



## Clinical trial results:

A phase III, open, randomized, controlled, multi-centre study to demonstrate the non-inferiority of the meningococcal serogroup C and the Haemophilus influenzae type b immune response of GlaxoSmithKline (GSK) Biologicals' conjugate Hib-MenC vaccine co-administered with GSK Biologicals' measles-mumps-rubella vaccine, Priorix™, versus MenC-CRM197 conjugate vaccine co-administered with GSK Biologicals' Hib vaccine, Hiberix™, and Priorix™ in 12- to 18-month-old toddlers primed in infancy with a Hib vaccine but not with a meningococcal serogroup C vaccine; and to evaluate the long-term antibody persistence up to 5 years after the administration of the Hib-MenC vaccine.

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2011-005032-26  |
| Trial protocol           | Outside EU/EEA  |
| Global end of trial date | 06 October 2012 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1            |
| This version publication date  | 03 March 2016 |
| First version publication date | 29 July 2015  |

### Trial information

#### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | 106445, |
|-----------------------|---------|

#### Additional study identifiers

|                                    |                                                                                                                   |
|------------------------------------|-------------------------------------------------------------------------------------------------------------------|
| ISRCTN number                      | -                                                                                                                 |
| ClinicalTrials.gov id (NCT number) | NCT00326118                                                                                                       |
| WHO universal trial number (UTN)   | -                                                                                                                 |
| Other trial identifiers            | 106449: eTrack number, 106446: eTrack number, 106450: eTrack number, 106452: eTrack number, 106454: eTrack number |

Notes:

### Sponsors

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

Notes:

### Paediatric regulatory details

|                                       |    |
|---------------------------------------|----|
| Is trial part of an agreed paediatric | No |
|---------------------------------------|----|

|                                                                      |     |
|----------------------------------------------------------------------|-----|
| investigation plan (PIP)                                             |     |
| 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                       | 08 February 2013 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 06 October 2012  |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 06 October 2012  |
| Was the trial ended prematurely?                     | No               |
| Notes:                                               |                  |

## General information about the trial

Main objective of the trial:

One month after vaccination, to demonstrate the non-inferiority of the meningococcal serogroup C and Hib responses induced by GSK Biologicals' Hib-MenC conjugate vaccine, compared to separately administered MenC-CRM197 and Hiberix™ (with Priorix™ co-administered in each group), when given as a single dose to toddlers 12-18 months of age primed with routine infant vaccines including Hib, but no meningococcal serogroup C vaccine, in terms of percentage of subjects with SBA-MenC titre  $\geq 1:8$  and percentage of subjects with Anti-PRP concentration  $\geq 0.15 \mu\text{g/mL}$ .

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 17 June 2011     |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 5 Years          |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                |
|--------------------------------------|----------------|
| Country: Number of subjects enrolled | Australia: 433 |
| Worldwide total number of subjects   | 433            |
| EEA total number of subjects         | 0              |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 433 |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 0   |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

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

### Period 1

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

### Arms

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

Arm description:

Subjects received a single dose of Menitorix™ vaccine co-administered with Priorix™ vaccine. Menitorix vaccine was administered intramuscularly in the left deltoid region and the Priorix vaccine was administered subcutaneously in the right upper arm.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Experimental      |
| Investigational medicinal product name | Menitorix™        |
| Investigational medicinal product code |                   |
| Other name                             | Hib-MenC          |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

One intramuscular dose at 12-18 months of age, administered in the left deltoid region.

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Priorix™         |
| Investigational medicinal product code |                  |
| Other name                             | MMR              |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

One subcutaneous dose at 12-18 months of age, administered in the right upper arm.

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Meningitec + Hiberix Group |
|------------------|----------------------------|

Arm description:

Subjects received a single dose of Meningitec™ vaccine co-administered with Hiberix™ and Priorix™ vaccines. The Meningitec vaccine was administered intramuscularly in the left deltoid region, the Hiberix vaccine was administered intramuscularly in the left thigh region and the Priorix vaccine was administered subcutaneously in the right upper arm.

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

Dosage and administration details:

One intramuscular dose at 12-18 months of age, administered in the left deltoid region.

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

Dosage and administration details:

One intramuscular dose at 12-18 months of age, administered in the left thigh region.

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Priorix™         |
| Investigational medicinal product code |                  |
| Other name                             | MMR              |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

One subcutaneous dose at 12-18 months of age, administered in the right upper arm.

| <b>Number of subjects in period 1</b> | Menitorix Group | Meningitec + Hiberix Group |
|---------------------------------------|-----------------|----------------------------|
| Started                               | 324             | 109                        |
| Completed                             | 320             | 108                        |
| Not completed                         | 4               | 1                          |
| Consent withdrawn by subject          | 3               | 1                          |
| Unspecified                           | 1               | -                          |

## Baseline characteristics

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Menitorix Group |
|-----------------------|-----------------|

Reporting group description:

Subjects received a single dose of Menitorix™ vaccine co-administered with Priorix™ vaccine. Menitorix vaccine was administered intramuscularly in the left deltoid region and the Priorix vaccine was administered subcutaneously in the right upper arm.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Meningitec + Hiberix Group |
|-----------------------|----------------------------|

Reporting group description:

Subjects received a single dose of Meningitec™ vaccine co-administered with Hiberix™ and Priorix™ vaccines. The Meningitec vaccine was administered intramuscularly in the left deltoid region, the Hiberix vaccine was administered intramuscularly in the left thigh region and the Priorix vaccine was administered subcutaneously in the right upper arm.

| Reporting group values                                | Menitorix Group | Meningitec + Hiberix Group | Total |
|-------------------------------------------------------|-----------------|----------------------------|-------|
| Number of subjects                                    | 324             | 109                        | 433   |
| Age categorical<br>Units: Subjects                    |                 |                            |       |
| In utero                                              |                 |                            | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) |                 |                            | 0     |
| Newborns (0-27 days)                                  |                 |                            | 0     |
| Infants and toddlers (28 days-23 months)              |                 |                            | 0     |
| Children (2-11 years)                                 |                 |                            | 0     |
| Adolescents (12-17 years)                             |                 |                            | 0     |
| Adults (18-64 years)                                  |                 |                            | 0     |
| From 65-84 years                                      |                 |                            | 0     |
| 85 years and over                                     |                 |                            | 0     |
| Age continuous<br>Units: months                       |                 |                            |       |
| arithmetic mean                                       | 12.5            | 12.5                       |       |
| standard deviation                                    | ± 0.94          | ± 0.75                     | -     |
| Gender categorical<br>Units: Subjects                 |                 |                            |       |
| Female                                                | 150             | 42                         | 192   |
| Male                                                  | 174             | 67                         | 241   |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                               |                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                         | Menitorix Group            |
| Reporting group description:<br>Subjects received a single dose of Menitorix™ vaccine co-administered with Priorix™ vaccine. Menitorix vaccine was administered intramuscularly in the left deltoid region and the Priorix vaccine was administered subcutaneously in the right upper arm.                                                                                                    |                            |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                         | Meningitec + Hiberix Group |
| Reporting group description:<br>Subjects received a single dose of Meningitec™ vaccine co-administered with Hiberix™ and Priorix™ vaccines. The Meningitec vaccine was administered intramuscularly in the left deltoid region, the Hiberix vaccine was administered intramuscularly in the left thigh region and the Priorix vaccine was administered subcutaneously in the right upper arm. |                            |

### Primary: Number of subjects with meningococcal polysaccharide C serum bactericidal assay, using baby rabbit complement (rSBA-MenC) titres $\geq 1:8$

|                                                      |                                                                                                                                             |
|------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                      | Number of subjects with meningococcal polysaccharide C serum bactericidal assay, using baby rabbit complement (rSBA-MenC) titres $\geq 1:8$ |
| End point description:                               |                                                                                                                                             |
| End point type                                       | Primary                                                                                                                                     |
| End point timeframe:<br>One month after vaccination. |                                                                                                                                             |

| End point values            | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 281             | 98                         |  |  |
| Units: Subjects             |                 |                            |  |  |
| rSBA-MenC, M1(N=281; 98)    | 280             | 98                         |  |  |

### Statistical analyses

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| Statistical analysis title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Difference in % subjects with rSBA-MenC $\geq 1:8$ |
| Statistical analysis description:<br>To demonstrate the non-inferiority of the meningococcal serogroup C and Hib responses induced by Hib-MenC vaccine, compared to separately administered MCC and Hib vaccines (with MMR co-administered in each group), when given as a single dose to toddlers 12-18 months of age primed with routine infant vaccines including Hib, but no MenC vaccine, in terms of percentage of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer $\geq 1:8$ . |                                                    |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Menitorix Group v Meningitec + Hiberix Group       |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 379                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[1]</sup> |
| Parameter estimate                      | Difference in percentage       |
| Point estimate                          | -0.36                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -1.99                          |
| upper limit                             | 3.43                           |

Notes:

[1] - Criterion for achieving the co-primary objectives: One month after vaccination, the lower limit of the standardized asymptotic 95% confidence interval on the difference between the study vaccine group and (minus) the control group was above -10%.

### **Primary: Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentrations $\geq 0.15$ $\mu\text{g/mL}$**

|                 |                                                                                                                           |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentrations $\geq 0.15$ $\mu\text{g/mL}$ |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

One month after vaccination.

| <b>End point values</b>                               | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-------------------------------------------------------|-----------------|----------------------------|--|--|
| Subject group type                                    | Reporting group | Reporting group            |  |  |
| Number of subjects analysed                           | 292             | 100                        |  |  |
| Units: Subjects                                       |                 |                            |  |  |
| Anti-PRP, M1, $\geq 0.15 \mu\text{g/mL}$ (N=292; 100) | 292             | 100                        |  |  |

### **Statistical analyses**

|                                   |                                                                     |
|-----------------------------------|---------------------------------------------------------------------|
| <b>Statistical analysis title</b> | Difference in % subjects with anti-PRP $\geq 0.15$ $\mu\text{g/mL}$ |
|-----------------------------------|---------------------------------------------------------------------|

Statistical analysis description:

To demonstrate the non-inferiority of the meningococcal serogroup C and Hib responses induced by Hib-MenC vaccine, compared to separately administered MCC and Hib vaccines (with MMR co-administered in each group), when given as a single dose to toddlers 12-18 months of age primed with routine infant vaccines including Hib, but no MenC vaccine, in terms of percentage of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration  $\geq 0.15$   $\mu\text{g/mL}$ .

|                                         |                                              |
|-----------------------------------------|----------------------------------------------|
| Comparison groups                       | Menitorix Group v Meningitec + Hiberix Group |
| Number of subjects included in analysis | 392                                          |
| Analysis specification                  | Pre-specified                                |
| Analysis type                           | non-inferiority <sup>[2]</sup>               |
| Parameter estimate                      | Difference in percentage                     |
| Point estimate                          | 0                                            |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.3    |
| upper limit         | 3.71    |

Notes:

[2] - Criterion for achieving the co-primary objectives: One month after vaccination, the lower limit of the standardized asymptotic 95% confidence interval on the difference between the study vaccine group and (minus) the control group was above -10%.

### Secondary: Number of subjects with rSBA-MenC titers $\geq$ 1:8

|                 |                                                     |
|-----------------|-----------------------------------------------------|
| End point title | Number of subjects with rSBA-MenC titers $\geq$ 1:8 |
|-----------------|-----------------------------------------------------|

End point description:

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

End point timeframe:

Prior to vaccination

| End point values            | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 255             | 83                         |  |  |
| Units: Subjects             |                 |                            |  |  |
| rSBA-MenC, PRE, (N=255; 83) | 37              | 7                          |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-PRP antibody concentrations $\geq$ 0.15 $\mu\text{g/mL}$

|                 |                                                                                       |
|-----------------|---------------------------------------------------------------------------------------|
| End point title | Number of subjects with anti-PRP antibody concentrations $\geq$ 0.15 $\mu\text{g/mL}$ |
|-----------------|---------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Prior to vaccination

| End point values            | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 285             | 98                         |  |  |
| Units: Subjects             |                 |                            |  |  |
| Anti-PRP, PRE, (N=285; 98)  | 219             | 82                         |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with rSBA-MenC titers $\geq$ 1:128

|                 |                                                       |
|-----------------|-------------------------------------------------------|
| End point title | Number of subjects with rSBA-MenC titers $\geq$ 1:128 |
|-----------------|-------------------------------------------------------|

End point description:

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

End point timeframe:

Prior to vaccination and one month after vaccination

| End point values            | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 281             | 98                         |  |  |
| Units: Subjects             |                 |                            |  |  |
| rSBA-MenC, PRE, (N=255; 83) | 15              | 3                          |  |  |
| rSBA-MenC, M1, (N=281; 98)  | 247             | 89                         |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: rSBA-MenC antibody titers

|                 |                           |
|-----------------|---------------------------|
| End point title | rSBA-MenC antibody titers |
|-----------------|---------------------------|

End point description:

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

End point timeframe:

Prior to vaccination and one month after vaccination

| End point values                         | Menitorix Group        | Meningitec + Hiberix Group |  |  |
|------------------------------------------|------------------------|----------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group            |  |  |
| Number of subjects analysed              | 281                    | 98                         |  |  |
| Units: Titers                            |                        |                            |  |  |
| geometric mean (confidence interval 95%) |                        |                            |  |  |
| rSBA-MenC, PRE, (N=255; 83)              | 6.3 (5.5 to 7.3)       | 5.5 (4.3 to 7.2)           |  |  |
| rSBA-MenC, M1, (N=281; 98)               | 482.8 (420.7 to 554.2) | 621 (480.3 to 802.9)       |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-PRP antibody concentrations $\geq 1.0$ $\mu\text{g/mL}$

|                 |                                                                                      |
|-----------------|--------------------------------------------------------------------------------------|
| End point title | Number of subjects with anti-PRP antibody concentrations $\geq 1.0$ $\mu\text{g/mL}$ |
|-----------------|--------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Prior to vaccination and one month after vaccination

| End point values            | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 292             | 100                        |  |  |
| Units: Subjects             |                 |                            |  |  |
| Anti-PRP, PRE, (N=285; 98)  | 77              | 22                         |  |  |
| Anti-PRP, M1, (N=292; 100)  | 286             | 100                        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PRP antibody concentrations

|                 |                                  |
|-----------------|----------------------------------|
| End point title | Anti-PRP antibody concentrations |
|-----------------|----------------------------------|

End point description:

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

End point timeframe:

Prior to vaccination and one month after vaccination

| <b>End point values</b>                  | Menitorix Group           | Meningitec + Hiberix Group |  |  |
|------------------------------------------|---------------------------|----------------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group            |  |  |
| Number of subjects analysed              | 292                       | 100                        |  |  |
| Units: µg/mL                             |                           |                            |  |  |
| geometric mean (confidence interval 95%) |                           |                            |  |  |
| Anti-PRP, PRE, (N=285; 98)               | 0.438 (0.374 to 0.512)    | 0.472 (0.364 to 0.611)     |  |  |
| Anti-PRP, M1, (N=292; 100)               | 46.652 (38.929 to 55.907) | 73.976 (57.624 to 94.968)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-polysaccharide C (anti-PSC) antibody concentrations $\geq 0.30$ µg/mL and $\geq 2.0$ µg/mL

|                                                      |                                                                                                                         |
|------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title                                      | Number of subjects with anti-polysaccharide C (anti-PSC) antibody concentrations $\geq 0.30$ µg/mL and $\geq 2.0$ µg/mL |
| End point description:                               |                                                                                                                         |
| End point type                                       | Secondary                                                                                                               |
| End point timeframe:                                 |                                                                                                                         |
| Prior to vaccination and one month after vaccination |                                                                                                                         |

| <b>End point values</b>                     | Menitorix Group | Meningitec + Hiberix Group |  |  |
|---------------------------------------------|-----------------|----------------------------|--|--|
| Subject group type                          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed                 | 290             | 100                        |  |  |
| Units: Subjects                             |                 |                            |  |  |
| Anti-PSC, PRE, $\geq 0.3$ µg/mL (N=283; 96) | 2               | 1                          |  |  |
| Anti-PSC, M1, $\geq 0.3$ µg/mL (N=290; 100) | 290             | 100                        |  |  |
| Anti-PSC, PRE, $\geq 2.0$ µg/mL (N=283; 96) | 0               | 0                          |  |  |
| Anti-PSC, M1, $\geq 2.0$ µg/mL (N=290; 100) | 289             | 96                         |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-polysaccharide C (anti-PSC) antibody concentrations

End point title Anti-polysaccharide C (anti-PSC) antibody concentrations

End point description:

End point type Secondary

End point timeframe:

Prior to vaccination and one month after vaccination

| End point values                         | Menitorix Group       | Meningitec + Hiberix Group |  |  |
|------------------------------------------|-----------------------|----------------------------|--|--|
| Subject group type                       | Reporting group       | Reporting group            |  |  |
| Number of subjects analysed              | 290                   | 100                        |  |  |
| Units: µg/mL                             |                       |                            |  |  |
| geometric mean (confidence interval 95%) |                       |                            |  |  |
| Anti-PSC, PRE, (N=283; 96)               | 0.15 (0.15 to 0.15)   | 0.15 (0.15 to 0.16)        |  |  |
| Anti-PSC, M1, (N=290; 100)               | 18.69 (17.1 to 20.42) | 7.95 (6.95 to 9.08)        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with rSBA-MenC titers $\geq 1:8$ and $\geq 1:128$

End point title Number of subjects with rSBA-MenC titers  $\geq 1:8$  and  $\geq 1:128$

End point description:

The cut-off values assessed were greater than or equal to ( $\geq$ ) 1:8 and  $\geq 1:128$  and starting with year 4 Public Health England (PHE) continued with the laboratory assay.

End point type Secondary

End point timeframe:

At 1, 2, 3, 4, and 5 years after vaccination

| End point values                   | Menitorix Group | Meningitec + Hiberix Group |  |  |
|------------------------------------|-----------------|----------------------------|--|--|
| Subject group type                 | Reporting group | Reporting group            |  |  |
| Number of subjects analysed        | 249             | 89                         |  |  |
| Units: Subjects                    |                 |                            |  |  |
| rSBA, M12, $\geq 1:8$ (N=249;89)   | 216             | 68                         |  |  |
| rSBA, M12, $\geq 1:128$ (N=249;89) | 117             | 37                         |  |  |
| rSBA, M24, $\geq 1:8$ (N=235;86)   | 164             | 52                         |  |  |
| rSBA, M24, $\geq 1:128$ (N=235;86) | 76              | 26                         |  |  |
| rSBA, M36, $\geq 1:8$ (N=226;77)   | 145             | 41                         |  |  |

|                                    |    |    |  |  |
|------------------------------------|----|----|--|--|
| rSBA, M36, $\geq 1:128$ (N=226;77) | 58 | 22 |  |  |
| rSBA, M48, $\geq 1:8$ (N=208;73)   | 26 | 9  |  |  |
| rSBA, M48, $\geq 1:128$ (N=208;73) | 7  | 4  |  |  |
| rSBA, M60, $\geq 1:8$ (N=195;68)   | 37 | 12 |  |  |
| rSBA, M60, $\geq 1:128$ (N=195;68) | 17 | 7  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: rSBA-MenC antibody titers

|                 |                           |
|-----------------|---------------------------|
| End point title | rSBA-MenC antibody titers |
|-----------------|---------------------------|

End point description:

The cut-off values assessed were greater than or equal to ( $\geq$ ) 1:8 and  $\geq 1:128$ . The analyses were performed at the GSK Biologicals' laboratory, and starting with year 4 GSK Biologicals laboratory was replaced with Public Health England (PHE) laboratory.

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

End point timeframe:

At 1, 2, 3, 4, and 5 years after vaccination

| End point values                         | Menitorix Group      | Meningitec + Hiberix Group |  |  |
|------------------------------------------|----------------------|----------------------------|--|--|
| Subject group type                       | Reporting group      | Reporting group            |  |  |
| Number of subjects analysed              | 249                  | 89                         |  |  |
| Units: Titers                            |                      |                            |  |  |
| geometric mean (confidence interval 95%) |                      |                            |  |  |
| rSBA, M12, (N=249;89)                    | 91.7 (75.6 to 111.3) | 63.8 (43.3 to 94.1)        |  |  |
| rSBA, M24, (N=235;86)                    | 39.3 (31.3 to 49.3)  | 30.6 (20.1 to 46.7)        |  |  |
| rSBA, M36, (N=226;77)                    | 29.8 (23.6 to 37.6)  | 21.8 (14.2 to 33.5)        |  |  |
| rSBA, M48, (N=208;73)                    | 5.3 (4.7 to 6)       | 6 (4.5 to 8)               |  |  |
| rSBA, M60, (N=195;68)                    | 6.6 (5.6 to 7.8)     | 8.5 (5.9 to 12.3)          |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-PRP $\geq 0.15$ $\mu\text{g/mL}$ , $\geq 1.0$ $\mu\text{g/mL}$

|                 |                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Number of subjects with anti-PRP $\geq 0.15$ $\mu\text{g/mL}$ , $\geq 1.0$ $\mu\text{g/mL}$ |
|-----------------|---------------------------------------------------------------------------------------------|

End point description:

The cut-off values assessed were greater than or equal to ( $\geq$ ) 0.15  $\mu\text{g/mL}$  and  $\geq 1.0$   $\mu\text{g/mL}$ . The analyses were performed at the GSK Biologicals' laboratory, and starting with year 4 GSK Biologicals laboratory was replaced with Public Health England (PHE) laboratory.

|                                              |           |
|----------------------------------------------|-----------|
| End point type                               | Secondary |
| End point timeframe:                         |           |
| At 1, 2, 3, 4, and 5 years after vaccination |           |

| End point values                                        | Menitorix Group | Meningitec + Hiberix Group |  |  |
|---------------------------------------------------------|-----------------|----------------------------|--|--|
| Subject group type                                      | Reporting group | Reporting group            |  |  |
| Number of subjects analysed                             | 255             | 91                         |  |  |
| Units: Subjects                                         |                 |                            |  |  |
| Anti-PRP, M12, $\geq 0.15 \mu\text{g/mL}$<br>(N=255;91) | 252             | 91                         |  |  |
| Anti-PRP, M12, $\geq 1.0 \mu\text{g/mL}$<br>(N=255;91)  | 209             | 80                         |  |  |
| Anti-PRP, M24, $\geq 0.15 \mu\text{g/mL}$<br>(N=237;84) | 235             | 84                         |  |  |
| Anti-PRP, M24, $\geq 1.0 \mu\text{g/mL}$<br>(N=237;84)  | 174             | 72                         |  |  |
| Anti-PRP, M36, $\geq 0.15 \mu\text{g/mL}$<br>(N=233;78) | 231             | 77                         |  |  |
| Anti-PRP, M36, $\geq 1.0 \mu\text{g/mL}$<br>(N=233;78)  | 164             | 64                         |  |  |
| Anti-PRP, M48, $\geq 0.15 \mu\text{g/mL}$<br>(N=204;73) | 202             | 73                         |  |  |
| Anti-PRP, M48, $\geq 1.0 \mu\text{g/mL}$<br>(N=204;73)  | 144             | 57                         |  |  |
| Anti-PRP, M60, $\geq 0.15 \mu\text{g/mL}$<br>(N=191;67) | 191             | 67                         |  |  |
| Anti-PRP, M60, $\geq 1.0 \mu\text{g/mL}$<br>(N=191;67)  | 129             | 47                         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-PRP antibody concentrations

|                                                                                                                                                                                                          |                                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| End point title                                                                                                                                                                                          | Anti-PRP antibody concentrations |
| End point description:                                                                                                                                                                                   |                                  |
| *The cut-off values assessed were greater than or equal to ( $\geq$ ) 1:8 and $\geq 1:128$ and starting with year 4 GSK Biologicals laboratory was replaced with Public Health England (PHE) laboratory. |                                  |
| End point type                                                                                                                                                                                           | Secondary                        |
| End point timeframe:                                                                                                                                                                                     |                                  |
| At 1, 2, 3, 4, and 5 years after vaccination                                                                                                                                                             |                                  |

| End point values                         | Menitorix Group        | Meningitec + Hiberix Group |  |  |
|------------------------------------------|------------------------|----------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group            |  |  |
| Number of subjects analysed              | 255                    | 91                         |  |  |
| Units: µg/mL                             |                        |                            |  |  |
| geometric mean (confidence interval 95%) |                        |                            |  |  |
| Anti-PRP, M12, (N=255; 91)               | 3.55 (2.988 to 4.218)  | 4.802 (3.708 to 6.218)     |  |  |
| Anti-PRP, M24, (N=237; 84)               | 2.5 (2.1 to 3)         | 3.3 (2.5 to 4.2)           |  |  |
| Anti-PRP, M36, (N=233; 78)               | 2.234 (1.886 to 2.647) | 2.751 (2.113 to 3.582)     |  |  |
| Anti-PRP, M48, (N=204; 73)               | 2.116 (1.773 to 2.524) | 2.964 (2.215 to 3.966)     |  |  |
| Anti-PRP, M60, (N=191; 67)               | 2.131 (1.752 to 2.592) | 2.537 (1.815 to 3.546)     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-PSC antibody concentrations $\geq 0.30$ µg/mL and $\geq 2.0$ µg/mL

|                                        |                                                                                                 |
|----------------------------------------|-------------------------------------------------------------------------------------------------|
| End point title                        | Number of subjects with anti-PSC antibody concentrations $\geq 0.30$ µg/mL and $\geq 2.0$ µg/mL |
| End point description:                 |                                                                                                 |
| End point type                         | Secondary                                                                                       |
| End point timeframe:                   |                                                                                                 |
| At 1, 2 and 3 years after vaccination. |                                                                                                 |

| End point values                           | Menitorix Group | Meningitec + Hiberix Group |  |  |
|--------------------------------------------|-----------------|----------------------------|--|--|
| Subject group type                         | Reporting group | Reporting group            |  |  |
| Number of subjects analysed                | 250             | 91                         |  |  |
| Units: Subjects                            |                 |                            |  |  |
| Anti-PSC, M12, $\geq 0.3$ µg/mL (N=250;91) | 95              | 91                         |  |  |
| Anti-PSC, M12, $\geq 2.0$ µg/mL (N=250;91) | 6               | 0                          |  |  |
| Anti-PSC, M24, $\geq 0.3$ µg/mL (N=233;84) | 47              | 17                         |  |  |
| Anti-PSC, M24, $\geq 2.0$ µg/mL (N=233;84) | 1               | 1                          |  |  |
| Anti-PSC, M36, $\geq 0.3$ µg/mL (N=230;79) | 24              | 8                          |  |  |
| Anti-PSC, M36, $\geq 2.0$ µg/mL (N=230;79) | 1               | 1                          |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PSC antibody concentrations

End point title Anti-PSC antibody concentrations

End point description:

End point type Secondary

End point timeframe:

At 1, 2 and 3 years after vaccination.

| End point values                         | Menitorix Group     | Meningitec + Hiberix Group |  |  |
|------------------------------------------|---------------------|----------------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group            |  |  |
| Number of subjects analysed              | 250 <sup>[3]</sup>  | 91 <sup>[4]</sup>          |  |  |
| Units: µg/mL                             |                     |                            |  |  |
| geometric mean (confidence interval 95%) |                     |                            |  |  |
| Anti-PSC, M12, (N=250; 91)               | 0.27 (0.24 to 0.3)  | 0.25 (0.21 to 0.29)        |  |  |
| Anti-PSC, M24, (N=233; 84)               | 0.2 (0.2 to 0.2)    | 0.2 (0.2 to 0.2)           |  |  |
| Anti-PSC, M36, (N=230; 79)               | 0.17 (0.16 to 0.19) | 0.17 (0.16 to 0.19)        |  |  |

Notes:

[3] - Lower and Upper limits of 95% confidence interval not reliable because of deviation from log normal

[4] - Lower and Upper limits of 95% confidence interval not reliable because of deviation from log normal

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any solicited local symptoms

End point title Number of subjects reporting any solicited local symptoms

End point description:

End point type Secondary

End point timeframe:

Within 4 days (Day 0-3) after vaccination

| End point values            | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 324             | 109                        |  |  |
| Units: Subjects             |                 |                            |  |  |
| Any pain                    | 91              | 42                         |  |  |
| Any redness                 | 146             | 64                         |  |  |

|              |    |    |  |  |
|--------------|----|----|--|--|
| Any swelling | 78 | 41 |  |  |
|--------------|----|----|--|--|

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any solicited general symptoms

|                 |                                                             |
|-----------------|-------------------------------------------------------------|
| End point title | Number of subjects reporting any solicited general symptoms |
|-----------------|-------------------------------------------------------------|

End point description:

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

End point timeframe:

Within 4 days (Day 0-3) after vaccination

| End point values            | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 324             | 109                        |  |  |
| Units: Subjects             |                 |                            |  |  |
| Any drowsiness              | 102             | 40                         |  |  |
| Any fever                   | 76              | 30                         |  |  |
| Any irritability/fussiness  | 154             | 69                         |  |  |
| Any loss of appetite        | 102             | 40                         |  |  |

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point timeframe:

Within 31 days (Days 0–30) after vaccination

| End point values            | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 324             | 109                        |  |  |
| Units: Subjects             |                 |                            |  |  |
| Any AE(s)                   | 217             | 81                         |  |  |

### Statistical analyses

No statistical analyses for this end point

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

|                                      |                                                                |
|--------------------------------------|----------------------------------------------------------------|
| End point title                      | Number of subjects reporting any serious adverse events (SAEs) |
| End point description:               |                                                                |
| End point type                       | Secondary                                                      |
| End point timeframe:                 |                                                                |
| During the Active Phase of the study |                                                                |

| End point values            | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 324             | 109                        |  |  |
| Units: Subjects             |                 |                            |  |  |
| Any SAE(s)                  | 4               | 2                          |  |  |

### Statistical analyses

No statistical analyses for this end point

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

|                                                                                              |                                                                  |
|----------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| End point title                                                                              | Number of subjects reporting any solicited adverse events (SAEs) |
| End point description:                                                                       |                                                                  |
| End point type                                                                               | Secondary                                                        |
| End point timeframe:                                                                         |                                                                  |
| At each visit of the long-term persistence phase (at 1 year up to 5 years after vaccination) |                                                                  |

| <b>End point values</b>     | Menitorix Group | Meningitec + Hiberix Group |  |  |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group            |  |  |
| Number of subjects analysed | 270             | 100                        |  |  |
| Units: Subjects             |                 |                            |  |  |
| Any SAE(s), Y1              | 0               | 0                          |  |  |
| Any SAE(s), Y2              | 0               | 0                          |  |  |
| Any SAE(s), Y3              | 0               | 0                          |  |  |
| Any SAE(s), Y4              | 0               | 0                          |  |  |
| Any SAE(s), Y5              | 0               | 0                          |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 4-day post-vaccination period, Unsolicited AEs during the 31-day post-vaccination period, SAEs during the entire period

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 15.1   |

### Reporting groups

|                                |                            |
|--------------------------------|----------------------------|
| Reporting group title          | Menitorix Group            |
| Reporting group description: - |                            |
| Reporting group title          | Meningitec + Hiberix Group |
| Reporting group description: - |                            |

| Serious adverse events                               | Menitorix Group | Meningitec + Hiberix Group |  |
|------------------------------------------------------|-----------------|----------------------------|--|
| Total subjects affected by serious adverse events    |                 |                            |  |
| subjects affected / exposed                          | 4 / 324 (1.23%) | 2 / 109 (1.83%)            |  |
| number of deaths (all causes)                        | 0               | 0                          |  |
| number of deaths resulting from adverse events       |                 |                            |  |
| Injury, poisoning and procedural complications       |                 |                            |  |
| Traumatic brain injury                               |                 |                            |  |
| subjects affected / exposed                          | 1 / 324 (0.31%) | 0 / 109 (0.00%)            |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0                      |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0                      |  |
| Nervous system disorders                             |                 |                            |  |
| Convulsion                                           |                 |                            |  |
| subjects affected / exposed                          | 1 / 324 (0.31%) | 0 / 109 (0.00%)            |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0                      |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0                      |  |
| General disorders and administration site conditions |                 |                            |  |
| Pyrexia                                              |                 |                            |  |
| subjects affected / exposed                          | 0 / 324 (0.00%) | 1 / 109 (0.92%)            |  |
| occurrences causally related to treatment / all      | 0 / 0           | 1 / 1                      |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0                      |  |
| Respiratory, thoracic and mediastinal                |                 |                            |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| disorders                                       |                 |                 |  |
| Asthma                                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 324 (0.00%) | 1 / 109 (0.92%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin and subcutaneous tissue disorders          |                 |                 |  |
| Rash                                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 324 (0.00%) | 1 / 109 (0.92%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psychiatric disorders                           |                 |                 |  |
| Breath holding                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 324 (0.31%) | 0 / 109 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Croup infectious                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 324 (0.31%) | 0 / 109 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 324 (0.31%) | 0 / 109 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 324 (0.00%) | 1 / 109 (0.92%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Menitorix Group    | Meningitec + Hiberix Group |  |
|-------------------------------------------------------|--------------------|----------------------------|--|
| Total subjects affected by non-serious adverse events |                    |                            |  |
| subjects affected / exposed                           | 217 / 324 (66.98%) | 81 / 109 (74.31%)          |  |

|                                                      |                    |                   |  |
|------------------------------------------------------|--------------------|-------------------|--|
| General disorders and administration site conditions |                    |                   |  |
| Pain                                                 |                    |                   |  |
| alternative assessment type: Systematic              |                    |                   |  |
| subjects affected / exposed                          | 91 / 324 (28.09%)  | 42 / 109 (38.53%) |  |
| occurrences (all)                                    | 91                 | 42                |  |
| Redness                                              |                    |                   |  |
| alternative assessment type: Systematic              |                    |                   |  |
| subjects affected / exposed                          | 146 / 324 (45.06%) | 64 / 109 (58.72%) |  |
| occurrences (all)                                    | 146                | 64                |  |
| Swelling                                             |                    |                   |  |
| alternative assessment type: Systematic              |                    |                   |  |
| subjects affected / exposed                          | 78 / 324 (24.07%)  | 41 / 109 (37.61%) |  |
| occurrences (all)                                    | 78                 | 41                |  |
| Drowsiness                                           |                    |                   |  |
| alternative assessment type: Systematic              |                    |                   |  |
| subjects affected / exposed                          | 102 / 324 (31.48%) | 40 / 109 (36.70%) |  |
| occurrences (all)                                    | 102                | 40                |  |
| Fever (Rectally)                                     |                    |                   |  |
| alternative assessment type: Systematic              |                    |                   |  |
| subjects affected / exposed                          | 76 / 324 (23.46%)  | 30 / 109 (27.52%) |  |
| occurrences (all)                                    | 76                 | 30                |  |
| Irritability/Fussiness (unsolicited general symptom) |                    |                   |  |
| alternative assessment type: Systematic              |                    |                   |  |
| subjects affected / exposed                          | 154 / 324 (47.53%) | 69 / 109 (63.30%) |  |
| occurrences (all)                                    | 154                | 69                |  |
| Loss of appetite                                     |                    |                   |  |
| alternative assessment type: Systematic              |                    |                   |  |
| subjects affected / exposed                          | 102 / 324 (31.48%) | 40 / 109 (36.70%) |  |
| occurrences (all)                                    | 102                | 40                |  |
| Injection site reaction                              |                    |                   |  |
| subjects affected / exposed                          | 0 / 324 (0.00%)    | 10 / 109 (9.17%)  |  |
| occurrences (all)                                    | 0                  | 10                |  |
| Irritability                                         |                    |                   |  |

|                                                  |                      |                      |  |
|--------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 324 (0.00%)<br>0 | 9 / 109 (8.26%)<br>9 |  |
| Gastrointestinal disorders                       |                      |                      |  |
| Diarrhea                                         |                      |                      |  |
| subjects affected / exposed                      | 25 / 324 (7.72%)     | 8 / 109 (7.34%)      |  |
| occurrences (all)                                | 25                   | 8                    |  |
| Vomiting                                         |                      |                      |  |
| subjects affected / exposed                      | 22 / 324 (6.79%)     | 9 / 109 (8.26%)      |  |
| occurrences (all)                                | 22                   | 9                    |  |
| Respiratory, thoracic and mediastinal disorders  |                      |                      |  |
| Rhinorrhoea                                      |                      |                      |  |
| subjects affected / exposed                      | 17 / 324 (5.25%)     | 0 / 109 (0.00%)      |  |
| occurrences (all)                                | 17                   | 0                    |  |
| Skin and subcutaneous tissue disorders           |                      |                      |  |
| Pyrexia (unsolicited symptom)                    |                      |                      |  |
| subjects affected / exposed                      | 37 / 324 (11.42%)    | 13 / 109 (11.93%)    |  |
| occurrences (all)                                | 37                   | 13                   |  |
| Rash (unsolicited symptom)                       |                      |                      |  |
| subjects affected / exposed                      | 24 / 324 (7.41%)     | 17 / 109 (15.60%)    |  |
| occurrences (all)                                | 24                   | 17                   |  |
| Dermatitis diaper                                |                      |                      |  |
| subjects affected / exposed                      | 0 / 324 (0.00%)      | 9 / 109 (8.26%)      |  |
| occurrences (all)                                | 0                    | 9                    |  |
| Infections and infestations                      |                      |                      |  |
| Upper respiratory tract infection                |                      |                      |  |
| subjects affected / exposed                      | 54 / 324 (16.67%)    | 13 / 109 (11.93%)    |  |
| occurrences (all)                                | 54                   | 13                   |  |
| Teething                                         |                      |                      |  |
| subjects affected / exposed                      | 40 / 324 (12.35%)    | 15 / 109 (13.76%)    |  |
| occurrences (all)                                | 40                   | 15                   |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 28 July 2006     | The primary vaccination calendar in Australia was modified since the release of the present protocol, ie Hib-TT combined with DTPa containing vaccine are now routinely given to infants in some regions. As a result, the inclusion criteria and the statistical section have been amended to take into account these changes.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 26 February 2007 | <p>In order to improve the enrolment of subjects in the study, some sites may perform home visits. At the first home visit, the parents/guardians will be asked to sign a preinformed consent to allow the sites to collect some personal identifying information. This information will be recorded on a register which will help GSK and the study staff better prepare for and manage the first study visit if the parent/guardian subsequently decide to have their child/ward participate in the study.</p> <p>In order to be consistent throughout all study visits, the physical examinations during the persistence phase of the study do not need to be performed by the investigator. In protocol amendment 1, it was planned to perform all laboratory assays at Rixensart. The protocol was amended to allow for other validated laboratories designated by GSK Biologicals to perform the assays, if needed.</p>                                                                                                                                                                                                                                                                                                                                                                                    |
| 27 March 2012    | <p>To support the data obtained by serum bactericidal assay (SBA) testing, antibody concentrations against meningococcal polysaccharides (PSs) were planned to be assessed by enzyme-linked immunosorbent assay (ELISA). The ELISA testing was performed at month 0, month 1 and 1, 2 and 3 years after vaccine administration, but the sponsor decided not to perform the ELISA testing at 4 and 5 years after vaccine administration for the following reasons:</p> <ul style="list-style-type: none"><li>- the World Health Organisation (WHO) considers SBA the primary means of assessing immune response to meningococcal conjugate vaccines [WHO, 2006; WHO, 1999].</li><li>- circulating bactericidal antibodies are more critical for persistent protection against meningococcal disease than non-functional antibodies against meningococcal polysaccharides [CDC, 2011; WHO, 2006].</li></ul> <p>Although antibody concentrations will not be determined by ELISA at 4 and 5 years after vaccine administration, all subjects will be informed of their SBA antibody titers at each immunogenicity time point when statistical analyses at that time point have been completed.</p> <p>In addition, the protocol amendment clarifies in which laboratory the different assays will be performed.</p> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported