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 November 2007

Results information

Result version number	v3 (current)
This version publication date	26 May 2022
First version publication date	29 July 2015
Version creation reason	• Correction of full data set Minor corrections in safety section.

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	106446: eTrack number, 106449: 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 investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 February 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 November 2007
Global end of trial reached?	Yes
Global end of trial date	06 November 2007
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 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 ≥ 1:8.
-Percentage of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration ≥ 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	01 June 2006
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:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	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
Arm title	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.

Arm title	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 tight 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.

Number of subjects in period 1	Menitorix Group	Meningitec + Hiberix Group
Started	324	109
Completed	320	108
Not completed	4	1
Consent withdrawn by subject	4	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			
Units: Subjects			
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 Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers Greater Than or Equal to 1:8 Titer

End point title	Number of Subjects With Meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers Greater Than or Equal to 1:8 Titer
End point description:	
rSBA-MenC titers greater than or equal to 1:8 titer are indicative of seroprotection.	
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 ≥ 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 ≥ 1:8.	
Comparison groups	Meningitec + Hiberix Group v Menitorix Group

Number of subjects included in analysis	379
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
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 Concentration Greater Than or Equal to 0.15 Micrograms Per Milliliter (µg/mL)

End point title	Number of Subjects With Anti-polyribosylribitol Phosphate (Anti-PRP) Antibody Concentration Greater Than or Equal to 0.15 Micrograms Per Milliliter (µg/mL)

End point description:

Anti-PRP antibody concentration greater than or equal to 0.15 µg/mL is indicative of short-term protection.

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	292	100		
Units: Subjects				
Anti-PRP, M1, >=0.15µg/mL (N=292; 100)	292	100		

Statistical analyses

Statistical analysis title	Difference in % subjects with anti-PRP ≥0.15 µg/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 ≥ 0.15 µg/mL.

Comparison groups	Menitorix Group v Meningitec + Hiberix Group

Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
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 meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers Above the Cut-off Values

End point title	Number of subjects with meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers Above the Cut-off Values

End point description:

The cut-off values assessed were greater than or equal to (≥) 1:8.

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-polyribosylribitol Phosphate (Anti-PRP) Antibody Concentration Above Cut-off Values

End point title	Number of subjects with anti-polyribosylribitol Phosphate (Anti-PRP) Antibody Concentration Above Cut-off Values

End point description:

Anti-PRP antibody concentration cut-off values assessed include 0.15 µg/mL (indicative of short-term protection)

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 meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers Greater Than or Equal to 1:128 titer

End point title	Number of subjects with meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers Greater Than or Equal to 1:128 titer

End point description:

rSBA-MenC titers cut-off values assessed were greater than or equal to (≥) 1:8 (indicative of seroprotection) and ≥ 1:128 titers.

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: Meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers

End point title	Meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers

End point description:

Titers are given as Geometric Mean Titers (GMTs). Functional anti-meningococcal serogroup C activity (SBA-MenC) was determined by a serum bactericidal test using rabbit complement.

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-polyribosylribitol Phosphate (Anti-PRP) Antibody Concentration Above Cut-off Values

End point title	Number of subjects with anti-polyribosylribitol Phosphate (Anti-PRP) Antibody Concentration Above Cut-off Values

End point description:

Anti-PRP antibody concentration cut-off values assessed include 1.0 µg/mL (indicative of long-term protection).

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-polyribosylribitol Phosphate (Anti-PRP) antibody concentrations

End point title	Anti-polyribosylribitol Phosphate (Anti-PRP) antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

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: 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 above the Cut-off Values

End point title	Number of subjects with anti-polysaccharide C (anti-PSC) antibody concentrations above the Cut-off Values

End point description:

Anti-PSC antibody concentration cut-off values assessed include greater than or equal to (≥) 0.30 µg/mL and ≥ 2.0 µg/mL.

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: Subjects				
Anti-PSC, PRE, >=0.3µg/mL (N=283; 96)	2	1		
Anti-PSC, M1, >=0.3µg/mL (N=290; 100)	290	100		
Anti-PSC, PRE, >=2.0µg/mL (N=283; 96)	0	0		

Anti-PSC, M1, >=2.0µg/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:

Concentrations given as Geometric Mean Concentrations (GMCs).

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 meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers Above the Cut-off Values

End point title	Number of subjects with meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers Above the Cut-off Values

End point description:

rSBA-MenC titers cut-off values assessed were greater than or equal to (≥) 1:8 (indicative of seroprotection) and ≥ 1:128 titers.
Functional anti-meningococcal serogroup C activity (SBA-MenC) was determined by a serum bactericidal test using rabbit complement. For SBA testing at a GlaxoSmithKline (GSK) laboratory up to Year 3 after vaccination, titers were expressed as the reciprocal of the dilution resulting in 50% inhibition. For SBA testing at the Public Health England (PHE), formerly known as Health Protection Agency (HPA), at Year 4, titers were expressed as the reciprocal of the last dilution resulting in at least 50% inhibition.

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, ≥ 1:8 (N=249;89)	216	68		
rSBA, M12, ≥ 1:128 (N=249;89)	117	37		
rSBA, M24, ≥ 1:8 (N=235;86)	164	52		
rSBA, M24, ≥ 1:128 (N=235;86)	76	26		
rSBA, M36, ≥ 1:8 (N=226;77)	145	41		
rSBA, M36, ≥ 1:128 (N=226;77)	58	22		
rSBA, M48, ≥ 1:8 (N=208;73)	26	9		
rSBA, M48, ≥ 1:128 (N=208;73)	7	4		
rSBA, M60, ≥ 1:8 (N=195;68)	37	17		
rSBA, M60, ≥ 1:128 (N=195;68)	12	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers

End point title	Meningococcal Serogroup C Serum Bactericidal Assay Using Rabbit Complement (rSBA-MenC) Titers

End point description:

Titers are given as Geometric Mean Titers (GMTs). Functional anti-meningococcal serogroup C activity (SBA-MenC) was determined by a serum bactericidal test using rabbit complement. For SBA testing at a GlaxoSmithKline (GSK) laboratory up to Year 3 after vaccination, titers were expressed as the reciprocal of the dilution resulting in 50% inhibition. For SBA testing at the PHE at year 4 after vaccination, titers were expressed as the reciprocal of the last dilution resulting in at least 50% inhibition.

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-polyribosylribitol Phosphate (Anti-PRP) Antibody Concentration Above Cut-off Values

End point title	Number of subjects with anti-polyribosylribitol Phosphate (Anti-PRP) Antibody Concentration Above Cut-off Values

End point description:

Anti-PRP antibody concentration cut-off values assessed include 0.15 µg/mL (indicative of short-term protection) and 1.0 µg/mL (indicative of long-term protection).

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, ≥ 0.15 µg/mL (N=255;91)	252	91		
Anti-PRP, M12, ≥ 1.0 µg/mL (N=255;91)	209	80		
Anti-PRP, M24, ≥ 0.15 µg/mL (N=237;84)	235	84		
Anti-PRP, M24, ≥ 1.0 µg/mL (N=237;84)	174	72		
Anti-PRP, M36, ≥ 0.15 µg/mL (N=233;78)	231	77		
Anti-PRP, M36, ≥ 1.0 µg/mL (N=233;78)	164	64		
Anti-PRP, M48, ≥ 0.15 µg/mL (N=204;73)	202	73		
Anti-PRP, M48, ≥ 1.0 µg/mL (N=204;73)	144	57		
Anti-PRP, M60, ≥ 0.15 µg/mL (N=191;67)	191	67		
Anti-PRP, M60, ≥ 1.0 µg/mL (N=191;67)	129	47		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosylribitol Phosphate (Anti-PRP) antibody concentrations

End point title	Anti-polyribosylribitol Phosphate (Anti-PRP) antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

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-polysaccharide C (Anti-PSC) Antibody Concentration Above the Cut-off Values

End point title	Number of subjects with anti-polysaccharide C (Anti-PSC) Antibody Concentration Above the Cut-off Values

End point description:

Anti-PSC antibody concentration cut-off values assessed include greater than or equal to (≥) 0.30 µg/mL and ≥ 2.0 µg/mL.

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, ≥ 0.3 µg/mL (N=250;91)	95	33		
Anti-PSC, M12, ≥ 2.0 µg/mL (N=250;91)	6	0		
Anti-PSC, M24, ≥ 0.3 µg/mL (N=233;84)	47	17		
Anti-PSC, M24, ≥ 2.0 µg/mL (N=233;84)	1	1		
Anti-PSC, M36, ≥ 0.3 µg/mL (N=230;79)	24	8		
Anti-PSC, M36, ≥ 2.0 µg/mL (N=230;79)	1	1		

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:

Concentrations given as Geometric Mean Concentrations (GMCs).

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[3]	91[4]		
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:

Assessed solicited local symptoms were pain, redness and swelling at the injection site. Any = Occurrence of any solicited local symptom regardless of their intensity grade.

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:

Solicited general symptoms assessed include drowsiness, fever (≥ 38°C), irritability and loss of appetite. Any = Occurrence of any solicited general symptom regardless of intensity grade or relationship to vaccination. Any Fever = Axillary temperature equal to or above (≥) 37.5 degrees Celsius (°C).

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 symptoms

End point title	Number of subjects reporting any unsolicited symptoms

End point description:

Unsolicited symptom: Any adverse event (AE) reported in addition to those solicited during the clinical study. Also any solicited symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited adverse event.

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:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination.

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:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination.

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)

End point values	Menitorix Group	Meningitec + Hiberix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	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

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

klUp to Year 5 for Serious Adverse Events. Within 31 days after vaccination for Other Adverse Events that were not systematically assessed. Within 4 days after vaccination for Other Adverse Events that were systematically assessed.

Adverse event reporting additional description:

For long-term persistence (Years 1 to 5), only SAEs that are determined by the investigator as causally related to vaccination will be described individually. No SAEs related to vaccination were reported between the end of the vaccination phase up to Year 5.

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 %

Non-serious adverse events	Menitorix Group	Meningitec + Hiberix Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	293 / 324 (90.43%)	104 / 109 (95.41%)	
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	7 / 324 (2.16%)	10 / 109 (9.17%)	
occurrences (all)	7	10	
Irritability			
subjects affected / exposed	0 / 324 (0.00%)	9 / 109 (8.26%)	
occurrences (all)	0	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%)	3 / 109 (2.75%)	
occurrences (all)	17	3	
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	9 / 324 (2.78%)	9 / 109 (8.26%)	
occurrences (all)	9	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	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. 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.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported