grade 3 Loss of appetite, Dose 2       | 0  | 0  |  |  |
| Related Loss of appetite, Dose 2       | 0  | 0  |  |  |
| Any Fever, Dose 2                      | 12 | 12 |  |  |
| Grade 3 Fever, Dose 2                  | 0  | 0  |  |  |
| Related Fever, Dose 2                  | 10 | 9  |  |  |
| Any Drowsiness, Dose 3                 | 0  | 0  |  |  |
| Grade 3 Drowsiness, Dose 3             | 0  | 0  |  |  |
| Related Drowsiness, Dose 3             | 0  | 0  |  |  |
| Any Irritability, Dose 3               | 0  | 0  |  |  |
| Grade 3 Irritability, Dose 3           | 0  | 0  |  |  |
| Related Irritability, Dose 3           | 0  | 0  |  |  |
| Any Loss of appetite, Dose 3           | 0  | 0  |  |  |
| Grade 3 Loss of appetite, Dose 3       | 0  | 0  |  |  |
| Related Loss of appetite, Dose 3       | 0  | 0  |  |  |
| Any Fever, Dose 3                      | 0  | 0  |  |  |
| Grade 3 Fever, Dose 3                  | 0  | 0  |  |  |
| Related Fever, Dose 3                  | 0  | 0  |  |  |
| Any Drowsiness, Across Doses           | 0  | 0  |  |  |
| Grade 3 Drowsiness, Across Doses       | 0  | 0  |  |  |
| Related Drowsiness, Across Doses       | 0  | 0  |  |  |
| Any Irritability, Across Doses         | 2  | 0  |  |  |
| Grade 3 Irritability, Across Doses     | 0  | 0  |  |  |
| Related Irritability, Across Doses     | 2  | 0  |  |  |
| Any Loss of appetite, Across Doses     | 0  | 1  |  |  |
| Grade 3 Loss of appetite, Across Doses | 0  | 0  |  |  |
| Related Loss of appetite, Across Doses | 0  | 1  |  |  |
| Any Fever, Across Doses                | 29 | 20 |  |  |
| Grade 3 Fever, Across Doses            | 0  | 0  |  |  |
| Related Fever, Across Doses            | 28 | 17 |  |  |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

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

End point timeframe:

|  |
|--|
| Within the 31-day (Days 0-30) post-primary and post-booster vaccination period |
|--|

| End point values                                 | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group | Synflorix 7-11NS Group |
|--|--|---|-----------------------|------------------------|
| Subject group type                               | Reporting group                          | Reporting group                           | Reporting group       | Reporting group        |
| Number of subjects analysed                      | 50                                       | 50  | 50                    | 50                     |
| Units: Subjects                                  |  |   |                       |                        |
| Any AEs post primary vaccination [N=50,50,50,50] | 37                                       | 34  | 32                    | 37                     |
| Any AEs post-booster vaccination [N=49,49,50,50] | 8  | 17  | 18                    | 12                     |

| End point values                                 | Synflorix 12-23S Group | Synflorix 12-23NS Group |  |  |
|--|------------------------|-------------------------|--|--|
| Subject group type                               | Reporting group        | Reporting group         |  |  |
| Number of subjects analysed                      | 50                     | 50                      |  |  |
| Units: Subjects                                  |                        |                         |  |  |
| Any AEs post primary vaccination [N=50,50,50,50] | 23                     | 25                      |  |  |
| Any AEs post-booster vaccination [N=49,49,50,50] | 0                      | 0                       |  |  |

**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:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

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

End point timeframe:

|  |
|--|
| During the entire study period from Month 0 to Month 9 |
|--|

| End point values            | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group | Synflorix 7-11NS Group |
|-----------------------------|--|---|-----------------------|------------------------|
| Subject group type          | Reporting group                          | Reporting group                           | Reporting group       | Reporting group        |
| Number of subjects analysed | 50                                       | 50  | 50                    | 50                     |
| Units: Subjects             |  |   |                       |                        |
| Any SAEs                    | 3  | 9   | 3                     | 4                      |

| End point values            | Synflorix 12-23S Group | Synflorix 12-23NS Group |  |  |
|-----------------------------|------------------------|-------------------------|--|--|
| Subject group type          | Reporting group        | Reporting group         |  |  |
| Number of subjects analysed | 50                     | 50                      |  |  |
| Units: Subjects             |                        |                         |  |  |
| Any SAEs                    | 2                      | 2                       |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any and grade 3 solicited local symptoms during the booster vaccination phase

|                 |   |
|-----------------|---|
| End point title | Number of subjects with any and grade 3 solicited local symptoms during the booster vaccination phase |
|-----------------|---|

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

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

End point timeframe:

During the 4-day (Days 0-3) post-booster vaccination period

| End point values            | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group | Synflorix 7-11NS Group |
|-----------------------------|--|---|-----------------------|------------------------|
| Subject group type          | Reporting group                          | Reporting group                           | Reporting group       | Reporting group        |
| Number of subjects analysed | 49                                       | 49  | 50                    | 50                     |
| Units: Subjects             |  |   |                       |                        |
| Any Pain                    | 11                                       | 6   | 3                     | 0                      |
| Grade 3 Pain                | 0  | 0   | 0                     | 0                      |
| Any Redness                 | 0  | 0   | 0                     | 0                      |
| Grade 3 Redness             | 0  | 0   | 0                     | 0                      |

|                  |   |   |   |   |
|------------------|---|---|---|---|
| Any Swelling     | 1 | 0 | 1 | 0 |
| Grade 3 Swelling | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any, grade 3 and related solicited general symptoms during the booster vaccination phase

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any, grade 3 and related solicited general symptoms during the booster vaccination phase |
|-----------------|--|

End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as rectal temperature equal to or above ( $\geq$ ) 38 degrees Celsius ( $^{\circ}$ C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever  $> 40.0^{\circ}$ 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-booster vaccination period

| End point values            | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group | Synflorix 7-11NS Group |
|-----------------------------|--|---|-----------------------|------------------------|
| Subject group type          | Reporting group                          | Reporting group                           | Reporting group       | Reporting group        |
| Number of subjects analysed | 49                                       | 49  | 50                    | 50                     |
| Units: Subjects             |  |   |                       |                        |
| Any Drowsiness              | 0  | 0   | 0                     | 0                      |
| Grade 3 Drowsiness          | 0  | 0   | 0                     | 0                      |
| Related Drowsiness          | 0  | 0   | 0                     | 0                      |
| Any Irritability            | 6  | 0   | 0                     | 0                      |
| Grade 3 Irritability        | 0  | 0   | 0                     | 0                      |
| Related Irritability        | 5  | 0   | 0                     | 0                      |
| Any Loss of appetite        | 0  | 0   | 0                     | 0                      |
| Grade 3 Loss of appetite    | 0  | 0   | 0                     | 0                      |
| Related Loss of appetite    | 0  | 0   | 0                     | 0                      |
| Any Fever                   | 38                                       | 31  | 14                    | 13                     |
| Grade 3 Fever               | 0  | 0   | 0                     | 0                      |
| Related Fever               | 35                                       | 28  | 13                    | 13                     |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentrations of antibodies against cross-reactive pneumococcal

## serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines

|                 |   |
|-----------------|---|
| End point title | Concentrations of antibodies against cross-reactive pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines <sup>[5]</sup> |
|-----------------|---|

### End point description:

Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A, -19A) were measured by 22F enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration  $\geq 0.05$  micrograms per milliliter (µg/mL). Antibody concentrations  $< 0.05$  µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

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

### End point timeframe:

Prior to (Month 0) and one month after primary vaccination (Month 3), prior to (Month 8) and one month after (Month 9) booster vaccination

### Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

| End point values                         | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |  |  |
|--|--|---|--|--|
| Subject group type                       | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed              | 48                                       | 45  |  |  |
| Units: Titer                             |  |   |  |  |
| geometric mean (confidence interval 95%) |  |   |  |  |
| Anti-6A [Month 0] (N=47,41)              | 0.10 (0.07 to 0.14)                      | 0.15 (0.1 to 0.23)                        |  |  |
| Anti-6A [Month 3] (N=46,43)              | 0.12 (0.08 to 0.17)                      | 0.10 (0.07 to 0.13)                       |  |  |
| Anti-6A [Month 8] (N=37,30)              | 0.40 (0.27 to 0.61)                      | 0.18 (0.1 to 0.3)                         |  |  |
| Anti-6A [Month 9] (N=36,29)              | 0.48 (0.31 to 0.74)                      | 0.36 (0.23 to 0.55)                       |  |  |
| Anti-19A [Month 0] (N=47,44)             | 0.24 (0.17 to 0.36)                      | 0.23 (0.16 to 0.33)                       |  |  |
| Anti-19A [Month 3] (N=48,45)             | 0.26 (0.17 to 0.39)                      | 0.25 (0.17 to 0.37)                       |  |  |
| Anti-19A [Month 8] (N=44,38)             | 0.23 (0.15 to 0.37)                      | 0.21 (0.13 to 0.35)                       |  |  |
| Anti-19A [Month 9] (N=44,37)             | 1.09 (0.65 to 1.83)                      | 0.85 (0.5 to 1.43)                        |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentrations of antibodies against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose

|                 |   |
|-----------------|---|
| End point title | Concentrations of antibodies against vaccine pneumococcal |
|-----------------|---|

## End point description:

Antibodies have been assessed against the following 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), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration  $\geq 0.05$  micrograms per milliliter (µg/mL). Antibody concentrations  $< 0.05$  µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type Secondary

## End point timeframe:

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

## Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

| End point values                         | Synflorix 7-11S Group | Synflorix 7-11NS Group |  |  |
|--|-----------------------|------------------------|--|--|
| Subject group type                       | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed              | 50                    | 50                     |  |  |
| Units: µg/mL                             |                       |                        |  |  |
| geometric mean (confidence interval 95%) |                       |                        |  |  |
| Anti-1 [Month 0] (N=48,46)               | 0.03 (0.03 to 0.03)   | 0.04 (0.03 to 0.05)    |  |  |
| Anti-1 [Month 2] (N=50,48)               | 5.48 (4.34 to 6.93)   | 3.99 (3.24 to 4.91)    |  |  |
| Anti-1 [Month 3] (N=50,49)               | 2.68 (2.12 to 3.39)   | 2.44 (1.99 to 2.98)    |  |  |
| Anti-1 [Month 4] (N=49,48)               | 5.51 (4.27 to 7.1)    | 4.92 (3.74 to 6.48)    |  |  |
| Anti-4 [Month 0] (N=49,50)               | 0.03 (0.03 to 0.04)   | 0.03 (0.02 to 0.04)    |  |  |
| Anti-4 [Month 2] (N=49,47)               | 10.88 (8.94 to 13.24) | 7.55 (6 to 9.5)        |  |  |
| Anti-4 [Month 3] (N=50,48)               | 5.72 (4.66 to 7.03)   | 4.32 (3.51 to 5.32)    |  |  |
| Anti-4 [Month 4] (N=49,48)               | 9.75 (7.67 to 12.39)  | 7.88 (6.28 to 9.89)    |  |  |
| Anti-5 [Month 0] (N=48,50)               | 0.04 (0.03 to 0.06)   | 0.06 (0.05 to 0.08)    |  |  |
| Anti-5 [Month 2] (N=50,47)               | 6.76 (5.14 to 8.89)   | 4.59 (3.58 to 5.88)    |  |  |
| Anti-5 [Month 3] (N=50,49)               | 3.68 (2.87 to 4.73)   | 3.4 (2.66 to 4.33)     |  |  |
| Anti-5 [Month 4] (N=49,48)               | 7.75 (6.05 to 9.92)   | 7.87 (6.02 to 10.29)   |  |  |
| Anti-6B [Month 0] (N=49,46)              | 0.03 (0.02 to 0.03)   | 0.03 (0.02 to 0.03)    |  |  |
| Anti-6B [Month 2] (N=49,49)              | 1.61 (1.03 to 2.52)   | 1.48 (1.02 to 2.13)    |  |  |
| Anti-6B [Month 3] (N=50,49)              | 1.51 (1.06 to 2.15)   | 1.35 (0.98 to 1.87)    |  |  |
| Anti-6B [Month 4] (N=49,48)              | 3.12 (2.1 to 4.64)    | 2.93 (2.17 to 3.95)    |  |  |
| Anti-7F [Month 0] (N=50,50)              | 0.04 (0.03 to 0.05)   | 0.04 (0.03 to 0.05)    |  |  |

|                              |                        |                        |  |  |
|------------------------------|------------------------|------------------------|--|--|
| Anti-7F [Month 2] (N=49,49)  | 8.51 (6.94 to 10.42)   | 6.67 (5.44 to 8.19)    |  |  |
| Anti-7F [Month 3] (N=50,49)  | 5.46 (4.37 to 6.83)    | 4.68 (3.76 to 5.81)    |  |  |
| Anti-7F [Month 4] (N=48,48)  | 11.08 (8.9 to 13.81)   | 10.29 (7.92 to 13.37)  |  |  |
| Anti-9V [Month 0] (N=49,48)  | 0.04 (0.03 to 0.05)    | 0.04 (0.03 to 0.05)    |  |  |
| Anti-9V [Month 2] (N=49,49)  | 2.55 (1.86 to 3.49)    | 1.67 (1.21 to 2.29)    |  |  |
| Anti-9V [Month 3] (N=50,49)  | 1.9 (1.42 to 2.56)     | 1.52 (1.16 to 2)       |  |  |
| Anti-9V [Month 4] (N=49,48)  | 4.73 (3.4 to 6.58)     | 3.76 (2.67 to 5.3)     |  |  |
| Anti-14 [Month 0] (N=47,48)  | 0.08 (0.06 to 0.12)    | 0.07 (0.05 to 0.1)     |  |  |
| Anti-14 [Month 2] (N=50,46)  | 4.91 (3.48 to 6.95)    | 4.81 (3.67 to 6.29)    |  |  |
| Anti-14 [Month 3] (N=50,49)  | 4.71 (3.45 to 6.43)    | 4.98 (4.01 to 6.2)     |  |  |
| Anti-14 [Month 4] (N=49,48)  | 10.24 (7.96 to 13.18)  | 10.69 (8.34 to 13.71)  |  |  |
| Anti-18C [Month 0] (N=50,49) | 0.03 (0.03 to 0.03)    | 0.03 (0.03 to 0.04)    |  |  |
| Anti-18C [Month 2] (N=49,47) | 12.92 (9.93 to 16.82)  | 14.62 (11.61 to 18.4)  |  |  |
| Anti-18C [Month 3] (N=50,49) | 8.43 (6.53 to 10.88)   | 11.49 (9.24 to 14.29)  |  |  |
| Anti-18C [Month 4] (N=49,48) | 23.57 (18.38 to 30.22) | 31.88 (25.34 to 40.11) |  |  |
| Anti-19F [Month 0] (N=49,48) | 0.05 (0.04 to 0.06)    | 0.04 (0.04 to 0.06)    |  |  |
| Anti-19F [Month 2] (N=50,49) | 11.13 (7.97 to 15.54)  | 9.77 (6.16 to 15.48)   |  |  |
| Anti-19F [Month 3] (N=50,49) | 6.54 (4.79 to 8.92)    | 7.39 (5.04 to 10.81)   |  |  |
| Anti-19F [Month 4] (N=49,48) | 15.59 (11.24 to 21.62) | 15.85 (10.52 to 23.89) |  |  |
| Anti-23F [Month 0] (N=48,48) | 0.03 (0.03 to 0.04)    | 0.04 (0.03 to 0.05)    |  |  |
| Anti-23F [Month 2] (N=50,48) | 1.29 (0.79 to 2.1)     | 0.93 (0.6 to 1.45)     |  |  |
| Anti-23F [Month 3] (N=50,48) | 1 (0.65 to 1.56)       | 1.08 (0.74 to 1.56)    |  |  |
| Anti-23F [Month 4] (N=49,48) | 3.11 (1.85 to 5.24)    | 3.17 (2.04 to 4.91)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentrations of antibodies against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose

|                 |   |
|-----------------|---|
| End point title | Concentrations of antibodies against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose <sup>[7]</sup> |
|-----------------|---|



**End point description:**

Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A, -19A) were measured by 22F enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration  $\geq 0.05$  micrograms per milliliter (µg/mL). Antibody concentrations  $< 0.05$  µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

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

**End point timeframe:**

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

**Notes:**

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

| End point values                         | Synflorix 7-11S Group | Synflorix 7-11NS Group |  |  |
|--|-----------------------|------------------------|--|--|
| Subject group type                       | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed              | 50                    | 49                     |  |  |
| Units: Titer                             |                       |                        |  |  |
| geometric mean (confidence interval 95%) |                       |                        |  |  |
| Anti-6A [Month 0] (N=47,44)              | 0.03 (0.03 to 0.04)   | 0.03 (0.03 to 0.04)    |  |  |
| Anti-6A [Month 2] (N=48,46)              | 0.18 (0.11 to 0.3)    | 0.16 (0.11 to 0.24)    |  |  |
| Anti-6A [Month3] (N=50,47)               | 0.23 (0.14 to 0.37)   | 0.22 (0.16 to 0.32)    |  |  |
| Anti-6A [Month 4] (N=48,48)              | 0.44 (0.28 to 0.7)    | 0.43 (0.3 to 0.62)     |  |  |
| Anti-19A [Month 0] (N=48,49)             | 0.04 (0.03 to 0.06)   | 0.06 (0.04 to 0.1)     |  |  |
| Anti-19A [Month 2] (N=50,49)             | 0.46 (0.28 to 0.76)   | 0.77 (0.5 to 1.18)     |  |  |
| Anti-19A [Month3] (N=50,48)              | 0.44 (0.27 to 0.7)    | 0.77 (0.51 to 1.17)    |  |  |
| Anti-19A [Month 4] (N=49,48)             | 1.49 (0.93 to 2.38)   | 2.35 (1.5 to 3.67)     |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Concentration of antibodies against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose**

|                 |   |
|-----------------|---|
| End point title | Concentration of antibodies against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose <sup>[8]</sup> |
|-----------------|---|

**End point description:**

Antibodies have been assessed against the following 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), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration  $\geq 0.05$  micrograms per milliliter (µg/mL). Antibody concentrations  $< 0.05$  µg/mL were given an arbitrary value of half the cut-off for the

purpose of GMC calculation.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose |           |

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

| End point values                         | Synflorix 12-23S Group | Synflorix 12-23NS Group |  |  |
|--|------------------------|-------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group         |  |  |
| Number of subjects analysed              | 48                     | 47                      |  |  |
| Units: µg/mL                             |                        |                         |  |  |
| geometric mean (confidence interval 95%) |                        |                         |  |  |
| Anti-1 [Month 0] (N=47,45)               | 0.04 (0.03 to 0.05)    | 0.04 (0.03 to 0.05)     |  |  |
| Anti-1 [Month 2] (N=48,47)               | 1.39 (1.07 to 1.8)     | 1.49 (1.18 to 1.89)     |  |  |
| Anti-1 [Month 3] (N=48,46)               | 4.67 (3.75 to 5.81)    | 4.26 (3.38 to 5.37)     |  |  |
| Anti-4 [Month 0] (N=48,47)               | 0.04 (0.03 to 0.05)    | 0.04 (0.03 to 0.05)     |  |  |
| Anti-4 [Month 2] (N=47,47)               | 4.22 (3.23 to 5.51)    | 3.74 (2.96 to 4.72)     |  |  |
| Anti-4 [Month 3] (N=47,46)               | 8.87 (7.03 to 11.19)   | 7.02 (5.85 to 8.43)     |  |  |
| Anti-5 [Month 0] (N=48,47)               | 0.06 (0.04 to 0.08)    | 0.08 (0.06 to 0.11)     |  |  |
| Anti-5 [Month 2] (N=48,47)               | 1.06 (0.77 to 1.47)    | 1.1 (0.83 to 1.44)      |  |  |
| Anti-5 [Month 3] (N=48,46)               | 5.52 (4.23 to 7.2)     | 4.07 (3.06 to 5.42)     |  |  |
| Anti-6B [Month 0] (N=48,47)              | 0.03 (0.03 to 0.04)    | 0.04 (0.03 to 0.05)     |  |  |
| Anti-6B [Month 2] (N=48,47)              | 0.41 (0.28 to 0.62)    | 0.34 (0.24 to 0.48)     |  |  |
| Anti-6B [Month 3] (N=48,46)              | 1.37 (0.91 to 2.07)    | 1.25 (0.87 to 1.79)     |  |  |
| Anti-7F [Month 0] (N=48,47)              | 0.07 (0.05 to 0.11)    | 0.05 (0.04 to 0.07)     |  |  |
| Anti-7F [Month 2] (N=48,47)              | 2.74 (2.13 to 3.52)    | 3.17 (2.56 to 3.93)     |  |  |
| Anti-7F [Month 3] (N=48,46)              | 6.81 (5.32 to 8.7)     | 6.36 (5.25 to 7.69)     |  |  |
| Anti-9V [Month 0] (N=48,47)              | 0.08 (0.05 to 0.12)    | 0.05 (0.04 to 0.07)     |  |  |
| Anti-9V [Month 2] (N=48,47)              | 0.99 (0.72 to 1.34)    | 0.83 (0.62 to 1.11)     |  |  |
| Anti-9V [Month 3] (N=48,46)              | 2.35 (1.85 to 3)       | 1.72 (1.31 to 2.25)     |  |  |
| Anti-14 [Month 0] (N=47,46)              | 0.11 (0.07 to 0.16)    | 0.09 (0.06 to 0.12)     |  |  |
| Anti-14 [Month 2] (N=48,47)              | 1.87 (1.46 to 2.4)     | 1.24 (0.92 to 1.66)     |  |  |
| Anti-14 [Month 3] (N=47,45)              | 7.59 (5.84 to 9.87)    | 5.75 (4.33 to 7.62)     |  |  |

|                              |                        |                        |  |  |
|------------------------------|------------------------|------------------------|--|--|
| Anti-18C [Month 0] (N=48,47) | 0.04 (0.03 to 0.06)    | 0.05 (0.04 to 0.07)    |  |  |
| Anti-18C [Month 2] (N=48,47) | 6.21 (4.77 to 8.1)     | 6.12 (4.56 to 8.21)    |  |  |
| Anti-18C [Month 3] (N=47,45) | 25.52 (20.66 to 31.53) | 22.64 (18.14 to 28.26) |  |  |
| Anti-19F [Month 0] (N=48,47) | 0.06 (0.04 to 0.09)    | 0.08 (0.05 to 0.12)    |  |  |
| Anti-19F [Month 2] (N=48,47) | 5.88 (4.44 to 7.8)     | 5.12 (3.79 to 6.94)    |  |  |
| Anti-19F [Month 3] (N=48,46) | 18 (13.97 to 23.2)     | 14.46 (10.81 to 19.34) |  |  |
| Anti-23F [Month 0] (N=48,47) | 0.03 (0.03 to 0.04)    | 0.05 (0.03 to 0.07)    |  |  |
| Anti-23F [Month 2] (N=48,47) | 0.5 (0.32 to 0.77)     | 0.35 (0.25 to 0.49)    |  |  |
| Anti-23F [Month 3] (N=47,46) | 1.95 (1.32 to 2.87)    | 1.4 (1.05 to 1.87)     |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentration of antibodies against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose

|                 |  |
|-----------------|--|
| End point title | Concentration of antibodies against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose <sup>[9]</sup> |
|-----------------|--|

End point description:

Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A, -19A) were measured by 22F enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 micrograms per milliliter (µg/mL). Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

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

End point timeframe:

Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

| End point values                         | Synflorix 12-23S Group | Synflorix 12-23NS Group |  |  |
|--|------------------------|-------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group         |  |  |
| Number of subjects analysed              | 48                     | 47                      |  |  |
| Units: Titers                            |                        |                         |  |  |
| geometric mean (confidence interval 95%) |                        |                         |  |  |
| Anti-6A [Month 0] (N=45,44)              | 0.03 (0.03 to 0.03)    | 0.04 (0.03 to 0.05)     |  |  |
| Anti-6A [Month 2] (N=47,47)              | 0.15 (0.1 to 0.23)     | 0.12 (0.08 to 0.18)     |  |  |

|                              |                     |                     |  |  |
|------------------------------|---------------------|---------------------|--|--|
| Anti-6A [Month 3] (N=47,46)  | 0.39 (0.23 to 0.66) | 0.31 (0.2 to 0.48)  |  |  |
| Anti-19A [Month 0] (N=47,45) | 0.06 (0.04 to 0.09) | 0.07 (0.04 to 0.11) |  |  |
| Anti-19A [Month 2] (N=48,47) | 0.77 (0.5 to 1.17)  | 0.75 (0.47 to 1.19) |  |  |
| Anti-19A [Month 3] (N=48,46) | 3.15 (2.13 to 4.65) | 2.79 (1.93 to 4.05) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines

|                 |  |
|-----------------|--|
| End point title | Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines <sup>[10]</sup> |
|-----------------|--|

End point description:

Opsonophagocytic activity has been assessed against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was  $\geq 8$ . Antibody titers  $< 8$  were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

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

End point timeframe:

Prior to (Month 0) and one month after (Month 3) primary vaccination, prior to (Month 8) and one month after (Month 9) booster vaccination

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

| End point values                         | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |  |  |
|--|--|---|--|--|
| Subject group type                       | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed              | 46                                       | 41  |  |  |
| Units: Titer                             |  |   |  |  |
| geometric mean (confidence interval 95%) |  |   |  |  |
| Opsono-1 Month 3 (N=45,41)               | 106.4 (56 to 202.2)                      | 94.6 (49.9 to 179.5)                      |  |  |
| Opsono-1 Month 8 (N=41,33)               | 11.7 (6.8 to 20.1)                       | 10.9 (6 to 20.1)                          |  |  |
| Opsono-1 Month 9 (N=41,35)               | 930.5 (606.3 to 1427.9)                  | 750.4 (401.4 to 1403)                     |  |  |
| Opsono-4 Month 3 (N=44,38)               | 1316.6 (1014 to 1709.7)                  | 992.5 (680 to 1448.4)                     |  |  |
| Opsono-4 Month 8 (N=40,31)               | 222.1 (130.6 to 377.8)                   | 108.3 (51.6 to 227.6)                     |  |  |
| Opsono-4 Month 9 (N=41,33)               | 2064.2 (1625.3 to 2621.8)                | 2079.3 (1425.7 to 3032.7)                 |  |  |

|                              |                            |                            |  |  |
|------------------------------|----------------------------|----------------------------|--|--|
| Opsono-5 Month 3 (N=44,41)   | 106.9 (66.8 to 171.2)      | 119.4 (81.4 to 175.2)      |  |  |
| Opsono-5 Month 8 (N=40,33)   | 14.9 (8.9 to 24.9)         | 15.8 (9.6 to 26.1)         |  |  |
| Opsono-5 Month 9 (N=41,33)   | 273.2 (200.6 to 372)       | 277.5 (168.8 to 456.1)     |  |  |
| Opsono-6B Month 3 (N=41,37)  | 1043.3 (605.3 to 1798.3)   | 446.2 (207.4 to 960)       |  |  |
| Opsono-6B Month 8 (N=39,32)  | 285.3 (150.1 to 542.1)     | 245.6 (115 to 524.3)       |  |  |
| Opsono-6B Month 9 (N=40,33)  | 952.2 (638.8 to 1419.3)    | 989.2 (530.6 to 1843.9)    |  |  |
| Opsono-7F Month 3 (N=42,37)  | 4644.1 (3519.3 to 6128.4)  | 4924.2 (3430.2 to 7068.8)  |  |  |
| Opsono-7F Month 8 (N=40,32)  | 1747.2 (1225.4 to 2491.3)  | 1585.7 (1133.8 to 2217.8)  |  |  |
| Opsono-7F Month 9 (N=39,32)  | 7262.9 (5257.6 to 10033.1) | 8120.3 (5802.1 to 11364.8) |  |  |
| Opsono-9V Month 3 (N=46,39)  | 1438.6 (1084 to 1909.3)    | 1116.8 (679.6 to 1835.2)   |  |  |
| Opsono-9V Month 8 (N=38,32)  | 215.5 (97.5 to 476.1)      | 244.5 (123.9 to 482.2)     |  |  |
| Opsono-9V Month 9 (N=40,32)  | 2062.3 (1569 to 2710.8)    | 2987.2 (2149.4 to 4151.6)  |  |  |
| Opsono-14 Month 3 (N=44,41)  | 1689.9 (1090.7 to 2618.2)  | 1062.3 (562.8 to 2005.2)   |  |  |
| Opsono-14 Month 8 (N=39,26)  | 215.9 (113.6 to 410.1)     | 132.5 (60.3 to 291.5)      |  |  |
| Opsono-14 Month 9 (N=40,33)  | 1571.5 (1114.2 to 2216.4)  | 1454.1 (741.8 to 2850.5)   |  |  |
| Opsono-18C Month 3 (N=40,37) | 873.8 (591.7 to 1290.4)    | 524.7 (319.6 to 861.6)     |  |  |
| Opsono-18C Month 8 (N=39,30) | 46.5 (28.5 to 75.7)        | 28.7 (17.5 to 47.3)        |  |  |
| Opsono-18C Month 9 (N=39,31) | 1246 (776.7 to 1999)       | 1011.8 (686.4 to 1491.4)   |  |  |
| Opsono-19F Month 3 (N=43,39) | 558.9 (376.3 to 830.2)     | 266.1 (148.2 to 477.8)     |  |  |
| Opsono-19F Month 8 (N=41,32) | 60.7 (37.1 to 99.3)        | 43.4 (22.6 to 83.2)        |  |  |
| Opsono-19F Month 9 (N=40,33) | 652.9 (413.3 to 1031.5)    | 486.7 (278.9 to 849.4)     |  |  |
| Opsono-23F Month 3 (N=44,37) | 705.1 (309.2 to 1607.8)    | 759.7 (326.7 to 1766.6)    |  |  |
| Opsono-23F Month 8 (N=36,31) | 85.2 (27.5 to 264.4)       | 41.6 (14.6 to 118.9)       |  |  |
| Opsono-23F Month 9 (N=39,33) | 4231.2 (2793.7 to 6408.3)  | 1454 (736.1 to 2872.3)     |  |  |

## Statistical analyses

**Secondary: Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines**

|                 |   |
|-----------------|---|
| End point title | Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines <sup>[11]</sup> |
|-----------------|---|

## End point description:

Opsonophagocytic activity has been assessed for cross-reactive vaccine pneumococcal serotypes 6A and 19A (Opsono-6A, Opsono-19A) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was  $\geq 8$ . Antibody titers  $< 8$  were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

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

## End point timeframe:

Prior to (Month 0) and one month after (Month 3) primary vaccination, prior to (Month 8) and one month after (Month 9) booster vaccination

## Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

| End point values                         | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |  |  |
|--|--|---|--|--|
| Subject group type                       | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed              | 42                                       | 41  |  |  |
| Units: Titers                            |  |   |  |  |
| geometric mean (confidence interval 95%) |  |   |  |  |
| Opsono-6A [Month 3] (N=42,41)            | 24.73 (11.46 to 53.37)                   | 9.45 (5.32 to 16.75)                      |  |  |
| Opsono-6A [Month 8] (N=40,33)            | 18.23 (8.97 to 37.09)                    | 17.59 (8.08 to 38.3)                      |  |  |
| Opsono-6A [Month 9] (N=38,32)            | 35.35 (15.6 to 80.12)                    | 30.7 (12.14 to 77.64)                     |  |  |
| Opsono-19A [Month 3] (N=38,34)           | 9.42 (5.65 to 15.7)                      | 5.04 (3.83 to 6.63)                       |  |  |
| Opsono-19A [Month 8] (N=34,23)           | 6.31 (4.28 to 9.32)                      | 5.83 (3.95 to 8.61)                       |  |  |
| Opsono-19A [Month 9] (N=26,28)           | 22.06 (9.49 to 51.3)                     | 19.44 (10.25 to 36.86)                    |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose**

|                 |  |
|-----------------|--|
| End point title | Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary |
|-----------------|--|

## End point description:

Opsonophagocytic activity has been assessed for cross-reactive vaccine pneumococcal serotypes 6A and 19A (Opsono-6A, Opsono-19A) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was  $\geq 8$ . Antibody titers  $< 8$  were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

## End point type

Secondary

## End point timeframe:

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

## Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

| End point values                         | Synflorix 7-11S Group   | Synflorix 7-11NS Group     |  |  |
|--|-------------------------|----------------------------|--|--|
| Subject group type                       | Reporting group         | Reporting group            |  |  |
| Number of subjects analysed              | 49                      | 45                         |  |  |
| Units: Titers                            |                         |                            |  |  |
| geometric mean (confidence interval 95%) |                         |                            |  |  |
| Opsono-6A [Month 2] (N=49,39)            | 40.59 (19.11 to 86.23)  | 51.23 (22.85 to 114.88)    |  |  |
| Opsono-6A [Month 3] (N=44,45)            | 38.11 (17.04 to 85.21)  | 36.27 (16.89 to 77.89)     |  |  |
| Opsono-6A [Month 4] (N=45,43)            | 77.09 (35.58 to 167.04) | 98.18 (43.05 to 223.96)    |  |  |
| Opsono-19A [Month 2] (N=40,31)           | 15.21 (7.95 to 29.08)   | 108.31 (49.55 to 236.78)   |  |  |
| Opsono-19A [Month 3] (N=37,26)           | 14.65 (7.71 to 27.81)   | 19.4 (8.04 to 46.82)       |  |  |
| Opsono-19A [Month 4] (N=31,29)           | 76.09 (30.5 to 189.83)  | 449.06 (170.05 to 1185.87) |  |  |
| Opsono-6A [Month 0] (N=46,40)            | 4.81 (3.71 to 6.24)     | 5.02 (3.64 to 6.90)        |  |  |
| Opsono-19A [Month 0] (N=41,40)           | 4.49 (3.91 to 5.16)     | 4.33 (3.68 to 5.10)        |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose**

## End point title

Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose<sup>[13]</sup>

## End point description:

Opsonophagocytic activity has been assessed against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was  $\geq 8$ . Antibody titers  $< 8$  were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

## End point type

Secondary

End point timeframe:

Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

| End point values                         | Synflorix 12-23S Group      | Synflorix 12-23NS Group     |  |  |
|--|-----------------------------|-----------------------------|--|--|
| Subject group type                       | Reporting group             | Reporting group             |  |  |
| Number of subjects analysed              | 47                          | 45                          |  |  |
| Units: Titer                             |                             |                             |  |  |
| geometric mean (confidence interval 95%) |                             |                             |  |  |
| Opsono-1 Month 2 (N=46,45)               | 9.3 (6.1 to 14.3)           | 10.9 (6.8 to 17.4)          |  |  |
| Opsono-1 Month 3 (N=45,43)               | 195.7 (119.9 to 319.3)      | 115.1 (64 to 206.8)         |  |  |
| Opsono-4 Month 2 (N=44,43)               | 1086.3 (758.4 to 1555.9)    | 1539.4 (1128.4 to 2100.1)   |  |  |
| Opsono-4 Month 3 (N=44,43)               | 2089.7 (1635 to 2670.8)     | 3193.9 (2241.3 to 4551.4)   |  |  |
| Opsono-5 Month 2 (N=45,45)               | 9.8 (7.1 to 13.7)           | 9.6 (6.6 to 13.7)           |  |  |
| Opsono-5 Month 3 (N=44,44)               | 151.3 (99.8 to 229.2)       | 84 (53.5 to 131.8)          |  |  |
| Opsono-6B Month 2 (N=41,42)              | 345.1 (172.4 to 690.7)      | 278.4 (131.8 to 588.4)      |  |  |
| Opsono-6B Month 3 (N=43,43)              | 748.4 (425.9 to 1315)       | 866.4 (511.8 to 1466.7)     |  |  |
| Opsono-7F Month 2 (N=44,45)              | 5462.3 (4108.9 to 7261.4)   | 5802.2 (4678.6 to 7195.6)   |  |  |
| Opsono-7F Month 3 (N=44,42)              | 10279.4 (7836.7 to 13483.6) | 10131.4 (8303.7 to 12361.6) |  |  |
| Opsono-9V Month 2 (N=43,44)              | 1976.2 (1392.6 to 2804.4)   | 2359 (1514.3 to 3674.9)     |  |  |
| Opsono-9V Month 3 (N=44,43)              | 3778.2 (2880 to 4956.4)     | 4276.8 (3122.3 to 5858.3)   |  |  |
| Opsono-14 Month 2 (N=42,40)              | 711.2 (400.7 to 1262.4)     | 865.6 (583.2 to 1284.9)     |  |  |
| Opsono-14 Month 3 (N=45,40)              | 2704.5 (1856.4 to 3940)     | 2737.5 (1890 to 3965.1)     |  |  |
| Opsono-18C Month 2 (N=32,34)             | 1035.5 (507.6 to 2112.5)    | 449.2 (222.8 to 905.9)      |  |  |
| Opsono-18C Month 3 (N=40,40)             | 2873.1 (2070 to 3987.6)     | 2126.8 (1509.7 to 2996.3)   |  |  |
| Opsono-19F Month 2 (N=44,43)             | 229.1 (132.9 to 395)        | 248 (143 to 430.1)          |  |  |
| Opsono-19F Month 3 (N=45,43)             | 1845.3 (1169.3 to 2912.1)   | 1271.4 (825.4 to 1958.3)    |  |  |



|                              |                           |                           |  |  |
|------------------------------|---------------------------|---------------------------|--|--|
| Opsono-23F Month 2 (N=44,44) | 2572.2 (1264.1 to 5233.9) | 2433.6 (1309.7 to 4522)   |  |  |
| Opsono-23F Month 3 (N=42,41) | 5016.6 (3176.6 to 7922.4) | 5325.4 (2857.8 to 9923.9) |  |  |
| Opsono-1 Month 0 (N=47,43)   | 6.9 (4.5 to 10.8)         | 5.6 (4.2 to 7.6)          |  |  |
| Opsono-4 Month 0 (N=46,44)   | 8.0 (4.7 to 13.6)         | 7.3 (4.3 to 12.3)         |  |  |
| Opsono-5 Month 0 (N=47,45)   | 5.5 (4.2 to 7.4)          | 4.4 (3.6 to 5.4)          |  |  |
| Opsono-6B Month 0 (N=41,38)  | 13.6 (6.7 to 27.6)        | 9.9 (5.2 to 18.7)         |  |  |
| Opsono-7F Month 0 (N=44,36)  | 1436.6 (1014.4 to 2034.6) | 1228.1 (783.3 to 1925.5)  |  |  |
| Opsono-9V Month 0 (N=40,37)  | 119.5 (50.4 to 283.2)     | 81.3 (35.7 to 185.0)      |  |  |
| Opsono-14 Month 0 (N=40,34)  | 16.3 (8.3 to 31.8)        | 12.0 (5.3 to 27.0)        |  |  |
| Opsono-18C Month 0 (N=44,40) | 4.9 (4.0 to 6.0)          | 4.0 (4.0 to 4.0)          |  |  |
| Opsono-19F Month 0 (N=46,42) | 5.5 (5.5 to 7.3)          | 4.0 (4.0 to 4.0)          |  |  |
| Opsono-23F Month 0 (N=39,38) | 68.1 (21.1 to 219.6)      | 37.6 (12.3 to 114.3)      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose

|                 |   |
|-----------------|---|
| End point title | Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose <sup>[14]</sup> |
|-----------------|---|

End point description:

Opsonophagocytic activity has been assessed for cross-reactive vaccine pneumococcal serotypes 6A and 19A (Opsono-6A, Opsono-19A) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was  $\geq 8$ . Antibody titers  $< 8$  were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

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

End point timeframe:

Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

| End point values                         | Synflorix 12-23S Group   | Synflorix 12-23NS Group  |  |  |
|--|--------------------------|--------------------------|--|--|
| Subject group type                       | Reporting group          | Reporting group          |  |  |
| Number of subjects analysed              | 44                       | 42                       |  |  |
| Units: Titers                            |                          |                          |  |  |
| geometric mean (confidence interval 95%) |                          |                          |  |  |
| Opsono-6A [Month 2] (N=44,42)            | 82.82 (40.27 to 170.33)  | 77.25 (31.81 to 187.64)  |  |  |
| Opsono-6A [Month 3] (N=40,39)            | 147.91 (63.11 to 346.68) | 157.37 (59.23 to 418.11) |  |  |
| Opsono-19A [Month 2] (N=23,27)           | 28.37 (11.84 to 67.98)   | 25.68 (11.6 to 56.84)    |  |  |
| Opsono-19A [Month 3] (N=19,23)           | 214.17 (75.58 to 606.93) | 321.14 (144.75 to 712.5) |  |  |
| Opsono-6A [Month 0] (N=44,40)            | 9.26 (5.76 to 14.89)     | 6.35 (4.02 to 10.02)     |  |  |
| Opsono-19A [Month 0] (N=44,40)           | 5.85 (4.27 to 8.01)      | 6.32 (4.09 to 9.76)      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentration of antibodies against protein D (PD) for subjects who received a two-dose primary vaccination followed by a booster dose

|                 |  |
|-----------------|--|
| End point title | Concentration of antibodies against protein D (PD) for subjects who received a two-dose primary vaccination followed by a booster dose <sup>[15]</sup> |
|-----------------|--|

End point description:

Anti-PD antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was an antibody concentration  $\geq 100$  EL.U/mL. Antibody concentrations  $< 100$  EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

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

End point timeframe:

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

| End point values                         | Synflorix 7-11S Group  | Synflorix 7-11NS Group  |  |  |
|--|------------------------|-------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group         |  |  |
| Number of subjects analysed              | 50                     | 50                      |  |  |
| Units: EL.U/mL                           |                        |                         |  |  |
| geometric mean (confidence interval 95%) |                        |                         |  |  |
| Anti-PD [Month 0] (N=47,48)              | 72.73 (57.23 to 92.42) | 88.74 (70.85 to 111.13) |  |  |

|                             |                                   |                                    |  |  |
|-----------------------------|-----------------------------------|------------------------------------|--|--|
| Anti-PD [Month 2] (N=50,50) | 1313.39<br>(1014.3 to<br>1700.67) | 1489.78<br>(1171.98 to<br>1893.76) |  |  |
| Anti-PD [Month 3] (N=50,49) | 932.52 (732.63<br>to 1186.96)     | 1063.54<br>(844.52 to<br>1339.37)  |  |  |
| Anti-PD [Month 4] (N=49,48) | 2695.5<br>(2150.74 to<br>3378.24) | 2638.27<br>(2049.91 to<br>3395.49) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Concentration of antibodies against protein D (PD) for subjects who received a two-dose primary vaccination without any booster dose

|                 |  |
|-----------------|--|
| End point title | Concentration of antibodies against protein D (PD) for subjects who received a two-dose primary vaccination without any booster dose <sup>[16]</sup> |
|-----------------|--|

End point description:

Anti-PD antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was an antibody concentration  $\geq 100$  EL.U/mL. Antibody concentrations  $< 100$  EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

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

End point timeframe:

Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

| End point values                         | Synflorix 12-23S Group       | Synflorix 12-23NS Group    |  |  |
|--|------------------------------|----------------------------|--|--|
| Subject group type                       | Reporting group              | Reporting group            |  |  |
| Number of subjects analysed              | 48                           | 47                         |  |  |
| Units: EL.U/mL                           |                              |                            |  |  |
| geometric mean (confidence interval 95%) |                              |                            |  |  |
| Anti-PD [Month 0] (N=47,46)              | 79.59 (62.08 to 102.04)      | 76.22 (61.39 to 94.63)     |  |  |
| Anti-PD [Month 2] (N=48,47)              | 199.23 (150.51 to 263.72)    | 184.34 (140.21 to 242.35)  |  |  |
| Anti-PD [Month 3] (N=48,46)              | 1376.56 (1020.71 to 1856.46) | 760.99 (553.23 to 1046.77) |  |  |

## Statistical analyses

**Secondary: Concentration of antibodies against diphtheria toxoid (DT) and tetanus toxoid (TT) for subjects who were co-administered Tritanrix-HepB/Hib vaccine**

|                 |   |
|-----------------|---|
| End point title | Concentration of antibodies against diphtheria toxoid (DT) and tetanus toxoid (TT) for subjects who were co-administered Tritanrix-HepB/Hib vaccine <sup>[17]</sup> |
|-----------------|---|

## End point description:

Anti-DT and anti-TT antibody concentrations are presented as geometric mean concentrations (GMCs) and expressed in international units per milliliter (IU/mL). Seroprotection status was defined as anti-DT or anti-TT antibody concentration  $\geq$  than 0.1 IU/mL.

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

## End point timeframe:

Prior to (Month 0) and one month after (Month 3) primary vaccination, prior to (Month 8) and one month after (Month 9) booster vaccination

## Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

| End point values                         | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |  |  |
|--|--|---|--|--|
| Subject group type                       | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed              | 48                                       | 46  |  |  |
| Units: IU/mL                             |  |   |  |  |
| geometric mean (confidence interval 95%) |  |   |  |  |
| Anti-DT Month 0 (N=48,45)                | 0.07 (0.05 to 0.08)                      | 0.06 (0.05 to 0.07)                       |  |  |
| Anti-DT Month 3 (N=48,46)                | 3.22 (2.59 to 4)                         | 3.5 (2.82 to 4.34)                        |  |  |
| Anti-DT Month 8 (N=44,37)                | 0.62 (0.5 to 0.77)                       | 0.9 (0.72 to 1.12)                        |  |  |
| Anti-DT Month 9 (N=44,38)                | 6.58 (5.44 to 7.97)                      | 7.55 (6.11 to 9.32)                       |  |  |
| Anti-TT Month 0 (N=48,46)                | 1.54 (1.13 to 2.09)                      | 1.22 (0.85 to 1.76)                       |  |  |
| Anti-TT Month 3 (N=48,46)                | 4.04 (3.26 to 5.01)                      | 4.13 (3.27 to 5.22)                       |  |  |
| Anti-TT Month 8 (N=44,38)                | 1.19 (0.96 to 1.48)                      | 1.33 (1.08 to 1.63)                       |  |  |
| Anti-TT Month 9 (N=44,38)                | 10.88 (9.24 to 12.81)                    | 11.11 (9.62 to 12.83)                     |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Concentrations of antibodies against Bordetella pertussis (BPT) for subjects who were co-administered Tritanrix-HepB/Hib vaccine**

|                 |  |
|-----------------|--|
| End point title | Concentrations of antibodies against Bordetella pertussis (BPT) for subjects who were co-administered Tritanrix-HepB/Hib |
|-----------------|--|

## End point description:

Anti-BPT antibody concentrations are presented as geometric mean concentrations (GMCs) and expressed in enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was an antibody concentration  $\geq 15$  EL.U/mL.

## End point type

Secondary

## End point timeframe:

Prior to (Month 0) and one month after (Month 3) primary vaccination, prior to (Month 8) and one month after (Month 9) booster vaccination

## Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

| End point values                         | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |  |  |
|--|--|---|--|--|
| Subject group type                       | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed              | 48                                       | 46  |  |  |
| Units: EL.U/mL                           |  |   |  |  |
| geometric mean (confidence interval 95%) |  |   |  |  |
| Anti-BPT Month 0 (N=48,46)               | 7.71 (7.29 to 8.16)                      | 7.77 (7.39 to 8.17)                       |  |  |
| Anti-BPT Month 3 (N=48,46)               | 105.61 (86.93 to 128.3)                  | 101.74 (84.56 to 122.42)                  |  |  |
| Anti-BPT Month 8 (N=44,38)               | 22.67 (17.45 to 29.45)                   | 22.69 (17.88 to 28.8)                     |  |  |
| Anti-BPT Month 9 (N=44,38)               | 177.87 (152.1 to 207.99)                 | 190.58 (167.67 to 216.63)                 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose

## End point title

Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose<sup>[19]</sup>

## End point description:

Opsonophagocytic activity has been assessed against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was  $\geq 8$ . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

## End point type

Secondary

## End point timeframe:

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

| End point values                         | Synflorix 7-11S Group       | Synflorix 7-11NS Group      |  |  |
|--|-----------------------------|-----------------------------|--|--|
| Subject group type                       | Reporting group             | Reporting group             |  |  |
| Number of subjects analysed              | 49                          | 47                          |  |  |
| Units: Titers                            |                             |                             |  |  |
| geometric mean (confidence interval 95%) |                             |                             |  |  |
| Opsono-1 Month 0 (N=47,43)               | 4.9 (3.8 to 6.3)            | 4.5 (3.6 to 5.7)            |  |  |
| Opsono-1 Month 2 (N=48,45)               | 134.7 (83.6 to 216.9)       | 88.1 (53.7 to 144.6)        |  |  |
| Opsono-1 Month 3 (N=48,46)               | 74.2 (42.6 to 129.3)        | 48 (26.6 to 86.7)           |  |  |
| Opsono-1 Month 4 (N=48,44)               | 516.0 (307.6 to 865.7)      | 511.3 (293.2 to 891.8)      |  |  |
| Opsono-4 Month 0 (N=44,44)               | 5.1 (3.6 to 7.2)            | 11.8 (5.7 to 24.5)          |  |  |
| Opsono-4 Month 2 (N=49,44)               | 1636.3 (1217.5 to 2199.2)   | 1771.1 (1359.0 to 2308.2)   |  |  |
| Opsono-4 Month 3 (N=45,45)               | 812.7 (584.5 to 1130.1)     | 1048.3 (790.4 to 1390.3)    |  |  |
| Opsono-4 Month 4 (N=48,43)               | 2130.5 (1639.1 to 2769.2)   | 2415.5 (1686.5 to 3459.8)   |  |  |
| Opsono-5 Month 0 (N=47,44)               | 4.4 (3.8 to 5.1)            | 4.0 (4.0 to 4.0)            |  |  |
| Opsono-5 Month 2 (N=49,46)               | 105.7 (67.7 to 165.1)       | 85.8 (59.4 to 124.0)        |  |  |
| Opsono-5 Month 3 (N=47,47)               | 54.1 (34.9 to 83.6)         | 49.2 (31.7 to 76.3)         |  |  |
| Opsono-5 Month 4 (N=48,43)               | 277.4 (180.7 to 425.7)      | 289.6 (190.9 to 439.3)      |  |  |
| Opsono-6B Month 0 (N=43,41)              | 7.9 (4.6 to 13.8)           | 8.5 (4.7 to 15.4)           |  |  |
| Opsono-6B Month 2 (N=48,43)              | 702.5 (413.2 to 1194.2)     | 696.6 (388.5 to 1249.2)     |  |  |
| Opsono-6B Month 3 (N=44,45)              | 708.3 (422.9 to 1186.1)     | 615.5 (337.3 to 1123.1)     |  |  |
| Opsono-6B Month 4 (N=46,43)              | 1360.0 (860.2 to 2150.3)    | 1305.4 (731.9 to 2328.4)    |  |  |
| Opsono-7F Month 0 (N=41,40)              | 215.3 (91.2 to 508.1)       | 643.5 (293.4 to 1411.7)     |  |  |
| Opsono-7F Month 2 (N=47,40)              | 6694.3 (5055.1 to 8864.9)   | 10452.0 (7782.7 to 14036.6) |  |  |
| Opsono-7F Month 3 (N=46,46)              | 7776.9 (6000.8 to 10078.7)  | 9336.3 (6752.4 to 12908.9)  |  |  |
| Opsono-7F Month 4 (N=47,39)              | 10854.8 (9051.6 to 13017.2) | 9362.8 (6882.3 to 12737.3)  |  |  |
| Opsono-9V Month 0 (N=42,44)              | 16.9 (8.3 to 34.5)          | 20.3 (9.2 to 44.5)          |  |  |
| Opsono-9V Month 2 (N=48,42)              | 2858.2 (1875.3 to 4356.2)   | 2667.9 (1677.9 to 4242.0)   |  |  |

|                              |                           |                           |  |  |
|------------------------------|---------------------------|---------------------------|--|--|
| Opsono-9V Month 3 (N=44,46)  | 1982.9 (1192.1 to 3298.2) | 1986.2 (1167.8 to 3378.2) |  |  |
| Opsono-9V Month 4 (N=48,41)  | 3047.9 (2389.7 to 3887.3) | 2719.2 (1681.0 to 4398.9) |  |  |
| Opsono-14 Month 0 (N=40,39)  | 5.5 (3.8 to 8.1)          | 5.9 (3.8 to 9.1)          |  |  |
| Opsono-14 Month 2 (N=44,43)  | 2109.5 (1299.0 to 3425.9) | 4009.9 (2501.9 to 6426.7) |  |  |
| Opsono-14 Month 3 (N=46,46)  | 1431.6 (865.2 to 2368.6)  | 2128.3 (1477.5 to 3065.9) |  |  |
| Opsono-14 Month 4 (N=46,40)  | 3414.9 (2237.4 to 5211.9) | 3717.3 (2403.9 to 5748.5) |  |  |
| Opsono-18C Month 0 (N=44,43) | 4.1 (3.9 to 4.5)          | 4.6 (3.4 to 6.2)          |  |  |
| Opsono-18C Month 2 (N=39,37) | 744.4 (393.3 to 1409.2)   | 1605.6 (937.1 to 2751.1)  |  |  |
| Opsono-18C Month 3 (N=40,42) | 411.4 (214.4 to 789.7)    | 746.4 (430.5 to 1294.1)   |  |  |
| Opsono-18C Month 4 (N=44,40) | 2218.9 (1577.5 to 3121.2) | 3238.7 (1874.7 to 5595.0) |  |  |
| Opsono-19F Month 0 (N=44,43) | 4.2 (3.8 to 4.7)          | 4.0 (4.0 to 4.0)          |  |  |
| Opsono-19F Month 2 (N=47,43) | 393.4 (393.4 to 722.0)    | 491.5 (256.8 to 940.6)    |  |  |
| Opsono-19F Month 3 (N=45,46) | 160.2 (86.8 to 295.6)     | 279.5 (161.1 to 484.9)    |  |  |
| Opsono-19F Month 4 (N=47,41) | 1347.7 (813.6 to 2232.3)  | 1174.4 (605.6 to 2277.3)  |  |  |
| Opsono-23F Month 0 (N=43,40) | 7.6 (4.1 to 13.9)         | 15.3 (6.4 to 36.6)        |  |  |
| Opsono-23F Month 2 (N=46,44) | 1545.1 (788.3 to 3028.2)  | 2107.5 (1155.0 to 3845.5) |  |  |
| Opsono-23F Month 3 (N=40,46) | 1168.8 (560.8 to 2435.8)  | 1026.2 (458.3 to 2298.0)  |  |  |
| Opsono-23F Month 4 (N=47,43) | 2038.8 (977.1 to 4254.4)  | 3525.1 (1974.2 to 6294.4) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: during the 4-day (Days 0-3) period following each vaccination dose; Unsolicited AEs: within the 31-day (Days 0-30) period following each vaccination; SAEs: throughout the study, from Day 0 up to Month 9.

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 | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Tritanrix-HepB/Hib+Polio Sabin <6S Group |
|-----------------------|--|

Reporting group description:

Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8

|                       |   |
|-----------------------|---|
| Reporting group title | Tritanrix-HepB/Hib+Polio Sabin <6NS Group |
|-----------------------|---|

Reporting group description:

Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Synflorix 7-11S Group |
|-----------------------|-----------------------|

Reporting group description:

Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Synflorix 7-11NS Group |
|-----------------------|------------------------|

Reporting group description:

Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Synflorix 12-23S Group |
|-----------------------|------------------------|

Reporting group description:

Children between 12-23 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Synflorix 12-23NS Group |
|-----------------------|-------------------------|

Reporting group description:

Healthy children between 12-23 months of age at time of enrolment, who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.

| Serious adverse events                            | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group |
|---|--|---|-----------------------|
| Total subjects affected by serious adverse events |  |   |                       |
| subjects affected / exposed                       | 3 / 50 (6.00%)                           | 9 / 50 (18.00%)                           | 3 / 50 (6.00%)        |
| number of deaths (all causes)                     | 1  | 1   | 1                     |
| number of deaths resulting from                   |  |   |                       |



|  |                |                 |                |
|--|----------------|-----------------|----------------|
| adverse events                                       |                |                 |                |
| General disorders and administration site conditions |                |                 |                |
| Pyrexia  |                |                 |                |
| alternative assessment type: Non-systematic          |                |                 |                |
| subjects affected / exposed                          | 0 / 50 (0.00%) | 0 / 50 (0.00%)  | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 1          |
| Gastrointestinal disorders                           |                |                 |                |
| Enteritis  |                |                 |                |
| alternative assessment type: Non-systematic          |                |                 |                |
| subjects affected / exposed                          | 0 / 50 (0.00%) | 0 / 50 (0.00%)  | 0 / 50 (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          |
| Infections and infestations                          |                |                 |                |
| Gastroenteritis                                      |                |                 |                |
| alternative assessment type: Non-systematic          |                |                 |                |
| subjects affected / exposed                          | 1 / 50 (2.00%) | 6 / 50 (12.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 6           | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0          |
| Malaria  |                |                 |                |
| alternative assessment type: Non-systematic          |                |                 |                |
| subjects affected / exposed                          | 3 / 50 (6.00%) | 3 / 50 (6.00%)  | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 3          | 0 / 3           | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0          |
| Sepsis   |                |                 |                |
| alternative assessment type: Non-systematic          |                |                 |                |
| subjects affected / exposed                          | 1 / 50 (2.00%) | 0 / 50 (0.00%)  | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0          |
| Pneumonia  |                |                 |                |
| alternative assessment type: Non-systematic          |                |                 |                |
| subjects affected / exposed                          | 0 / 50 (0.00%) | 1 / 50 (2.00%)  | 0 / 50 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Bronchitis                                      |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 0 / 50 (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          |
| Gastroenteritis rotavirus                       |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 50 (2.00%) | 0 / 50 (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          |
| Meningitis Salmonella                           |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 1 / 50 (2.00%) | 0 / 50 (0.00%) | 0 / 50 (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          |
| Osteomyelitis acute                             |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 0 / 50 (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          |
| Urinary tract infection                         |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 50 (2.00%) | 0 / 50 (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          |
| Metabolism and nutrition disorders              |                |                |                |
| Malnutrition                                    |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 50 (2.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |

|                                    |                        |                        |                         |
|------------------------------------|------------------------|------------------------|-------------------------|
| <b>Serious adverse events</b>      | Synflorix 7-11NS Group | Synflorix 12-23S Group | Synflorix 12-23NS Group |
| Total subjects affected by serious |                        |                        |                         |

|  |                |                |                |
|--|----------------|----------------|----------------|
| adverse events                                       |                |                |                |
| subjects affected / exposed                          | 4 / 50 (8.00%) | 2 / 50 (4.00%) | 2 / 50 (4.00%) |
| number of deaths (all causes)                        | 0              | 0              | 0              |
| number of deaths resulting from adverse events       |                |                |                |
| General disorders and administration site conditions |                |                |                |
| Pyrexia  |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 0 / 50 (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          |
| Gastrointestinal disorders                           |                |                |                |
| Enteritis  |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 1 / 50 (2.00%) | 0 / 50 (0.00%) | 0 / 50 (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                          |                |                |                |
| Gastroenteritis                                      |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 2 / 50 (4.00%) | 0 / 50 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Malaria  |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 1 / 50 (2.00%) | 1 / 50 (2.00%) | 2 / 50 (4.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          | 0 / 2          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Sepsis   |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia  |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 50 (2.00%) | 0 / 50 (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          |
| Bronchitis                                      |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 1 / 50 (2.00%) | 0 / 50 (0.00%) | 0 / 50 (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          |
| Gastroenteritis rotavirus                       |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 0 / 50 (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          |
| Meningitis Salmonella                           |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 0 / 50 (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          |
| Osteomyelitis acute                             |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 50 (2.00%) | 0 / 50 (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          |
| Urinary tract infection                         |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 0 / 50 (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          |
| Metabolism and nutrition disorders              |                |                |                |
| Malnutrition                                    |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 0 / 50 (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          |

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

| <b>Non-serious adverse events</b>                     | Tritanrix-HepB/Hib+Polio Sabin <6S Group | Tritanrix-HepB/Hib+Polio Sabin <6NS Group | Synflorix 7-11S Group |
|---|--|---|-----------------------|
| Total subjects affected by non-serious adverse events |  |   |                       |
| subjects affected / exposed                           | 50 / 50 (100.00%)                        | 49 / 50 (98.00%)                          | 47 / 50 (94.00%)      |
| Congenital, familial and genetic disorders            |  |   |                       |
| Sickle cell anaemia with crisis                       |  |   |                       |
| subjects affected / exposed                           | 1 / 50 (2.00%)                           | 0 / 50 (0.00%)                            | 3 / 50 (6.00%)        |
| occurrences (all)                                     | 1  | 0   | 5                     |
| General disorders and administration site conditions  |  |   |                       |
| Pain  |  |   |                       |
| subjects affected / exposed                           | 23 / 50 (46.00%)                         | 26 / 50 (52.00%)                          | 15 / 50 (30.00%)      |
| occurrences (all)                                     | 30                                       | 31  | 17                    |
| Pyrexia   |  |   |                       |
| subjects affected / exposed                           | 49 / 50 (98.00%)                         | 47 / 50 (94.00%)                          | 37 / 50 (74.00%)      |
| occurrences (all)                                     | 143                                      | 123                                       | 63                    |
| Eye disorders   |  |   |                       |
| Conjunctivitis  |  |   |                       |
| subjects affected / exposed                           | 2 / 50 (4.00%)                           | 3 / 50 (6.00%)                            | 1 / 50 (2.00%)        |
| occurrences (all)                                     | 2  | 3   | 1                     |
| Gastrointestinal disorders                            |  |   |                       |
| Diarrhoea   |  |   |                       |
| subjects affected / exposed                           | 8 / 50 (16.00%)                          | 6 / 50 (12.00%)                           | 4 / 50 (8.00%)        |
| occurrences (all)                                     | 8  | 6   | 4                     |
| Enteritis   |  |   |                       |
| subjects affected / exposed                           | 2 / 50 (4.00%)                           | 5 / 50 (10.00%)                           | 7 / 50 (14.00%)       |
| occurrences (all)                                     | 2  | 5   | 7                     |
| Abdominal pain  |  |   |                       |
| subjects affected / exposed                           | 3 / 50 (6.00%)                           | 1 / 50 (2.00%)                            | 2 / 50 (4.00%)        |
| occurrences (all)                                     | 3  | 1   | 2                     |
| Respiratory, thoracic and mediastinal                 |  |   |                       |

|  |                        |                        |                        |
|--|------------------------|------------------------|------------------------|
| disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)                     | 4 / 50 (8.00%)<br>4    | 5 / 50 (10.00%)<br>5   | 3 / 50 (6.00%)<br>3    |
| Psychiatric disorders<br>Irritability<br>subjects affected / exposed<br>occurrences (all)  | 9 / 50 (18.00%)<br>9   | 6 / 50 (12.00%)<br>6   | 0 / 50 (0.00%)<br>0    |
| Infections and infestations<br>Malaria<br>subjects affected / exposed<br>occurrences (all) | 10 / 50 (20.00%)<br>10 | 13 / 50 (26.00%)<br>14 | 18 / 50 (36.00%)<br>19 |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                             | 9 / 50 (18.00%)<br>10  | 10 / 50 (20.00%)<br>12 | 6 / 50 (12.00%)<br>6   |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                        | 6 / 50 (12.00%)<br>6   | 6 / 50 (12.00%)<br>7   | 3 / 50 (6.00%)<br>3    |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)                               | 4 / 50 (8.00%)<br>4    | 7 / 50 (14.00%)<br>7   | 5 / 50 (10.00%)<br>6   |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                        | 7 / 50 (14.00%)<br>7   | 5 / 50 (10.00%)<br>6   | 3 / 50 (6.00%)<br>3    |
| Gastrointestinal fungal infection<br>subjects affected / exposed<br>occurrences (all)      | 4 / 50 (8.00%)<br>5    | 6 / 50 (12.00%)<br>6   | 3 / 50 (6.00%)<br>3    |
| Ear infection<br>subjects affected / exposed<br>occurrences (all)                          | 3 / 50 (6.00%)<br>3    | 2 / 50 (4.00%)<br>2    | 0 / 50 (0.00%)<br>0    |

| <b>Non-serious adverse events</b>   | Synflorix 7-11NS<br>Group | Synflorix 12-23S<br>Group | Synflorix 12-23NS<br>Group |
|---|---------------------------|---------------------------|----------------------------|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed | 47 / 50 (94.00%)          | 41 / 50 (82.00%)          | 31 / 50 (62.00%)           |
| Congenital, familial and genetic<br>disorders<br>Sickle cell anaemia with crisis        |                           |                           |                            |

|   |                     |                        |                     |
|---|---------------------|------------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)        | 0 / 50 (0.00%)<br>0 | 10 / 50 (20.00%)<br>13 | 0 / 50 (0.00%)<br>0 |
| General disorders and administration<br>site conditions |                     |                        |                     |
| Pain  |                     |                        |                     |
| subjects affected / exposed                             | 15 / 50 (30.00%)    | 14 / 50 (28.00%)       | 9 / 50 (18.00%)     |
| occurrences (all)                                       | 17                  | 16                     | 9                   |
| Pyrexia   |                     |                        |                     |
| subjects affected / exposed                             | 35 / 50 (70.00%)    | 29 / 50 (58.00%)       | 21 / 50 (42.00%)    |
| occurrences (all)                                       | 52                  | 33                     | 28                  |
| Eye disorders   |                     |                        |                     |
| Conjunctivitis  |                     |                        |                     |
| subjects affected / exposed                             | 1 / 50 (2.00%)      | 2 / 50 (4.00%)         | 0 / 50 (0.00%)      |
| occurrences (all)                                       | 1                   | 2                      | 0                   |
| Gastrointestinal disorders                              |                     |                        |                     |
| Diarrhoea   |                     |                        |                     |
| subjects affected / exposed                             | 4 / 50 (8.00%)      | 1 / 50 (2.00%)         | 1 / 50 (2.00%)      |
| occurrences (all)                                       | 4                   | 1                      | 1                   |
| Enteritis   |                     |                        |                     |
| subjects affected / exposed                             | 4 / 50 (8.00%)      | 0 / 50 (0.00%)         | 1 / 50 (2.00%)      |
| occurrences (all)                                       | 4                   | 0                      | 1                   |
| Abdominal pain  |                     |                        |                     |
| subjects affected / exposed                             | 0 / 50 (0.00%)      | 0 / 50 (0.00%)         | 0 / 50 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                      | 0                   |
| Respiratory, thoracic and mediastinal<br>disorders      |                     |                        |                     |
| Cough   |                     |                        |                     |
| subjects affected / exposed                             | 2 / 50 (4.00%)      | 1 / 50 (2.00%)         | 0 / 50 (0.00%)      |
| occurrences (all)                                       | 2                   | 1                      | 0                   |
| Psychiatric disorders                                   |                     |                        |                     |
| Irritability  |                     |                        |                     |
| subjects affected / exposed                             | 0 / 50 (0.00%)      | 2 / 50 (4.00%)         | 0 / 50 (0.00%)      |
| occurrences (all)                                       | 0                   | 2                      | 0                   |
| Infections and infestations                             |                     |                        |                     |
| Malaria   |                     |                        |                     |
| subjects affected / exposed                             | 18 / 50 (36.00%)    | 10 / 50 (20.00%)       | 8 / 50 (16.00%)     |
| occurrences (all)                                       | 20                  | 10                     | 8                   |
| Bronchitis  |                     |                        |                     |

|                                   |                 |                |                 |
|-----------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed       | 9 / 50 (18.00%) | 1 / 50 (2.00%) | 4 / 50 (8.00%)  |
| occurrences (all)                 | 10              | 1              | 4               |
| Gastroenteritis                   |                 |                |                 |
| subjects affected / exposed       | 7 / 50 (14.00%) | 1 / 50 (2.00%) | 5 / 50 (10.00%) |
| occurrences (all)                 | 7               | 1              | 5               |
| Rhinitis                          |                 |                |                 |
| subjects affected / exposed       | 4 / 50 (8.00%)  | 3 / 50 (6.00%) | 4 / 50 (8.00%)  |
| occurrences (all)                 | 4               | 3              | 4               |
| Nasopharyngitis                   |                 |                |                 |
| subjects affected / exposed       | 8 / 50 (16.00%) | 4 / 50 (8.00%) | 5 / 50 (10.00%) |
| occurrences (all)                 | 8               | 4              | 5               |
| Gastrointestinal fungal infection |                 |                |                 |
| subjects affected / exposed       | 1 / 50 (2.00%)  | 0 / 50 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)                 | 1               | 0              | 0               |
| Ear infection                     |                 |                |                 |
| subjects affected / exposed       | 1 / 50 (2.00%)  | 0 / 50 (0.00%) | 1 / 50 (2.00%)  |
| occurrences (all)                 | 1               | 0              | 1               |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 15 April 2010     | The oral polio vaccine was to be provided in multidose vials<br>Changes in the randomization of treatment<br>Inconsistencies regarding the age for booster vaccination in the 7-11 month groups<br>Changes in the priority ranking of immunological assays<br>Changes in the definition of the Epochs<br>Update of Rationale of the study  |
| 03 September 2010 | <ul style="list-style-type: none"><li>•For clarification, the inclusion criteria for children with sickle cell disease have been further detailed.</li><li>•An additional blood sample for SCD testing was planned to be taken at the pre-vaccination timepoint from subjects aged 7-11 and 12-23 months without hemoglobin status confirmed by electrophoresis available.</li><li>•Presentation of oral polio vaccine that was to be used has changed: 10- or 20-dose vials were used. In addition, the use of one 10- or 20-dose vial to vaccinate up to 10 or 20 subjects, respectively, on the same day was allowed.</li><li>•The immunogenicity objectives related to the co-administered OPV have been removed since there are no plans to test poliovirus immune response.</li><li>•The contact details for the emergency code break have been clarified.</li></ul> |
| 08 May 2012       | The main changes and their rationale are the following: <ul style="list-style-type: none"><li>•Additional information was given about administration of vaccines through the local EPI program.</li><li>•Extension of the recruitment period due to a lower enrolment rate than expected.</li><li>•Additional exclusion criterion for children of the &lt;6S and &lt;6NS groups to clarify differences between groups with regard to administration of vaccines included in the EPI program either as study vaccines or outside the study.</li><li>•Additional exclusion criterion for all groups, i.e. exclusion of subjects being heterozygous or carriers of abnormal haemoglobin (e.g. haemoglobin S, haemoglobin C) who are not considered to have SCD, to avoid potential bias and to keep homogeneity of the examined groups.</li></ul>                             |
| 09 April 2013     | In the past few months, GSK Biologicals has been investigating the quality of some serology assays used in clinical studies, including the Streptococcus pneumonia opsonophagocytic activity (OPA) assay used in the present trial. This protocol amendment reflected the fact that delays in the availability of the assay results would lead to changes in the analysis plan.<br>Therefore, the sequence of analysis has been modified to perform study analysis in one final step on all immunogenicity and safety data obtained up to one month after administration of the last dose of study vaccine for all study groups. The results of this final analysis were presented in a final clinical study report.   |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported