



## Clinical trial results:

**A Phase III, open, multicentre study to assess the long-term persistence of a booster dose of GlaxoSmithKline (GSK) Biologicals' Haemophilus influenzae type b-meningococcal serogroup C conjugate vaccine (Hib-MenC) compared to a booster dose of Infanrix™ hexa (combined diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated polio-Hib vaccine) when given to 14-month-old subjects who were primed in study 217744/097 (DTPa-HBV-IPV-097) and boosted in study Hib-MenC-TT-010 BST: DTPa-HBV-IPV-097**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2006-000518-19    |
| Trial protocol           | ES                |
| Global end of trial date | 08 September 2010 |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1           |
| This version publication date  | 20 June 2016 |
| First version publication date | 22 May 2015  |

### Trial information

#### Trial identification

|                       |                                 |
|-----------------------|---------------------------------|
| Sponsor protocol code | 106672;106673;106675;106679;-80 |
|-----------------------|---------------------------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00322335 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                                        |
|------------------------------|--------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | GlaxoSmithKline Biologicals                                                                            |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330                                                       |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                   |
|------------------------------------------------------|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 20 May 2011       |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 08 September 2010 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 08 September 2010 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the persistence of Meningococcal C antibodies on a yearly basis for a period of 5.5 years after booster vaccination.

To evaluate the persistence of Haemophilus influenzae type b antibodies on a yearly basis for a period of 5.5 years after booster vaccination

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the day of vaccination and the subsequent 30 days after the last vaccination administration.

Background therapy: -

Evidence for comparator: -

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 11 May 2010 |
| Long term follow-up planned                               | Yes         |
| Long term follow-up rationale                             | Efficacy    |
| Long term follow-up duration                              | 4 Years     |
| Independent data monitoring committee (IDMC) involvement? | No          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |            |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Spain: 184 |
| Worldwide total number of subjects   | 184        |
| EEA total number of subjects         | 184        |

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) | 0   |
| Children (2-11 years)                    | 184 |
| 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.

### Pre-assignment period milestones

|                              |     |
|------------------------------|-----|
| Number of subjects started   | 184 |
| Number of subjects completed | 184 |

### Period 1

|                              |                             |
|------------------------------|-----------------------------|
| Period 1 title               | Month 18                    |
| 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>             | Menitorix/Pediarix Group Month 18 |

Arm description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                                        |                                                            |
|----------------------------------------|------------------------------------------------------------|
| Arm type                               | Experimental                                               |
| Investigational medicinal product name | Menitorix™                                                 |
| Investigational medicinal product code |                                                            |
| Other name                             | Haemophilus influenzae type b- and meningococcal (vaccine) |
| Pharmaceutical forms                   | Injection                                                  |
| Routes of administration               | Intramuscular use                                          |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ penta   |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

|                  |                                                     |
|------------------|-----------------------------------------------------|
| <b>Arm title</b> | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18 |
|------------------|-----------------------------------------------------|

Arm description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with

Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                                        |                                                            |
|----------------------------------------|------------------------------------------------------------|
| Arm type                               | Active comparator                                          |
| Investigational medicinal product name | Menitorix™                                                 |
| Investigational medicinal product code |                                                            |
| Other name                             | Haemophilus influenzae type b- and meningococcal (vaccine) |
| Pharmaceutical forms                   | Injection                                                  |
| Routes of administration               | Intramuscular use                                          |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ Hexa    |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Engerix-B         |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as a birth dose

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | NeisVac-C™        |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age.

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ IPV/HIB |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 4 months of age.

|                  |                                         |
|------------------|-----------------------------------------|
| <b>Arm title</b> | Infanrix hexa/Meningitec Group Month 18 |
|------------------|-----------------------------------------|

Arm description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Infanrix™ Hexa    |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

**Dosage and administration details:**

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Meningitec™       |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

**Dosage and administration details:**

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

| Number of subjects in period 1 | Menitorix/Pediarix Group Month 18 | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18 | Infanrix hexa/Meningitec Group Month 18 |
|--------------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|
|                                |                                   |                                                     |                                         |
| Started                        | 58                                | 123                                                 | 3                                       |
| Completed                      | 58                                | 123                                                 | 3                                       |

**Period 2**

|                              |                             |
|------------------------------|-----------------------------|
| Period 2 title               | Month 30                    |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

**Arms**

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | Menitorix/Pediarix Group Month 30 |

**Arm description:**

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                                        |                                                            |
|----------------------------------------|------------------------------------------------------------|
| Arm type                               | Experimental                                               |
| Investigational medicinal product name | Menitorix™                                                 |
| Investigational medicinal product code |                                                            |
| Other name                             | Haemophilus influenzae type b- and meningococcal (vaccine) |
| Pharmaceutical forms                   | Injection                                                  |
| Routes of administration               | Intramuscular use                                          |

**Dosage and administration details:**

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

|                                        |                 |
|----------------------------------------|-----------------|
| Investigational medicinal product name | Infanrix™ penta |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Injection       |

|                          |                   |
|--------------------------|-------------------|
| Routes of administration | Intramuscular use |
|--------------------------|-------------------|

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

|                  |                                                     |
|------------------|-----------------------------------------------------|
| <b>Arm title</b> | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30 |
|------------------|-----------------------------------------------------|

Arm description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of **Infanrix™** hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of **NeisVac-C™** administered intramuscularly in the left thigh at 2 and 4 months of age or with **Engerix-B** at birth intramuscularly in the right thigh, **Infanrix™** hexa intramuscularly in the right thigh at 2 and 6 months of age and **NeisVac-C™** intramuscularly in the left thigh at 2 and 4 months of age, **Infanrix™** IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with **Menitorix™** administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                                        |                                                                   |
|----------------------------------------|-------------------------------------------------------------------|
| Arm type                               | Active comparator                                                 |
| Investigational medicinal product name | <b>Menitorix™</b>                                                 |
| Investigational medicinal product code |                                                                   |
| Other name                             | <b>Haemophilus influenzae type b- and meningococcal (vaccine)</b> |
| Pharmaceutical forms                   | Injection                                                         |
| Routes of administration               | Intramuscular use                                                 |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

|                                        |                         |
|----------------------------------------|-------------------------|
| Investigational medicinal product name | <b>Infanrix™ Hexa</b>   |
| Investigational medicinal product code |                         |
| Other name                             | <b>DTPa-HBV-IPV/Hib</b> |
| Pharmaceutical forms                   | Injection               |
| Routes of administration               | Intramuscular use       |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | <b>Engerix-B</b>  |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as a birth dose

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | <b>NeisVac-C™</b> |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age.

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | <b>Infanrix™ IPV/HIB</b> |
| Investigational medicinal product code |                          |
| Other name                             | <b>DTPa-HBV-IPV/Hib</b>  |
| Pharmaceutical forms                   | Injection                |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 4 months of age

|                  |                                         |
|------------------|-----------------------------------------|
| <b>Arm title</b> | Infanrix hexa/Meningitec Group Month 30 |
|------------------|-----------------------------------------|

Arm description:

Subjects were primed with **Infanrix™** hexa co-administered intramuscularly with **Meningitec™** in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of **Infanrix™** hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Infanrix™ Hexa    |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Meningitec™       |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Menitorix/Pediarix Group Month 30 | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30 | Infanrix hexa/Meningitec Group Month 30 |
|-----------------------------------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|
|                                                     |                                   |                                                     |                                         |
| Started                                             | 54                                | 119                                                 | 3                                       |
| Completed                                           | 54                                | 119                                                 | 57                                      |

|                            |   |   |    |
|----------------------------|---|---|----|
| Joined                     | 0 | 0 | 54 |
| Late return to study visit | - | - | 54 |

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: Not all subjects completing one period came to the next study visit; however, a subject missing a previous visit was allowed to return to a subsequent one. Thus, the number of subjects starting every study period is based on the actual rate of return.

**Period 3**

|                              |                             |
|------------------------------|-----------------------------|
| Period 3 title               | Month 42                    |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

**Arms**

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|



|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                            |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Menitorix/Pediarix Group Month 42                          |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                            |
| Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.                                                                                                                                                                                                                                                                                                                                                                            |                                                            |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Experimental                                               |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Menitorix™                                                 |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                            |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Haemophilus influenzae type b- and meningococcal (vaccine) |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Injection                                                  |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Intramuscular use                                          |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                            |
| Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                            |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Infanrix™ penta                                            |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                            |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                            |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Injection                                                  |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Intramuscular use                                          |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                            |
| Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                            |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42        |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                            |
| Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study. |                                                            |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Active comparator                                          |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Menitorix™                                                 |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                            |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Haemophilus influenzae type b- and meningococcal (vaccine) |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Injection                                                  |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Intramuscular use                                          |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                            |
| Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                            |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Infanrix™ Hexa                                             |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                            |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | DTPa-HBV-IPV/Hib                                           |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Injection                                                  |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Intramuscular use                                          |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                            |
| Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                            |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Engerix-B                                                  |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                            |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                            |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Injection                                                  |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Intramuscular use                                          |

|                                                        |                   |
|--------------------------------------------------------|-------------------|
| Dosage and administration details:                     |                   |
| Intramuscular injection into the thigh as a birth dose |                   |
| Investigational medicinal product name                 | NeisVac-C™        |
| Investigational medicinal product code                 |                   |
| Other name                                             |                   |
| Pharmaceutical forms                                   | Injection         |
| Routes of administration                               | Intramuscular use |

|                                                                                         |                   |
|-----------------------------------------------------------------------------------------|-------------------|
| Dosage and administration details:                                                      |                   |
| Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age. |                   |
| Investigational medicinal product name                                                  | Infanrix™ IPV/HIB |
| Investigational medicinal product code                                                  |                   |
| Other name                                                                              | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                                                                    | Injection         |
| Routes of administration                                                                | Intramuscular use |

|                                                                                   |                                         |
|-----------------------------------------------------------------------------------|-----------------------------------------|
| Dosage and administration details:                                                |                                         |
| Intramuscular injection into the thigh as primary vaccination at 4 months of age. |                                         |
| <b>Arm title</b>                                                                  | Infanrix hexa/Meningitec Group Month 42 |

Arm description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Infanrix™ Hexa    |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

|                                                                                                                                                                                       |                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Dosage and administration details:                                                                                                                                                    |                   |
| Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM). |                   |
| Investigational medicinal product name                                                                                                                                                | Meningitec™       |
| Investigational medicinal product code                                                                                                                                                |                   |
| Other name                                                                                                                                                                            |                   |
| Pharmaceutical forms                                                                                                                                                                  | Injection         |
| Routes of administration                                                                                                                                                              | Intramuscular use |

|                                                                                           |  |
|-------------------------------------------------------------------------------------------|--|
| Dosage and administration details:                                                        |  |
| Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age |  |

| Number of subjects in period 3 <sup>[2]</sup> | Menitorix/Pediarix Group Month 42 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42 | Infanrix hexa/Meningitec Group Month 42 |
|-----------------------------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|
|                                               |                                   |                                                     |                                         |
| Started                                       | 51                                | 113                                                 | 56                                      |
| Completed                                     | 51                                | 113                                                 | 56                                      |

Notes:

[2] - 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: Not all subjects completing one period came to the next study visit; however, a subject missing a previous visit was allowed to return to a subsequent one. Thus, the number of subjects starting every study period is based on the actual rate of return.

#### Period 4

|                              |                             |
|------------------------------|-----------------------------|
| Period 4 title               | Month 54                    |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

#### Arms

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | Menitorix/Pediarix Group Month 54 |

Arm description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                                        |                                                            |
|----------------------------------------|------------------------------------------------------------|
| Arm type                               | Experimental                                               |
| Investigational medicinal product name | Menitorix™                                                 |
| Investigational medicinal product code |                                                            |
| Other name                             | Haemophilus influenzae type b- and meningococcal (vaccine) |
| Pharmaceutical forms                   | Injection                                                  |
| Routes of administration               | Intramuscular use                                          |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ penta   |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

|                  |                                                     |
|------------------|-----------------------------------------------------|
| <b>Arm title</b> | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54 |
|------------------|-----------------------------------------------------|

Arm description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                                        |                                                            |
|----------------------------------------|------------------------------------------------------------|
| Arm type                               | Active comparator                                          |
| Investigational medicinal product name | Menitorix™                                                 |
| Investigational medicinal product code |                                                            |
| Other name                             | Haemophilus influenzae type b- and meningococcal (vaccine) |
| Pharmaceutical forms                   | Injection                                                  |
| Routes of administration               | Intramuscular use                                          |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group

HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ Hexa    |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Engerix-B         |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as a birth dose

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | NeisVac-C™        |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age.

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ IPV/HIB |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 4 months of age.

|                  |                                         |
|------------------|-----------------------------------------|
| <b>Arm title</b> | Infanrix hexa/Meningitec Group Month 54 |
|------------------|-----------------------------------------|

Arm description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Infanrix™ Hexa    |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Meningitec™       |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

| Number of subjects in period 4[3] | Menitorix/Pediarix Group Month 54 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54 | Infanrix hexa/Meningitec Group Month 54 |
|-----------------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|
|                                   |                                   |                                                     |                                         |
| Started                           | 50                                | 108                                                 | 56                                      |
| Completed                         | 50                                | 108                                                 | 56                                      |

Notes:

[3] - 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: Not all subjects completing one period came to the next study visit; however, a subject missing a previous visit was allowed to return to a subsequent one. Thus, the number of subjects starting every study period is based on the actual rate of return.

## Period 5

|                              |                             |
|------------------------------|-----------------------------|
| Period 5 title               | Month 66                    |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

## Arms

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| Arm title                    | Menitorix/Pediarix Group Month 66 |

Arm description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                                        |                                                            |
|----------------------------------------|------------------------------------------------------------|
| Arm type                               | Experimental                                               |
| Investigational medicinal product name | Menitorix™                                                 |
| Investigational medicinal product code |                                                            |
| Other name                             | Haemophilus influenzae type b- and meningococcal (vaccine) |
| Pharmaceutical forms                   | Injection                                                  |
| Routes of administration               | Intramuscular use                                          |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ penta   |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

|           |                                                     |
|-----------|-----------------------------------------------------|
| Arm title | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66 |
|-----------|-----------------------------------------------------|

Arm description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of

age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                                        |                                                            |
|----------------------------------------|------------------------------------------------------------|
| Arm type                               | Active comparator                                          |
| Investigational medicinal product name | Menitorix™                                                 |
| Investigational medicinal product code |                                                            |
| Other name                             | Haemophilus influenzae type b- and meningococcal (vaccine) |
| Pharmaceutical forms                   | Injection                                                  |
| Routes of administration               | Intramuscular use                                          |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ Hexa    |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Engerix-B         |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as a birth dose

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | NeisVac-C™        |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age.

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ IPV/HIB |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 4 months of age.

|                  |                                         |
|------------------|-----------------------------------------|
| <b>Arm title</b> | Infanrix hexa/Meningitec Group Month 66 |
|------------------|-----------------------------------------|

Arm description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

|          |                   |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Infanrix™ Hexa    |
| Investigational medicinal product code |                   |
| Other name                             | DTPa-HBV-IPV/Hib  |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Meningitec™       |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

| Number of subjects in period<br>5 <sup>[4]</sup> | Menitorix/Pediarix<br>Group Month 66 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad Group<br>Month 66 | Infanrix<br>hexa/Meningitec<br>Group Month 66 |
|--------------------------------------------------|--------------------------------------|--------------------------------------------------------------|-----------------------------------------------|
|                                                  |                                      |                                                              |                                               |
| Started                                          | 48                                   | 104                                                          | 53                                            |
| Completed                                        | 48                                   | 104                                                          | 53                                            |

Notes:

[4] - 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: Not all subjects completing one period came to the next study visit; however, a subject missing a previous visit was allowed to return to a subsequent one. Thus, the number of subjects starting every study period is based on the actual rate of return.

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Menitorix/Pediarix Group Month 18                   |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.                                                                                                                                                                                                                                                                                                                                                                            |                                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18 |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study. |                                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Infanrix hexa/Meningitec Group Month 18             |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.                                                                                                                                                                                                                                                                                                                                                                                            |                                                     |

| Reporting group values                                                                                                                                                                                                                                    | Menitorix/Pediarix Group Month 18 | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18 | Infanrix hexa/Meningitec Group Month 18 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|
| Number of subjects                                                                                                                                                                                                                                        | 58                                | 123                                                 | 3                                       |
| Age categorical<br>Units: Subjects                                                                                                                                                                                                                        |                                   |                                                     |                                         |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                                   |                                                     |                                         |
| Age continuous<br>Units: months                                                                                                                                                                                                                           |                                   |                                                     |                                         |
| arithmetic mean                                                                                                                                                                                                                                           | 31.3                              | 31.4                                                | 31.3                                    |
| standard deviation                                                                                                                                                                                                                                        | ± 0.54                            | ± 0.64                                              | ± 0.58                                  |
| Gender categorical<br>Units: Subjects                                                                                                                                                                                                                     |                                   |                                                     |                                         |
| Female                                                                                                                                                                                                                                                    | 27                                | 55                                                  | 1                                       |
| Male                                                                                                                                                                                                                                                      | 31                                | 68                                                  | 2                                       |



|                                                       |       |  |  |
|-------------------------------------------------------|-------|--|--|
| <b>Reporting group values</b>                         | Total |  |  |
| Number of subjects                                    | 184   |  |  |
| Age categorical                                       |       |  |  |
| 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)           | 0     |  |  |
| Children (2-11 years)                                 | 0     |  |  |
| Adolescents (12-17 years)                             | 0     |  |  |
| Adults (18-64 years)                                  | 0     |  |  |
| From 65-84 years                                      | 0     |  |  |
| 85 years and over                                     | 0     |  |  |
| Age continuous                                        |       |  |  |
| Units: months                                         |       |  |  |
| arithmetic mean                                       |       |  |  |
| standard deviation                                    | -     |  |  |
| Gender categorical                                    |       |  |  |
| Units: Subjects                                       |       |  |  |
| Female                                                | 83    |  |  |
| Male                                                  | 101   |  |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Menitorix/Pediarix Group Month 18                   |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.                                                                                                                                                                                                                                                                                                                                                                            |                                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18 |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study. |                                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Infanrix hexa/Meningitec Group Month 18             |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.                                                                                                                                                                                                                                                                                                                                                                                            |                                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Menitorix/Pediarix Group Month 30                   |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.                                                                                                                                                                                                                                                                                                                                                                            |                                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30 |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study. |                                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Infanrix hexa/Meningitec Group Month 30             |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.                                                                                                                                                                                                                                                                                                                                                                                            |                                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Menitorix/Pediarix Group Month 42                   |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                     |
| Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.                                                                                                                                                                                                                                                                                                                                                                            |                                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42 |

Reporting group description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                       |                                         |
|-----------------------|-----------------------------------------|
| Reporting group title | Infanrix hexa/Meningitec Group Month 42 |
|-----------------------|-----------------------------------------|

Reporting group description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Menitorix/Pediarix Group Month 54 |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                       |                                                     |
|-----------------------|-----------------------------------------------------|
| Reporting group title | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54 |
|-----------------------|-----------------------------------------------------|

Reporting group description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                       |                                         |
|-----------------------|-----------------------------------------|
| Reporting group title | Infanrix hexa/Meningitec Group Month 54 |
|-----------------------|-----------------------------------------|

Reporting group description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Menitorix/Pediarix Group Month 66 |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                       |                                                     |
|-----------------------|-----------------------------------------------------|
| Reporting group title | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66 |
|-----------------------|-----------------------------------------------------|

Reporting group description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramuscularly in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

|                       |                                         |
|-----------------------|-----------------------------------------|
| Reporting group title | Infanrix hexa/Meningitec Group Month 66 |
|-----------------------|-----------------------------------------|

Reporting group description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term

**Primary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:8**

|                 |                                                                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:8 <sup>[1][2]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

18, 30, 42, 54 and 66 months after booster dose (Day 0)

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: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

| End point values            | Menitorix/Pedia<br>rix Group<br>Month 18 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>18 | Menitorix/Pedia<br>rix Group<br>Month 30 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>30 |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                          | Reporting group                                                 |
| Number of subjects analysed | 45                                       | 96                                                              | 48                                       | 101                                                             |
| Units: Subjects             | 44                                       | 93                                                              | 39                                       | 96                                                              |

| End point values            | Infanrix<br>hexa/Meningite<br>c Group Month<br>30 | Menitorix/Pedia<br>rix Group<br>Month 42 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>42 | Infanrix<br>hexa/Meningite<br>c Group Month<br>42 |
|-----------------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|
| Subject group type          | Reporting group                                   | Reporting group                          | Reporting group                                                 | Reporting group                                   |
| Number of subjects analysed | 45                                                | 50                                       | 110                                                             | 52                                                |
| Units: Subjects             | 31                                                | 39                                       | 106                                                             | 33                                                |

| End point values            | Menitorix/Pedia<br>rix Group<br>Month 54 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>54 | Infanrix<br>hexa/Meningite<br>c Group Month<br>54 | Menitorix/Pedia<br>rix Group<br>Month 66 |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                                   | Reporting group                          |
| Number of subjects analysed | 49                                       | 106                                                             | 51                                                | 46                                       |
| Units: Subjects             | 38                                       | 103                                                             | 33                                                | 38                                       |

| <b>End point values</b>     | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66 | Infanrix hexa/Meningite c Group Month 66 |  |  |
|-----------------------------|-----------------------------------------------------|------------------------------------------|--|--|
| Subject group type          | Reporting group                                     | Reporting group                          |  |  |
| Number of subjects analysed | 101                                                 | 46                                       |  |  |
| Units: Subjects             | 95                                                  | 28                                       |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:32

|                 |                                                                                                                                                                                 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:32 <sup>[3][4]</sup> |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

18, 30, 42, 54 and 66 months after booster dose (Day 0)

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: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

| <b>End point values</b>     | Menitorix/Pediarix Group Month 18 | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18 | Menitorix/Pediarix Group Month 30 | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30 |
|-----------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------|-----------------------------------------------------|
| Subject group type          | Reporting group                   | Reporting group                                     | Reporting group                   | Reporting group                                     |
| Number of subjects analysed | 45                                | 96                                                  | 48                                | 101                                                 |
| Units: Subjects             | 40                                | 93                                                  | 36                                | 94                                                  |

| <b>End point values</b> | Infanrix hexa/Meningite c Group Month 30 | Menitorix/Pediarix Group Month 42 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42 | Infanrix hexa/Meningite c Group Month 42 |
|-------------------------|------------------------------------------|-----------------------------------|-----------------------------------------------------|------------------------------------------|
|-------------------------|------------------------------------------|-----------------------------------|-----------------------------------------------------|------------------------------------------|

|                             |                 |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 45              | 50              | 110             | 52              |
| Units: Subjects             | 25              | 38              | 100             | 30              |

|                             |                                          |                                                                 |                                                   |                                          |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|
| <b>End point values</b>     | Menitorix/Pedia<br>rix Group<br>Month 54 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>54 | Infanrix<br>hexa/Meningite<br>c Group Month<br>54 | Menitorix/Pedia<br>rix Group<br>Month 66 |
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                                   | Reporting group                          |
| Number of subjects analysed | 49                                       | 106                                                             | 51                                                | 46                                       |
| Units: Subjects             | 37                                       | 100                                                             | 29                                                | 37                                       |

|                             |                                                                 |                                                   |  |  |
|-----------------------------|-----------------------------------------------------------------|---------------------------------------------------|--|--|
| <b>End point values</b>     | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>66 | Infanrix<br>hexa/Meningite<br>c Group Month<br>66 |  |  |
| Subject group type          | Reporting group                                                 | Reporting group                                   |  |  |
| Number of subjects analysed | 101                                                             | 46                                                |  |  |
| Units: Subjects             | 88                                                              | 25                                                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:128

|                 |                                                                                                                                                                                              |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:128 <sup>[5]</sup> <sup>[6]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

18, 30, 42, 54 and 66 months after booster dose (Day 0)

Notes:

[5] - 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.

[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: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

| End point values            | Menitorix/Pedia<br>rix Group<br>Month 18 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>18 | Menitorix/Pedia<br>rix Group<br>Month 30 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>30 |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                          | Reporting group                                                 |
| Number of subjects analysed | 45                                       | 96                                                              | 48                                       | 101                                                             |
| Units: Subjects             | 27                                       | 82                                                              | 27                                       | 80                                                              |

| End point values            | Infanrix<br>hexa/Meningite<br>c Group Month<br>30 | Menitorix/Pedia<br>rix Group<br>Month 42 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>42 | Infanrix<br>hexa/Meningite<br>c Group Month<br>42 |
|-----------------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|
| Subject group type          | Reporting group                                   | Reporting group                          | Reporting group                                                 | Reporting group                                   |
| Number of subjects analysed | 45                                                | 50                                       | 110                                                             | 52                                                |
| Units: Subjects             | 12                                                | 30                                       | 89                                                              | 13                                                |

| End point values            | Menitorix/Pedia<br>rix Group<br>Month 54 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>54 | Infanrix<br>hexa/Meningite<br>c Group Month<br>54 | Menitorix/Pedia<br>rix Group<br>Month 66 |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                                   | Reporting group                          |
| Number of subjects analysed | 49                                       | 106                                                             | 51                                                | 46                                       |
| Units: Subjects             | 27                                       | 86                                                              | 15                                                | 28                                       |

| End point values            | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>66 | Infanrix<br>hexa/Meningite<br>c Group Month<br>66 |  |  |
|-----------------------------|-----------------------------------------------------------------|---------------------------------------------------|--|--|
| Subject group type          | Reporting group                                                 | Reporting group                                   |  |  |
| Number of subjects analysed | 101                                                             | 46                                                |  |  |
| Units: Subjects             | 69                                                              | 18                                                |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: rSBA-MenC titers

End point title rSBA-MenC titers<sup>[7]</sup><sup>[8]</sup>

End point description:

End point type Primary

End point timeframe:

18, 30, 42, 54 and 66 months after booster dose (Day 0)

Notes:

[7] - 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.

[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: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

| End point values                            | Menitorix/Pedia<br>rix Group<br>Month 18 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>18 | Menitorix/Pedia<br>rix Group<br>Month 30 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>30 |
|---------------------------------------------|------------------------------------------|-----------------------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|
| Subject group type                          | Reporting group                          | Reporting group                                                 | Reporting group                          | Reporting group                                                 |
| Number of subjects analysed                 | 45                                       | 96                                                              | 48                                       | 101                                                             |
| Units: Titers                               |                                          |                                                                 |                                          |                                                                 |
| geometric mean (confidence interval<br>95%) | 221.5 (137.2<br>to 357.7)                | 801.1 (570.3<br>to 1125.3)                                      | 109.1 (61.9 to<br>192.3)                 | 441.7 (309.4<br>to 630.6)                                       |

| End point values                            | Infanrix<br>hexa/Meningite<br>c Group Month<br>30 | Menitorix/Pedia<br>rix Group<br>Month 42 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>42 | Infanrix<br>hexa/Meningite<br>c Group Month<br>42 |
|---------------------------------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|
| Subject group type                          | Reporting group                                   | Reporting group                          | Reporting group                                                 | Reporting group                                   |
| Number of subjects analysed                 | 45                                                | 50                                       | 110                                                             | 52                                                |
| Units: Titers                               |                                                   |                                          |                                                                 |                                                   |
| geometric mean (confidence interval<br>95%) | 40.3 (21.9 to<br>74.1)                            | 98.9 (56.7 to<br>172.5)                  | 409.8 (297.7<br>to 564.2)                                       | 36.1 (20.4 to<br>63.8)                            |

| End point values                            | Menitorix/Pedia<br>rix Group<br>Month 54 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>54 | Infanrix<br>hexa/Meningite<br>c Group Month<br>54 | Menitorix/Pedia<br>rix Group<br>Month 66 |
|---------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|
| Subject group type                          | Reporting group                          | Reporting group                                                 | Reporting group                                   | Reporting group                          |
| Number of subjects analysed                 | 49                                       | 106                                                             | 51                                                | 46                                       |
| Units: Titers                               |                                          |                                                                 |                                                   |                                          |
| geometric mean (confidence interval<br>95%) | 90.4 (52.8 to<br>154.8)                  | 344.6 (255.9<br>to 463.9)                                       | 36.7 (21.1 to<br>64)                              | 121.5 (71 to<br>207.9)                   |

| End point values | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>66 | Infanrix<br>hexa/Meningite<br>c Group Month<br>66 |  |  |
|------------------|-----------------------------------------------------------------|---------------------------------------------------|--|--|
|------------------|-----------------------------------------------------------------|---------------------------------------------------|--|--|



|                                          |                        |                     |  |  |
|------------------------------------------|------------------------|---------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group     |  |  |
| Number of subjects analysed              | 101                    | 46                  |  |  |
| Units: Titers                            |                        |                     |  |  |
| geometric mean (confidence interval 95%) | 227.6 (160.2 to 323.3) | 42.7 (22.3 to 81.8) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 0.15 µg/mL

|                 |                                                                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 0.15 µg/mL <sup>[9]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

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

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

| End point values            | Menitorix/Pedia<br>rix Group<br>Month 18 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>18 | Infanrix<br>hexa/Meningite<br>c Group Month<br>18 | Menitorix/Pedia<br>rix Group<br>Month 30 |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                                   | Reporting group                          |
| Number of subjects analysed | 56                                       | 122                                                             | 3                                                 | 53                                       |
| Units: Subjects             | 56                                       | 121                                                             | 3                                                 | 53                                       |

| End point values            | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>30 | Infanrix<br>hexa/Meningite<br>c Group Month<br>30 | Menitorix/Pedia<br>rix Group<br>Month 42 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>42 |
|-----------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|
| Subject group type          | Reporting group                                                 | Reporting group                                   | Reporting group                          | Reporting group                                                 |
| Number of subjects analysed | 113                                                             | 53                                                | 50                                       | 110                                                             |
| Units: Subjects             | 112                                                             | 53                                                | 50                                       | 109                                                             |

| End point values | Infanrix<br>hexa/Meningite<br>c Group Month<br>42 | Menitorix/Pedia<br>rix Group<br>Month 54 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>54 | Infanrix<br>hexa/Meningite<br>c Group Month<br>54 |
|------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|
|------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|

| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Number of subjects analysed | 51              | 49              | 106             | 52              |
| Units: Subjects             | 51              | 49              | 105             | 52              |

| End point values            | Menitorix/Pedia<br>rix Group<br>Month 66 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>66 | Infanrix<br>hexa/Meningite<br>c Group Month<br>66 |  |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|--|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                                   |  |
| Number of subjects analysed | 47                                       | 101                                                             | 47                                                |  |
| Units: Subjects             | 47                                       | 101                                                             | 46                                                |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 1.0 µg/mL

|                 |                                                                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 1.0 µg/mL <sup>[10]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

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

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

| End point values            | Menitorix/Pedia<br>rix Group<br>Month 18 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>18 | Infanrix<br>hexa/Meningite<br>c Group Month<br>18 | Menitorix/Pedia<br>rix Group<br>Month 30 |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                                   | Reporting group                          |
| Number of subjects analysed | 56                                       | 122                                                             | 3                                                 | 53                                       |
| Units: Subjects             | 44                                       | 112                                                             | 3                                                 | 36                                       |

| End point values            | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>30 | Infanrix<br>hexa/Meningite<br>c Group Month<br>30 | Menitorix/Pedia<br>rix Group<br>Month 42 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>42 |
|-----------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|
| Subject group type          | Reporting group                                                 | Reporting group                                   | Reporting group                          | Reporting group                                                 |
| Number of subjects analysed | 113                                                             | 53                                                | 50                                       | 110                                                             |

|                 |    |    |    |    |
|-----------------|----|----|----|----|
| Units: Subjects | 98 | 40 | 33 | 91 |
|-----------------|----|----|----|----|

| End point values            | Infanrix hexa/Meningitec Group Month 42 | Menitorix/Pediarix Group Month 54 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54 | Infanrix hexa/Meningitec Group Month 54 |
|-----------------------------|-----------------------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|
| Subject group type          | Reporting group                         | Reporting group                   | Reporting group                                     | Reporting group                         |
| Number of subjects analysed | 51                                      | 49                                | 106                                                 | 52                                      |
| Units: Subjects             | 34                                      | 27                                | 86                                                  | 35                                      |

| End point values            | Menitorix/Pediarix Group Month 66 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66 | Infanrix hexa/Meningitec Group Month 66 |  |
|-----------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|--|
| Subject group type          | Reporting group                   | Reporting group                                     | Reporting group                         |  |
| Number of subjects analysed | 47                                | 101                                                 | 47                                      |  |
| Units: Subjects             | 26                                | 84                                                  | 26                                      |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Anti-PRP concentrations

End point title Anti-PRP concentrations<sup>[11]</sup>

End point description:

End point type Primary

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

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

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

| End point values                         | Menitorix/Pediarix Group Month 18 | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18 | Infanrix hexa/Meningitec Group Month 18 | Menitorix/Pediarix Group Month 30 |
|------------------------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|-----------------------------------|
| Subject group type                       | Reporting group                   | Reporting group                                     | Reporting group                         | Reporting group                   |
| Number of subjects analysed              | 56                                | 122                                                 | 3                                       | 53                                |
| Units: µg/mL                             |                                   |                                                     |                                         |                                   |
| geometric mean (confidence interval 95%) | 2.921 (2.15 to 3.968)             | 5.45 (4.39 to 6.766)                                | 2.547 (0.39 to 16.651)                  | 1.914 (1.383 to 2.648)            |

| End point values                         | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30 | Infanrix hexa/Meningite c Group Month 30 | Menitorix/Pedia rix Group Month 42 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42 |
|------------------------------------------|-----------------------------------------------------|------------------------------------------|------------------------------------|-----------------------------------------------------|
| Subject group type                       | Reporting group                                     | Reporting group                          | Reporting group                    | Reporting group                                     |
| Number of subjects analysed              | 113                                                 | 53                                       | 50                                 | 110                                                 |
| Units: µg/mL                             |                                                     |                                          |                                    |                                                     |
| geometric mean (confidence interval 95%) | 3.524 (2.813 to 4.415)                              | 2.224 (1.578 to 3.133)                   | 1.735 (1.243 to 2.423)             | 2.986 (2.395 to 3.722)                              |

| End point values                         | Infanrix hexa/Meningite c Group Month 42 | Menitorix/Pedia rix Group Month 54 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54 | Infanrix hexa/Meningite c Group Month 54 |
|------------------------------------------|------------------------------------------|------------------------------------|-----------------------------------------------------|------------------------------------------|
| Subject group type                       | Reporting group                          | Reporting group                    | Reporting group                                     | Reporting group                          |
| Number of subjects analysed              | 51                                       | 49                                 | 106                                                 | 52                                       |
| Units: µg/mL                             |                                          |                                    |                                                     |                                          |
| geometric mean (confidence interval 95%) | 2.005 (1.365 to 2.946)                   | 1.552 (1.154 to 2.087)             | 2.688 (2.149 to 3.361)                              | 1.799 (1.267 to 2.555)                   |

| End point values                         | Menitorix/Pedia rix Group Month 66 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66 | Infanrix hexa/Meningite c Group Month 66 |  |
|------------------------------------------|------------------------------------|-----------------------------------------------------|------------------------------------------|--|
| Subject group type                       | Reporting group                    | Reporting group                                     | Reporting group                          |  |
| Number of subjects analysed              | 47                                 | 101                                                 | 47                                       |  |
| Units: µg/mL                             |                                    |                                                     |                                          |  |
| geometric mean (confidence interval 95%) | 1.602 (1.107 to 2.32)              | 2.625 (2.113 to 3.261)                              | 1.763 (1.17 to 2.657)                    |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of subjects with anti-polysaccharide C (Anti-PSC) concentrations equal to or above cut-off value of 0.3 µg/mL

|                        |                                                                                                                                          |
|------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | Number of subjects with anti-polysaccharide C (Anti-PSC) concentrations equal to or above cut-off value of 0.3 µg/mL <sup>[12][13]</sup> |
| End point description: |                                                                                                                                          |
| End point type         | Primary                                                                                                                                  |

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

[12] - 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.

[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: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

| <b>End point values</b>     | Menitorix/Pedia<br>rix Group<br>Month 18 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>18 | Menitorix/Pedia<br>rix Group<br>Month 30 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>30 |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                          | Reporting group                                                 |
| Number of subjects analysed | 56                                       | 122                                                             | 52                                       | 108                                                             |
| Units: Subjects             | 38                                       | 100                                                             | 19                                       | 58                                                              |

| <b>End point values</b>     | Infanrix<br>hexa/Meningite<br>c Group Month<br>30 | Menitorix/Pedia<br>rix Group<br>Month 42 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>42 | Infanrix<br>hexa/Meningite<br>c Group Month<br>42 |
|-----------------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|
| Subject group type          | Reporting group                                   | Reporting group                          | Reporting group                                                 | Reporting group                                   |
| Number of subjects analysed | 53                                                | 49                                       | 107                                                             | 52                                                |
| Units: Subjects             | 19                                                | 17                                       | 52                                                              | 17                                                |

| <b>End point values</b>     | Menitorix/Pedia<br>rix Group<br>Month 54 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>54 | Infanrix<br>hexa/Meningite<br>c Group Month<br>54 | Menitorix/Pedia<br>rix Group<br>Month 66 |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                                   | Reporting group                          |
| Number of subjects analysed | 46                                       | 105                                                             | 52                                                | 45                                       |
| Units: Subjects             | 14                                       | 52                                                              | 17                                                | 12                                       |

| <b>End point values</b>     | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>66 | Infanrix<br>hexa/Meningite<br>c Group Month<br>66 |  |  |
|-----------------------------|-----------------------------------------------------------------|---------------------------------------------------|--|--|
| Subject group type          | Reporting group                                                 | Reporting group                                   |  |  |
| Number of subjects analysed | 99                                                              | 45                                                |  |  |
| Units: Subjects             | 34                                                              | 11                                                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with anti-polysaccharide C (Anti-PSC) concentrations equal to or above cut-off value of 2.0 µg/mL

|                 |                                                                                                                                          |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with anti-polysaccharide C (Anti-PSC) concentrations equal to or above cut-off value of 2.0 µg/mL <sup>[14][15]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

[14] - 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.

[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: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

| End point values            | Menitorix/Pedia<br>rix Group<br>Month 18 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>18 | Menitorix/Pedia<br>rix Group<br>Month 30 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>30 |
|-----------------------------|------------------------------------------|-----------------------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|
| Subject group type          | Reporting group                          | Reporting group                                                 | Reporting group                          | Reporting group                                                 |
| Number of subjects analysed | 56                                       | 122                                                             | 52                                       | 108                                                             |
| Units: Subjects             | 1                                        | 31                                                              | 1                                        | 18                                                              |

| End point values            | Infanrix<br>hexa/Meningite<br>c Group Month<br>30 | Menitorix/Pedia<br>rix Group<br>Month 42 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>42 | Infanrix<br>hexa/Meningite<br>c Group Month<br>42 |
|-----------------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|
| Subject group type          | Reporting group                                   | Reporting group                          | Reporting group                                                 | Reporting group                                   |
| Number of subjects analysed | 53                                                | 49                                       | 107                                                             | 52                                                |
| Units: Subjects             | 3                                                 | 0                                        | 14                                                              | 2                                                 |

| End point values            | Menitorix/Pediarix Group Month 54 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54 | Infanrix hexa/Meningitec Group Month 54 | Menitorix/Pediarix Group Month 66 |
|-----------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|-----------------------------------|
| Subject group type          | Reporting group                   | Reporting group                                     | Reporting group                         | Reporting group                   |
| Number of subjects analysed | 46                                | 105                                                 | 52                                      | 45                                |
| Units: Subjects             | 1                                 | 10                                                  | 1                                       | 0                                 |

| End point values            | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66 | Infanrix hexa/Meningitec Group Month 66 |  |  |
|-----------------------------|-----------------------------------------------------|-----------------------------------------|--|--|
| Subject group type          | Reporting group                                     | Reporting group                         |  |  |
| Number of subjects analysed | 99                                                  | 45                                      |  |  |
| Units: Subjects             | 8                                                   | 0                                       |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of subjects with serious adverse events

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Number of subjects with serious adverse events <sup>[16]</sup> |
|-----------------|----------------------------------------------------------------|

End point description:

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

End point timeframe:

From last study contact of the booster study (NCT00323050) to Month 66 after booster dose (Day 0)

Notes:

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

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

| End point values            | Menitorix/Pediarix Group Month 18 | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18 | Infanrix hexa/Meningitec Group Month 18 | Menitorix/Pediarix Group Month 30 |
|-----------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|-----------------------------------|
| Subject group type          | Reporting group                   | Reporting group                                     | Reporting group                         | Reporting group                   |
| Number of subjects analysed | 58                                | 123                                                 | 3                                       | 54                                |
| Units: Subjects             | 0                                 | 0                                                   | 0                                       | 0                                 |

| End point values | Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30 | Infanrix hexa/Meningitec Group Month 30 | Menitorix/Pediarix Group Month 42 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42 |
|------------------|-----------------------------------------------------|-----------------------------------------|-----------------------------------|-----------------------------------------------------|
|------------------|-----------------------------------------------------|-----------------------------------------|-----------------------------------|-----------------------------------------------------|

| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Number of subjects analysed | 119             | 57              | 51              | 113             |
| Units: Subjects             | 0               | 0               | 0               | 0               |

| End point values            | Infanrix hexa/Meningitec Group Month 42 | Menitorix/Pediarix Group Month 54 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54 | Infanrix hexa/Meningitec Group Month 54 |
|-----------------------------|-----------------------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|
| Subject group type          | Reporting group                         | Reporting group                   | Reporting group                                     | Reporting group                         |
| Number of subjects analysed | 56                                      | 50                                | 108                                                 | 56                                      |
| Units: Subjects             | 0                                       | 0                                 | 0                                                   | 0                                       |

| End point values            | Menitorix/Pediarix Group Month 66 | Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66 | Infanrix hexa/Meningitec Group Month 66 |  |
|-----------------------------|-----------------------------------|-----------------------------------------------------|-----------------------------------------|--|
| Subject group type          | Reporting group                   | Reporting group                                     | Reporting group                         |  |
| Number of subjects analysed | 48                                | 104                                                 | 53                                      |  |
| Units: Subjects             | 0                                 | 0                                                   | 0                                       |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Anti-PSC concentrations

|                 |                                              |
|-----------------|----------------------------------------------|
| End point title | Anti-PSC concentrations <sup>[17]</sup> [18] |
|-----------------|----------------------------------------------|

End point description:

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

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

[17] - 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.

[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: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.



| End point values                            | Menitorix/Pedia<br>rix Group<br>Month 18 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>18 | Menitorix/Pedia<br>rix Group<br>Month 30 | Infanrix<br>hexa/Infanrix<br>IPV-Hib co-ad<br>Group Month<br>30 |
|---------------------------------------------|------------------------------------------|-----------------------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|
| Subject group type                          | Reporting group                          | Reporting group                                                 | Reporting group                          | Reporting group                                                 |
| Number of subjects analysed                 | 56                                       | 122                                                             | 52                                       | 108                                                             |
| Units: µg/mL                                |                                          |                                                                 |                                          |                                                                 |
| geometric mean (confidence interval<br>95%) | 0.5 (0.39 to<br>0.64)                    | 1.01 (0.8 to<br>1.29)                                           | 0.26 (0.21 to<br>0.33)                   | 0.47 (0.37 to<br>0.61)                                          |

| End point values                            | Infanrix<br>hexa/Meningite<br>c Group Month<br>30 | Menitorix/Pedia<br>rix Group<br>Month 42 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>42 | Infanrix<br>hexa/Meningite<br>c Group Month<br>42 |
|---------------------------------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|
| Subject group type                          | Reporting group                                   | Reporting group                          | Reporting group                                                 | Reporting group                                   |
| Number of subjects analysed                 | 53                                                | 49                                       | 107                                                             | 52                                                |
| Units: µg/mL                                |                                                   |                                          |                                                                 |                                                   |
| geometric mean (confidence interval<br>95%) | 0.3 (0.23 to<br>0.39)                             | 0.25 (0.2 to<br>0.31)                    | 0.4 (0.32 to<br>0.51)                                           | 0.28 (0.21 to<br>0.37)                            |

| End point values                            | Menitorix/Pedia<br>rix Group<br>Month 54 | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>54 | Infanrix<br>hexa/Meningite<br>c Group Month<br>54 | Menitorix/Pedia<br>rix Group<br>Month 66 |
|---------------------------------------------|------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|------------------------------------------|
| Subject group type                          | Reporting group                          | Reporting group                                                 | Reporting group                                   | Reporting group                          |
| Number of subjects analysed                 | 46                                       | 105                                                             | 52                                                | 45                                       |
| Units: µg/mL                                |                                          |                                                                 |                                                   |                                          |
| geometric mean (confidence interval<br>95%) | 0.24 (0.19 to<br>0.3)                    | 0.36 (0.29 to<br>0.45)                                          | 0.26 (0.2 to<br>0.32)                             | 0.22 (0.18 to<br>0.27)                   |

| End point values                            | Infanrix<br>hexa/Infanrix<br>IPV/Hib co-ad<br>Group Month<br>66 | Infanrix<br>hexa/Meningite<br>c Group Month<br>66 |  |  |
|---------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------|--|--|
| Subject group type                          | Reporting group                                                 | Reporting group                                   |  |  |
| Number of subjects analysed                 | 99                                                              | 45                                                |  |  |
| Units: µg/mL                                |                                                                 |                                                   |  |  |
| geometric mean (confidence interval<br>95%) | 0.29 (0.23 to<br>0.36)                                          | 0.22 (0.18 to<br>0.28)                            |  |  |

## Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

From last study contact of the booster study (NCT00323050) to Month 66 after booster dose (Day 0)

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 10.0 |
|--------------------|------|

### Reporting groups

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Menitorix/Pediarix Group |
|-----------------------|--------------------------|

Reporting group description: -

|                       |                                                                |
|-----------------------|----------------------------------------------------------------|
| Reporting group title | Infanrix hexa (or IPV/Hib)/NeisVac-C/Engerix-B/Menitorix Group |
|-----------------------|----------------------------------------------------------------|

Reporting group description: -

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Infanrix hexa/Meningitec Group |
|-----------------------|--------------------------------|

Reporting group description: -

| <b>Serious adverse events</b>                     | Menitorix/Pediarix Group | Infanrix hexa (or IPV/Hib)/NeisVac-C/Engerix-B/Menitorix Group | Infanrix hexa/Meningitec Group |
|---------------------------------------------------|--------------------------|----------------------------------------------------------------|--------------------------------|
| Total subjects affected by serious adverse events |                          |                                                                |                                |
| subjects affected / exposed                       | 0 / 58 (0.00%)           | 0 / 123 (0.00%)                                                | 0 / 3 (0.00%)                  |
| number of deaths (all causes)                     | 0                        | 0                                                              | 0                              |
| number of deaths resulting from adverse events    |                          |                                                                |                                |

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

| <b>Non-serious adverse events</b>                     | Menitorix/Pediarix Group | Infanrix hexa (or IPV/Hib)/NeisVac-C/Engerix-B/Menitorix Group | Infanrix hexa/Meningitec Group |
|-------------------------------------------------------|--------------------------|----------------------------------------------------------------|--------------------------------|
| Total subjects affected by non-serious adverse events |                          |                                                                |                                |
| subjects affected / exposed                           | 0 / 58 (0.00%)           | 0 / 123 (0.00%)                                                | 0 / 3 (0.00%)                  |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events were collected in this study.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported