

**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,
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**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
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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 µg/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
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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
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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
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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 Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: months			
arithmetic mean	12.5	12.5	
standard deviation	± 0.94	± 0.75	-
Gender categorical Units: Subjects			
Female	150	42	192
Male	174	67	241

## End points

### End points 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.	

### 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: 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: 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 $\geq 0.15$ $\mu\text{g/mL}$
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End point description:

End point type	Primary
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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 $\geq 0.15$ $\mu\text{g/mL}$
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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 $\geq 1:8$
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End point description:

End point type	Secondary
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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 $\geq 0.15$ $\mu\text{g/mL}$
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End point description:

End point type	Secondary
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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
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End point description:

End point type	Secondary
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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
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End point description:

End point type	Secondary
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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 $\geq 1.0$ $\mu\text{g/mL}$
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End point description:

End point type	Secondary
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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
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End point description:

End point type	Secondary
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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
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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
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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 $\geq 0.15$ $\mu\text{g/mL}$ , $\geq 1.0$ $\mu\text{g/mL}$
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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, $\geq 0.15 \mu\text{g/mL}$ (N=255;91)	252	91		
Anti-PRP, M12, $\geq 1.0 \mu\text{g/mL}$ (N=255;91)	209	80		
Anti-PRP, M24, $\geq 0.15 \mu\text{g/mL}$ (N=237;84)	235	84		
Anti-PRP, M24, $\geq 1.0 \mu\text{g/mL}$ (N=237;84)	174	72		
Anti-PRP, M36, $\geq 0.15 \mu\text{g/mL}$ (N=233;78)	231	77		
Anti-PRP, M36, $\geq 1.0 \mu\text{g/mL}$ (N=233;78)	164	64		
Anti-PRP, M48, $\geq 0.15 \mu\text{g/mL}$ (N=204;73)	202	73		
Anti-PRP, M48, $\geq 1.0 \mu\text{g/mL}$ (N=204;73)	144	57		
Anti-PRP, M60, $\geq 0.15 \mu\text{g/mL}$ (N=191;67)	191	67		
Anti-PRP, M60, $\geq 1.0 \mu\text{g/mL}$ (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		
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### 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
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End point description:

End point type	Secondary
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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)
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End point description:

End point type	Secondary
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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
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### 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 occurrences (all)	0 / 324 (0.00%) 0	9 / 109 (8.26%) 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