Clinical trial results:
A phase III, randomized, multinational study, double-blinded for the immunogenicity and consistency evaluation of 3 Hib-MenCY-TT vaccine lots and single-blinded and controlled for the evaluation of safety and immunogenicity of GSK Biologicals' Haemophilus influenzae type b and Neisseria meningitidis serogroups C and Y-tetanus toxoid conjugate vaccine combined (Hib-MenCY-TT) compared to monovalent Hib vaccine in healthy infants at 2, 4, 6, and 12 to 15 months of age.

Summary

EudraCT number	2005-002352-18
Trial protocol	Outside EU/EEA
Global end of trial date	26 February 2008

Results information

Result version number	v3 (current)
This version publication date	08 April 2023
First version publication date	02 July 2015
Version creation reason	• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification

Sponsor protocol code	103813,105067

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00289783
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No	No

1901/2006 apply to this trial?	
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	21 April 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 August 2007
Global end of trial reached?	Yes
Global end of trial date	26 February 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate: the lot-to-lot consistency of 3 lots of Hib-MenCY-TT co-administered with DTPa-HBV-IPV following 3 doses, in terms of PRP, MenC and MenY; the immune response to PRP in the group that received 3 doses of Hib-MenCY-TT and a 4th dose of Hib-MenCY-TT was non-inferior to the group that received Hib and Hib-OMP. To evaluate the immunogenicity of a 4th dose of Hib-MenCY-TT co-administered with DTPa-HBV-IPV, MMR and Var. To evaluate the effect of a 4th dose of Hib-MenCY-TT co-administered with MMR and Var, in terms of a vaccine response; the non-inferiority of Hib-MenCY-TT compared to Hib, co-administered with DTPa-HBV-IPV, in terms of PRP; the non-inferiority of MMR when co-administered with a 4th dose of Hib-MenCY-TT compared to MMR co-administered with a 4th dose of Hib-OMP, co-administered with Var; the non-inferiority of Var co-administered with a 4th dose of Hib-MenCY-TT compared to Var co-administered with a 4th dose of Hib-OMP, co-administered with MMR.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 3037
Country: Number of subjects enrolled	Australia: 604
Country: Number of subjects enrolled	Mexico: 800
Worldwide total number of subjects	4441
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)	4441
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:

Subjects were randomized at the beginning of the primary phase and kept their group assignment during the fourth dose vaccination phase. The study protocol identified 3 different study cohorts : United States (US) Safety and Immunogenicity (Cohort 1), Safety Only (Cohort 2: from all investigation sites), Non-US Safety and Immunogenicity (Cohort 3).

Pre-assignment

Screening details:

The data for 261 subjects from one study center in the US were not included in the analyses as vaccine accountability could not be fully reconciled (i.e. treatment group assignment for the different subjects could not be verified).

Period 1

Period 1 title	Primary phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Blinding implementation details:

Double-blind for the immunogenicity and consistency evaluation of the 3 Hib-MenCY-TT vaccine lots and single-blind and controlled for the evaluation of safety and immunogenicity of Hib-MenCY-TT compared to monovalent Hib vaccine, randomized study with 4 parallel treatment groups (1:1:1:1).

Arms

Are arms mutually exclusive?	Yes
Arm title	Menhibrix Group

Arm description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' Haemophilus influenzae type b and Neisseria meningitidis 792014 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-doses administered at 2, 4 and 6 months of age, and 1 booster dose at 12 to 15 months of age.The vaccines were administered intramuscularly in the right upper thigh.

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

Dosage and administration details:

A 3-dose injection at 2, 4 and 6 months of age, administered intramuscularly in the left upper thigh.

Investigational medicinal product name	Prevnar
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection at 2, 4 and 6 months of age, and 1 booster dose by intramuscular injection at 12 to 15 months of age.

Investigational medicinal product name	M-M-R II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 booster dose by subcutaneous injection at 12 to 15 months of age.

Investigational medicinal product name	Varivax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 booster dose by subcutaneous injection at 12 to 15 months of age

Arm title	ActHIB Group

Arm description:

Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Arm type	Active comparator
Investigational medicinal product name	ActHIB
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose injection administered at 2, 4 and 6 months of age, intramuscularly in the right upper thigh.

Investigational medicinal product name	PedvaxHIB
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose by intramuscular injection at 12 to 15 months of age, administered in the left lower deltoid or tight

Number of subjects in period 1[1]	Menhibrix Group	ActHIB Group
Started	3136	1044
Completed	2888	961
Not completed	248	83
Adverse event, serious fatal	7	-

Consent withdrawn by subject	93	40
Adverse event, non-fatal	3	1
Unspecified	32	12
Lost to follow-up	60	14
Migration from the study area	26	10
Protocol deviation	27	6

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The data for 261 subjects from one study center in the US were not included in the analyses as vaccine accountability could not be fully reconciled (i.e. treatment group assignment for the different subjects could not be verified).

Period 2

Period 2 title	Fourth dose phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Menhibrix Group

Arm description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' Haemophilus influenzae type b and Neisseria meningitidis 792014 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-doses administered at 2, 4 and 6 months of age, and 1 booster dose at 12 to 15 months of age.The vaccines were administered intramuscularly in the right upper thigh.

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

Dosage and administration details:

A 3-dose injection at 2, 4 and 6 months of age, administered intramuscularly in the left upper thigh.

Investigational medicinal product name	Prevnar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:	
3-dose intramuscular injection at 2, 4 and 6 months of age, and 1 booster dose by intramuscular injection at 12 to 15 months of age.	
Investigational medicinal product name	M-M-R II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
1 booster dose by subcutaneous injection at 12 to 15 months of age.	
Investigational medicinal product name	Varivax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
1 booster dose by subcutaneous injection at 12 to 15 months of age	
Arm title	ActHIB Group
Arm description:	
Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.	
Arm type	Active comparator
Investigational medicinal product name	ActHIB
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3-dose injection administered at 2, 4 and 6 months of age, intramuscularly in the right upper thigh.	
Investigational medicinal product name	PedvaxHIB
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
1 booster dose by intramuscular injection at 12 to 15 months of age, administered in the left lower deltoid or tight	

Number of subjects in period 2[2]	Menhibrix Group	ActHIB Group
Started	2769	923
Completed	2682	899
Not completed	87	24
Consent withdrawn by subject	10	1
Adverse event	1	-

Unspecified	22	10
Lost to follow-up	53	12
Migration from the study area	1	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects were randomized at the beginning of the primary phase and kept their group assignment during the fourth dose vaccination phase.

Baseline characteristics

Reporting groups	
Reporting group title	Menhibrix Group
Reporting group description:	
Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.	
Reporting group title	ActHIB Group
Reporting group description:	
Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.	

Reporting group values	Menhibrix Group	ActHIB Group	Total
Number of subjects	3136	1044	4180
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	2.11	2.11	
standard deviation	± 0.26	± 0.27	-
Gender categorical Units: Subjects			
Female	1523	498	2021
Male	1613	546	2159

End points reporting groups

Reporting group title	Menhibrix Group

Reporting group description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Reporting group title	ActHIB Group

Reporting group description:

Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Reporting group title	Menhibrix Group

Reporting group description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Reporting group title	ActHIB Group

Reporting group description:

Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Subject analysis set title	Menhibrix A Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Subject analysis set title	Menhibrix B Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot B co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Subject analysis set title	Menhibrix C Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh,

respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Primary: Anti-Polyribosyl Ribitol Phosphate (PRP) antibody concentrations

End point title	Anti-Polyribosyl Ribitol Phosphate (PRP) antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Primary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	518	171	162	180
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	11.021 (10.027 to 12.114)	6.463 (5.288 to 7.9)	10.17 (8.855 to 11.681)	11.424 (9.71 to 13.441)

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	176			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	11.438 (9.503 to 13.768)			

Statistical analyses

Statistical analysis title	GMC ratio anti-PRP LotB / LotA

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for polyribosylribitol phosphate (PRP) as measured by ELISA.

Comparison groups	Menhibrix B Group v Menhibrix A Group

Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	GMC ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.42

Notes:

[1] - Criteria for lot-to-lot consistency (1 month after primary vaccination):
For each pair of lots and for the immune response to anti-PRP measured by ELISA the two-sided 95% confidence interval (CI) on the geometric mean concentrations (GMCs) ratio between lots is within the [0.5; 2.0] interval.

Statistical analysis title	GMC ratio anti-PRP LotC / LotA

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for polyribosylribitol phosphate (PRP) as measured by ELISA.

Comparison groups	Menhibrix A Group v Menhibrix C Group
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	GMC ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.42

Notes:

[2] - Criteria for lot-to-lot consistency (1 month after primary vaccination):
For each pair of lots and for the immune response to anti-PRP measured by ELISA the two-sided 95% confidence interval (CI) on the geometric mean concentrations (GMCs) ratio between lots is within the [0.5; 2.0] interval.

Statistical analysis title	GMC ratio anti-PRP LotC / LotB

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for polyribosylribitol phosphate (PRP) as measured by ELISA.

Comparison groups	Menhibrix B Group v Menhibrix C Group
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	GMC ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.26

Notes:

[3] - Criteria for lot-to-lot consistency (1 month after primary vaccination):
For each pair of lots and for the immune response to anti-PRP measured by ELISA the two-sided 95% confidence interval (CI) on the geometric mean concentrations (GMCs) ratio between lots is within the [0.5; 2.0] interval.

Primary: Neisseria meningitidis serogroup C (MenC) serum bactericidal assay using human complement (hSBA) antibody titers

End point title	Neisseria meningitidis serogroup C (MenC) serum bactericidal assay using human complement (hSBA) antibody titers

End point description:

Titers were expressed as Geometric Mean Titers (GMTs). This analysis occured on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Primary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	491	164	158	168
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenC	967.6 (864 to 1083.5)	2.5 (2.2 to 2.9)	910 (754.6 to 1097.3)	1118 (931.1 to 1342.5)

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	165			
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenC	885.7 (712.4 to 1101.2)			

Statistical analyses

Statistical analysis title	GMT ratio hSBA-MenC Lot B/Lot A

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup C (MenC) as measured by a serum bactericidal assay using human complement (hSBA).

Comparison groups	Menhibrix A Group v Menhibrix B Group

Number of subjects included in analysis	326
Analysis specification	Pre-specified
Analysis type	other[4]
Parameter estimate	GMT ratio
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.62

Notes:

[4] - For each pair of lots and for the immune response to hSBA-MenC, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

Statistical analysis title	GMT ratio hSBA-MenC Lot C/Lot A

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup C (MenC) as measured by a serum bactericidal assay using human complement (hSBA).

Comparison groups	Menhibrix C Group v Menhibrix A Group
Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	other[5]
Parameter estimate	GMT ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.29

Notes:

[5] - For each pair of lots and for the immune response to hSBA-MenC, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

Statistical analysis title	GMT ratio hSBA-MenC Lot C/Lot B

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup C (MenC) as measured by a serum bactericidal assay using human complement (hSBA).

Comparison groups	Menhibrix B Group v Menhibrix C Group
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	GMT ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.04

Notes:

[6] - For each pair of lots and for the immune response to hSBA-MenC, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

Primary: Neisseria meningitidis serogroup Y (MenY) serum bactericidal assay using human complement (hSBA) antibody titers

End point title	Neisseria meningitidis serogroup Y (MenY) serum bactericidal assay using human complement (hSBA) antibody titers

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Primary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	481	162	150	168
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenY	236.6 (205.7 to 272.1)	2.2 (2 to 2.4)	178.9 (136.4 to 234.6)	288.1 (232.8 to 356.6)

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	163			
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenY	249.6 (195.6 to 318.7)			

Statistical analyses

Statistical analysis title	GMT ratio hSBA-MenY Lot B/Lot A

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup Y (MenY) as measured by a serum bactericidal assay using human complement (hSBA).

Comparison groups	Menhibrix A Group v Menhibrix B Group

Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	other[7]
Parameter estimate	GMT ratio
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	2.27

Notes:

[7] - For each pair of lots and for the immune response to hSBA-MenY, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

Statistical analysis title	GMT ratio hSBA-MenY Lot C/Lot A

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup Y (MenY) as measured by a serum bactericidal assay using human complement (hSBA).

Comparison groups	Menhibrix A Group v Menhibrix C Group
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	other[8]
Parameter estimate	GMT ratio
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.97

Notes:

[8] - For each pair of lots and for the immune response to hSBA-MenY, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

Statistical analysis title	GMT ratio hSBA-MenC Lot C/Lot B

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup Y (MenY) as measured by a serum bactericidal assay using human complement (hSBA).

Comparison groups	Menhibrix B Group v Menhibrix C Group
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	GMT ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.21

Notes:

[9] - For each pair of lots and for the immune response to hSBA-MenY, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

Primary: hSBA-MenC antibody titers

End point title	hSBA-MenC antibody titers

End point description:

Titers are expressed as Geometric Mean Titers (GMTs). This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Primary

End point timeframe:

Prior to the fourth dose vaccination and 42 days after the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	331	119		
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenC [post-dose 4] (N=331;119)	2039.8 (1746.3 to 2382.6)	4.3 (3.2 to 5.8)		
hSBA-MenC [pre-dose 4] (N=329;104)	180.3 (155.6 to 208.8)	3 (2.4 to 3.7)		

Statistical analyses

Statistical analysis title	1.hSBA-MenC GMT ratio - Post-dose 4/Pre-dose 4

Statistical analysis description:

To evaluate the specific effect of a fourth dose of Menhibrix vaccine co-administered with M-M-R II and Varivax vaccines at 12 to 15 months of age in terms of a fourth dose vaccine response as measured by hSBA-MenC.

Comparison groups	Menhibrix Group v ActHIB Group
Number of subjects included in analysis	450
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	GMT ratio
Point estimate	12
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.4
upper limit	13.8

Notes:

[10] - Criteria for immunogenicity of MenC (42 days after the fourth dose): Lower limit of the asymptotic 95% CI for the geometric mean of individual ratio of post-dose 4/pre-dose 4 is ≥ 2.

Statistical analysis title	2.hSBA-MenC GMT ratio - Post-dose 4/Pre-dose 4

Statistical analysis description:

To evaluate the specific effect of a fourth dose of Menhibrix vaccine co-administered with M-M-R II and Varivax vaccines at 12 to 15 months of age in terms of a fourth dose vaccine response as measured by hSBA-MenC.

Comparison groups	Menhibrix Group v ActHIB Group
Number of subjects included in analysis	450
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	GMT ratio
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	1.4

Notes:

[11] - Point estimate = Lower limit (LL) = Upper limit (UL) as LL and UL values were not available due to the departure from lognormal distribution (large number of imputed values).

Primary: hSBA-MenY antibody titers

End point title	hSBA-MenY antibody titers

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Primary

End point timeframe:

Prior to the fourth dose vaccination and 42 days after the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342	120		
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenY [post-dose 4] (N=342;120)	1389.5 (1205 to 1602.2)	48.6 (31.9 to 74)		
hSBA-MenY [pre-dose 4] (N=329;103)	119.1 (101.1 to 140.3)	2.5 (2.1 to 2.9)		

Statistical analyses

Statistical analysis title	1.hSBA-MenY GMT ratio - Post-dose 4/Pre-dose 4

Statistical analysis description:

To evaluate the specific effect of a fourth dose of Menhibrix vaccine co-administered with M-M-R II and Varivax vaccines at 12 to 15 months of age in terms of a fourth dose vaccine response as measured by hSBA-MenY.

Comparison groups	Menhibrix Group v ActHIB Group

Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	GMT ratio
Point estimate	11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.2
upper limit	13.8

Notes:

[12] - Criteria for immunogenicity of MenY (42 days after the fourth dose): Lower limit of the asymptotic 95% CI for the geometric mean of individual ratio of post-dose 4/pre-dose 4 is ≥ 2.

Statistical analysis title	2.hSBA-MenY GMT ratio - Post-dose 4/Pre-dose 4

Statistical analysis description:

To evaluate the specific effect of a fourth dose of Menhibrix vaccine co-administered with M-M-R II and Varivax vaccines at 12 to 15 months of age in terms of a fourth dose vaccine response as measured by hSBA-MenY.

Comparison groups	ActHIB Group v Menhibrix Group
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Parameter estimate	GMT ratio
Point estimate	21.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.1
upper limit	21.1

Notes:

[13] - Point estimate = Lower limit (LL) = Upper limit (UL) as LL and UL values were not available due to the departure from lognormal distribution (large number of imputed values).

Primary: Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter (µg/mL)

End point title	Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter (µg/mL)[14]

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Primary

End point timeframe:

One month after primary vaccination

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	518	171	162	180
Units: Subjects				
Anti-PRP	499	156	158	175

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	176			
Units: Subjects				
Anti-PRP	166			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hSBA-MenC titer equal to or above 1:8

End point title	Number of subjects with hSBA-MenC titer equal to or above 1:8[15]

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Primary

End point timeframe:

42 days after the fourth dose

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	331	119		
Units: Subjects				
hSBA-MenC	326	26		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hSBA-MenY titer equal to or above 1:8

End point title	Number of subjects with hSBA-MenY titer equal to or above

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Primary

End point timeframe:

42 days after the fourth dose

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342	120		
Units: Subjects				
hSBA-MenY	338	87		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-measles antibody concentrations equal to or above 150 milli-international units per milliliter (mIU/mL)

End point title	Number of subjects with anti-measles antibody concentrations equal to or above 150 milli-international units per milliliter (mIU/mL)

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-measles antibody concentrations below 150 mIU/mL. Co-administration with MMR-II vaccine

End point type	Primary

End point timeframe:

42 days after the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	852	286		
Units: Subjects				
Anti-measles	815	274		

Statistical analyses

Statistical analysis title	Serostatus for anti-measles antibodies

Statistical analysis description:

To demonstrate the non-inferiority of M-M-R II vaccine when co-administered with a fourth dose of

Menhibrix vaccine compared to M-M-R II vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with Varivax vaccine.

Comparison groups	Menhibrix Group v ActHIB Group
Number of subjects included in analysis	1138
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
Parameter estimate	Difference in percentage
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.56
upper limit	3.06

Notes:

[17] - Lower limit of the standardized asymptotic 95% CI for the difference (Menhibrix vaccine fourth dose group minus ActHIB fourth dose group) in the percentage of subjects with seroconversion ≥ 150 mIU/mL, in initially seronegative subjects (<150 mIU/mL), for anti-measles antibody is ≥-5% (clinical limit for non-inferiority).

Primary: Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter

End point title	Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Primary

End point timeframe:

42 days after the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	126		
Units: Subjects				
Anti-PRP	358	125		

Statistical analyses

Statistical analysis title	Serostatus for anti-PRP

Statistical analysis description:

To demonstrate that, following a fourth dose, the immune response to Hib polysaccharide (PRP) in the group that received 3 primary vaccine doses of Menhibrix vaccine and a fourth dose of Menhibrix vaccine coadministered with M-M-R II and Varivax vaccines was non-inferior to the corresponding immune response in the group that received 3 primary vaccine doses of ActHIB vaccine and a fourth dose of PedvaxHIB vaccine co-administered with M-M-R II and Varivax vaccines.

Comparison groups	Menhibrix Group v ActHIB Group

Number of subjects included in analysis	487
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	Difference in percentage
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.78
upper limit	3.57

Notes:

[18] - Criteria for non-inferiority (42 days after the fourth dose): Lower limit of the two-sided standardized asymptotic 95% CI on the difference (Menhibrix vaccine fourth dose group minus ActHIB fourth dose group) in the percentage of subjects with anti-PRP concentration ≥ 1.0 µg/mL is ≥ -10% (clinical limit for non-inferiority).

Primary: Number of subjects with anti-mumps titer equal to or above 28 estimated dose 50 (ED50)

End point title	Number of subjects with anti-mumps titer equal to or above 28 estimated dose 50 (ED50)

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-mumps antibody titers below 28 ED50. Co-administration with MMR-II vaccine.

End point type	Primary

End point timeframe:

42 days after the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	601	191		
Units: Subjects				
Anti-mumps	595	191		

Statistical analyses

Statistical analysis title	Serostatus for anti-mumps antibodies ≥ 28 ED50

Statistical analysis description:

To demonstrate the non-inferiority of M-M-R II vaccine when co-administered with a fourth dose of Menhibrix vaccine compared to M--M-R II vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with Varivax vaccine.

Comparison groups	Menhibrix Group v ActHIB Group
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
Parameter estimate	Difference in percentage
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.16
upper limit	0.98

Notes:

[19] - Criterion for non-inferiority (42 days after fourth dose vaccination): Lower limit of the standardized asymptotic 95% CI for the difference (Menhibrix vaccine fourth dose group minus ActHIB fourth dose group) in the percentage of subjects with a seroconversion ≥28 ED50, in subjects with initial anti-mumps antibody < 28 ED50, for anti-mumps antibody is ≥ -5% (clinical limit for non-inferiority).

Primary: Number of subjects with anti-rubella antibody concentrations equal to or above 10 international units per millilitre (IU/mL)

End point title	Number of subjects with anti-rubella antibody concentrations equal to or above 10 international units per millilitre (IU/mL)

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-rubella antibody concentrations below 4 IU/mL. Co-administration with MMR-II vaccine.

End point type	Primary

End point timeframe:

42 days after the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	850	285		
Units: Subjects				
Anti-rubella	848	284		

Statistical analyses

Statistical analysis title	Serostatus for anti-rubella antibodies ≥ 10 IU/mL

Statistical analysis description:

To demonstrate the non-inferiority of M-M-R II vaccine when co-administered with a fourth dose of Menhibrix vaccine compared to M-M-R II vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with Varivax vaccine.

Comparison groups	Menhibrix Group v ActHIB Group
Number of subjects included in analysis	1135
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Parameter estimate	Difference in percentage
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	1.73

Notes:

[20] - To demonstrate the non-inferiority of M-M-R II vaccine when co-administered with a fourth dose of Menhibrix vaccine compared to M-M-R II vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with Varivax vaccine.

Primary: Number of subjects with anti-varicella titers equal to or above 1:5

End point title	Number of subjects with anti-varicella titers equal to or above 1:5

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-varicella antibody titers below 1:5. Co-administration with Varivax vaccine.

End point type	Primary

End point timeframe:

42 days after the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	723	223		
Units: Subjects				
Anti-varicella	722	223		

Statistical analyses

Statistical analysis title	Serostatus for anti-varicella antibodies (≥ 1:5)

Statistical analysis description:

To demonstrate the non-inferiority of Varivax vaccine co-administered with a fourth dose of Menhibrix vaccine compared to Varivax vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with M-M-R II vaccine in terms of immunogenicity to varicella as measured by fluorescent antibody to membrane antigen (FAMA).

Comparison groups	Menhibrix Group v ActHIB Group
Number of subjects included in analysis	946
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Parameter estimate	Difference in percentage
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	1.56

Notes:

[21] - Criterion for non-inferiority (42 days after the fourth dose vaccination): Lower limit of the standardized asymptotic 95% CI for the difference (Menhibrix vaccine fourth dose group minus ActHIB fourth dose group) in the percentage of subjects with seroconversion ≥ 1:5 dilution, in initially seronegative subjects (< 1:5), for anti-varicella antibody is ≥ -10% (clinical limit for non-inferiority).

Secondary: Number of subjects with anti-tetanus (anti-T) and anti-diphtheria toxoid (anti-D) antibody concentrations equal to or above 0.1 international units per millilitre (IU/mL)

End point title	Number of subjects with anti-tetanus (anti-T) and anti-

	diphtheria toxoid (anti-D) antibody concentrations equal to or above 0.1 international units per millilitre (IU/mL)

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	365	120		
Units: Subjects				
Anti-D	365	120		
Anti-T	365	120		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D and anti-T antibody concentrations

End point title	Anti-D and anti-T antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in international units per milliliter (IU/mL). This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	365	120		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D	2 (1.9 to 2.2)	2.2 (2 to 2.5)		
Anti-T	3.9 (3.7 to 4.1)	1.9 (1.7 to 2.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above 10.0 milli-international units per millilitre (mIU/mL)

End point title	Number of subjects with anti hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above 10.0 milli-international units per millilitre (mIU/mL)

End point description:

Results are stratified by the presence or absence of a birth dose of hepatitis B vaccine. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	47		
Units: Subjects				
Anti-HBs with Hepatitis B at birth (N=194;47)	193	47		
Anti-HBs without Hepatitis B at birth (N=18;8)	17	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in milli-International units per milliliter (mIU/mL) Results are stratified by the presence or absence of a birth dose of hepatitis B vaccine. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	47		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs with Hepatitis B at birth (N=194;47)	1963.2 (1684.8 to 2287.7)	2187.6 (1551.4 to 3084.5)		
Anti-HBs without Hepatitis B at birth (N=18;8)	1672.7 (730.9 to 3827.8)	3593.2 (1499.4 to 8611.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous hemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations equal to or above 5 ELISA units per millilitre (EL.U/mL)

End point title	Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous hemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations equal to or above 5 ELISA units per millilitre (EL.U/mL)

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	327	101		
Units: Subjects				
Anti-PT (N=327;100)	327	100		
Anti-FHA (N=324;97)	324	97		
Anti-PRN (N=322;101)	321	99		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	327	101		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT (N=327;100)	57.7 (54 to 61.7)	65.6 (58.3 to 73.9)		
Anti-FHA (N=324;97)	243.8 (227.9 to 260.9)	293.6 (261.4 to 329.8)		
Anti-PRN (N=322;101)	98.6 (89.5 to 108.6)	103.1 (82.8 to 128.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-poliovirus types 1, 2 and 3 equal to or above 8 estimated dose 50 (ED50)

End point title	Number of subjects with anti-poliovirus types 1, 2 and 3 equal to or above 8 estimated dose 50 (ED50)

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	285	90		
Units: Subjects				
Anti-Polio 1 (N=285;90)	285	90		
Anti-Polio 2 (N=285;90)	285	90		
Anti-Polio 3 (N=285;89)	285	89		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-poliovirus types 1, 2 and 3 titers

End point title	Anti-poliovirus types 1, 2 and 3 titers

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	285	90		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1 (N=285;90)	591.8 (525 to 667)	590.7 (462.7 to 754.1)		
Anti-Polio 2 (N=285;90)	496.7 (435.9 to 566)	452.7 (360.3 to 568.8)		
Anti-Polio 3 (N=285;89)	1367.7 (1209.9 to 1546)	1239.2 (973.5 to 1577.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibodies to Neisseria meningitidis serogroup C and Y polysaccharide capsule (anti-PSC and anti-PSY) concentrations equal to or above the cut-off values

End point title	Number of subjects with antibodies to Neisseria meningitidis serogroup C and Y polysaccharide capsule (anti-PSC and anti-PSY) concentrations equal to or above the cut-off values

End point description:

Anti-PSC and anti-PSY antibody cut-off values assessed were >=0.3 microgram per milliliter (µg/mL) and >=2.0 µg/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	404		
Units: Subjects				
Anti-PSC >=0.3 µg/mL (N=421;119)	418	5		
Anti-PSY >=0.3 µg/mL (N=404;109)	402	1		
Anti-PSC >=2.0 µg/mL (N=421;119)	379	2		
Anti-PSY >=2.0 µg/mL (N=404;109)	396	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PSC and anti-PSY antibody concentrations

End point title	Anti-PSC and anti-PSY antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per milliliter (µg/mL) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after primary vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	119		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSC (N=421;119)	5.8 (5.3 to 6.2)	0.2 (0.2 to 0.2)		
Anti-PSY (N=404;109)	17.5 (16 to 19.1)	0.2 (0.1 to 0.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off values

End point description:

Anti-PRP antibody cut-off values assessed were >=0.15 microgram per milliliter (µg/mL) and >=1.0 µg/mL. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after the primary vaccination course

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	134	46	49	42
Units: Subjects				
Anti-PRP >=0.15 µg/mL	134	46	49	42
Anti-PRP >=1.0 µg/mL	134	46	49	42

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: Subjects				
Anti-PRP >=0.15 µg/mL	43			
Anti-PRP >=1.0 µg/mL	43			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off values

End point description:

Anti-PRP antibody cut-off values assessed were >=0.15 microgram per milliliter (µg/mL) and >=1.0 µg/mL. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	13		
Units: Subjects				
Anti-PRP pre-dose 4 >=0.15 µg/mL (N=38;12)	38	12		
Anti-PRP pre-dose 4 >=1.0 µg/mL (N=38;12)	33	11		
Anti-PRP post-dose 4 >=0.15 µg/mL (N=40;13)	40	13		
Anti-PRP post-dose 4 >=1.0 µg/mL (N=40;13)	40	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL) The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after the primary vaccination course

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	134	46	49	42
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	23.165 (20.012 to 26.815)	29.759 (22.729 to 38.965)	24.984 (19.674 to 31.728)	24.05 (18.327 to 31.561)

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	43			

Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	20.489 (15.653 to 26.819)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL) The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	13		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP Pre-dose 4 (N=38;12)	3.34 (2.407 to 4.636)	4.123 (1.981 to 8.583)		
Anti-PRP Post-dose 4 (N=40;13)	132.965 (97.131 to 182.019)	92.8 (45.636 to 188.709)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenC and hSBA-MenY titers equal to or above the cut-off values

End point title	Number of subjects with hSBA-MenC and hSBA-MenY titers equal to or above the cut-off values

End point description:

hSBA-MenC/Y antibody cut-off values assessed were >=1:4 and >=1:8. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after the primary vaccination course

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	135	46	49	42
Units: Subjects				
hSBA-MenC >=1:4 (N=134;46;48;42;44)	133	2	47	42
hSBA-MenC >=1:8 (N=134;46;48;42;44)	133	2	47	42
hSBA-MenY >=1:4 (N=135;45;49;42;44)	134	1	48	42
hSBA-MenY >=1:8 (N=135;45;49;42;44)	134	1	48	42

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: Subjects				
hSBA-MenC >=1:4 (N=134;46;48;42;44)	44			
hSBA-MenC >=1:8 (N=134;46;48;42;44)	44			
hSBA-MenY >=1:4 (N=135;45;49;42;44)	44			
hSBA-MenY >=1:8 (N=135;45;49;42;44)	44			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenC and hSBA-MenY titers equal to or above the cut-off values

End point title	Number of subjects with hSBA-MenC and hSBA-MenY titers equal to or above the cut-off values

End point description:

hSBA-MenC/Y antibody cut-off values assessed were >=1:4 and >=1:8. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	13		
Units: Subjects				
hSBA-MenC pre-dose 4 >=1:4 (N=39;13)	39	2		
hSBA-MenC pre-dose 4 >=1:8 (N=39;13)	39	2		
hSBA-MenC post-dose 4 >=1:4 (N=39;13)	39	1		
hSBA-MenC post-dose 4 >=1:8 (N=39;13)	39	1		
hSBA-MenY pre-dose 4 >=1:4 (N=39;13)	39	3		
hSBA-MenY pre-dose 4 >=1:8 (N=39;13)	39	3		
hSBA-MenY post-dose 4 >=1:4 (N=40;13)	40	7		
hSBA-MenY post-dose 4 >=1:8 (N=40;13)	40	7		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenC and hSBA-MenY antibody titers

End point title	hSBA-MenC and hSBA-MenY antibody titers

End point description:

Titres are expressed as Geometric Mean Titers (GMTs). The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after the primary vaccination course

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	135	46	49	42
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenC (N=134;46;48;42;44)	3172.6 (2657.9 to 3786.8)	2.4 (1.8 to 3.1)	3055.8 (2096.8 to 4453.6)	3370.7 (2545.4 to 4463.6)

hSBA-MenY (N=135;45;49;42;44)	837.2 (696.4 to 1006.3)	2.2 (1.8 to 2.5)	666.5 (464 to 957.3)	916.7 (666.9 to 1260.1)

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenC (N=134;46;48;42;44)	3119.3 (2418.9 to 4022.4)			
hSBA-MenY (N=135;45;49;42;44)	989.6 (756.7 to 1294.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenC and hSBA-MenY antibody titers

End point title	hSBA-MenC and hSBA-MenY antibody titers

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	13		
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenC pre-dose 4 (N=39;13)	504.7 (366.2 to 695.5)	3.6 (1.5 to 8.7)		
hSBA-MenC post-dose 4 (N=39;13)	10132.9 (8008 to 12821.7)	2.5 (1.6 to 3.8)		
hSBA-MenY pre-dose 4 (N=39;13)	446.5 (328.3 to 607.3)	5.3 (1.7 to 16.7)		
hSBA-MenY post-dose 4 (N=40;13)	5775.8 (4488.9 to 7431.7)	27.4 (5.8 to 129)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values

End point description:

Anti-PSC and anti-PSY antibody cut-off values assessed were >=0.3 microgram per milliliter (µg/mL) and >=2.0 µg/mL. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after the primary vaccination course

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	46		
Units: Subjects				
Anti-PSC >=0.3 µg/mL (N=134;46)	134	2		
Anti-PSC >=2.0 µg/mL (N=134;46)	134	1		
Anti-PSY >=0.3 µg/mL (N=130;46)	130	1		
Anti-PSY >=2.0 µg/mL (N=130;46)	130	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values

End point description:

Anti-PSC and anti-PSY antibody cut-off values assessed were >=0.3 µg/mL and >=2.0 µg/mL. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	13		
Units: Subjects				
Anti-PSC pre-dose 4 >=0.3 µg/mL (N=40;13)	40	0		
Anti-PSC pre-dose 4 >=2.0 µg/mL (N=40;13)	22	0		
Anti-PSC post-dose 4 >=0.3 µg/mL (N=39;13)	39	0		
Anti-PSC post-dose 4 >=2.0 µg/mL (N=39;13)	39	0		
Anti-PSY pre-dose 4 >=0.3 µg/mL (N=40;13)	40	0		
Anti-PSY pre-dose 4 >=2.0 µg/mL (N=40;13)	36	0		
Anti-PSY post-dose 4 >=0.3 µg/mL (N=40;13)	40	0		
Anti-PSY post-dose 4 >=2.0 µg/mL (N=40;13)	40	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PSC and anti-PSY antibodies concentrations

End point title	Anti-PSC and anti-PSY antibodies concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per milliliter (µg/mL). The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after the primary vaccination course

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	46		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSC (N=134;46)	13.4 (12.1 to 15)	0.2 (0.1 to 0.2)		

Anti-PSY (N=130;46)	36.7 (32.2 to 41.8)	0.2 (0.1 to 0.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PSC and anti-PSY antibody concentrations

End point title	Anti-PSC and anti-PSY antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL). The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	13		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSC pre-dose 4 (N=40;13)	2.2 (1.72 to 2.83)	0.15 (0.15 to 0.15)		
Anti-PSC post-dose 4 (N=39;13)	15.63 (13.3 to 18.37)	0.15 (0.15 to 0.15)		
Anti-PSY pre-dose 4 (N=40;13)	5.7 (4.18 to 7.78)	0.15 (0.15 to 0.15)		
Anti-PSY post-dose 4 (N=40;13)	64.66 (52.35 to 79.86)	0.15 (0.15 to 0.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off value

End point title	Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off value

End point description:

Anti-PRP antibody cut-off values assessed were >=0.15 µg/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after the primary vaccination course

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	518	171	162	180
Units: Subjects				
Anti-PRP post-primary >=0.15 µg/mL	518	168	162	180

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	176			
Units: Subjects				
Anti-PRP post-primary >=0.15 µg/mL	176			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL). This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after the primary vaccination course and prior to the fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	469	160		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP post-primary (N=469;160)	10.802 (9.767 to 11.947)	6.086 (4.897 to 7.564)		
Anti-PRP pre-dose 4 (N=441;147)	1.615 (1.439 to 1.812)	0.832 (0.664 to 1.042)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenC and hSBA-MenY antibody titers equal to or above the cut-off values

End point title	Number of subjects with hSBA-MenC and hSBA-MenY antibody titers equal to or above the cut-off values

End point description:

hSBA-MenC and hSBA-MenY antibody cut-off values assessed were >=1:4 and >=1:8. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

One month after the primary vaccination course

End point values	Menhibrix Group	ActHIB Group	Menhibrix A Group	Menhibrix B Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	491	164	158	168
Units: Subjects				
hSBA-MenC >=1:4 (N=491;164;158;168;165)	485	11	156	167
hSBA-MenC >=1:8 (N=491;164;158;168;165)	485	11	156	167
hSBA-MenY >=1:4 (N=481;162;150;168;163)	463	3	141	165
hSBA-MenY >=1:8 (N=481;162;150;168;163)	461	3	140	165

End point values	Menhibrix C Group			
Subject group type	Subject analysis set			
Number of subjects analysed	165			
Units: Subjects				
hSBA-MenC >=1:4 (N=491;164;158;168;165)	162			
hSBA-MenC >=1:8 (N=491;164;158;168;165)	162			
hSBA-MenY >=1:4 (N=481;162;150;168;163)	157			
hSBA-MenY >=1:8 (N=481;162;150;168;163)	156			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values

End point description:

Anti-PSC and anti-PSY antibody cut-off values assessed were >=0.3 µg/mL and >=2.0 µg/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and 42 days after fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	109		
Units: Subjects				
Anti-PSC pre-dose 4 >=0.3 µg/mL (N=327;99)	300	3		
Anti-PSC pre-dose 4 >=2.0 µg/mL (N=327;99)	73	0		
Anti-PSC post-dose 4 >=0.3 µg/mL (N=316;106)	313	9		
Anti-PSC post-dose 4 >=2.0 µg/mL (N=316;106)	262	6		
Anti-PSY pre-dose 4 >=0.3 µg/mL (N=325;93)	320	1		
Anti-PSY pre-dose 4 >=2.0 µg/mL (N=325;93)	235	0		
Anti-PSY post-dose 4 >=0.3 µg/mL (N=334;109)	332	6		
Anti-PSY post-dose 4 >=2.0 µg/mL (N=334;109)	325	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PSC and anti-PSY antibody concentrations

End point title	Anti-PSC and anti-PSY antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL). This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and 42 days after fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	109		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSC pre-dose 4 (N=327;99)	1.04 (0.94 to 1.16)	0.16 (0.15 to 0.17)		
Anti-PSC post-dose 4 (N=316;106)	4.81 (4.33 to 5.34)	0.19 (0.16 to 0.23)		
Anti-PSY pre-dose 4 (N=325;93)	3.15 (2.83 to 3.5)	0.15 (0.15 to 0.15)		
Anti-PSY post-dose 4 (N=334;109)	18.26 (16.41 to 20.31)	0.18 (0.15 to 0.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PRP antibody concentrations equal to or above 0.15 microgram per milliliter (µg/mL)

End point title	Number of subjects with anti-PRP antibody concentrations equal to or above 0.15 microgram per milliliter (µg/mL)

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and 42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	126		
Units: Subjects				
Anti-PRP [post-dose 4] (N=361;126)	361	126		
Anti-PRP [pre-dose 4] (N=341;112)	329	98		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth vaccination and 42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	126		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP [post-dose 4] (N=361;126)	34.851 (30.664 to 39.61)	20.2 (16.373 to 24.92)		
Anti-PRP [pre-dose 4] (N=341;112)	1.617 (1.42 to 1.842)	0.759 (0.589 to 0.978)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenC and hSBA-MenY antibody concentrations equal to or above 1:4

End point title	Number of subjects with hSBA-MenC and hSBA-MenY antibody concentrations equal to or above 1:4

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and 42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342	120		
Units: Subjects				
hSBA-MenC [post-dose 4] (N=331;119)	326	26		
hSBA-MenY [post-dose 4](N=342;120)	338	87		
hSBA-MenC [pre-dose 4] (N=329;104)	318	12		
hSBA-MenY [pre-dose 4](N=329;103)	309	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-measles antibody concentrations equal to or above 200 milli-international units per millilitre (mIU/mL)

End point title	Number of subjects with anti-measles antibody concentrations equal to or above 200 milli-international units per millilitre (mIU/mL)

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-measles antibody concentrations below 150 mIU/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

42 days after the fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	852	286		
Units: Subjects				
Anti-measles	812	273		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-measles antibody concentrations

End point title	Anti-measles antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in milli-international units per milliliter (mIU/mL). The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-measles antibody concentrations below 150 mIU/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	852	286		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-measles	1990 (1852.2 to 2138)	1989.5 (1765.4 to 2242.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-mumps titer equal to or above the cut-off values

End point title	Number of subjects with anti-mumps titer equal to or above the cut-off values

End point description:

Anti-mumps antibody cut-off values assessed were >=28 estimated dose 50 (ED50) and >=51 ED50. The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-mumps antibody titers below 24 ED50. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	536	176		
Units: Subjects				
Anti-mumps >=28 ED50	532	176		
Anti-mumps >=51 ED50	490	160		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-mumps antibody titers

End point title	Anti-mumps antibody titers

End point description:

Titers are expressed as Geometric Mean Titers (GMTs). The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-measles antibody titers below 24 ED50. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	536	176		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-mumps	123.9 (116.9 to 131.3)	114.3 (103.7 to 126)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-rubella antibody concentrations equal to or above 4 international units per millilitre (IU/mL)

End point title	Number of subjects with anti-rubella antibody concentrations equal to or above 4 international units per millilitre (IU/mL)

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-rubella antibody concentrations below 4 IU/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	850	285		
Units: Subjects				
Anti-rubella	850	285		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rubella antibody concentrations

End point title	Anti-rubella antibody concentrations

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in international units per milliliter (IU/mL). The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-rubella antibody concentrations below 4 IU/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	850	285		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-rubella	81.4 (77.5 to 85.4)	74.9 (68.9 to 81.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-varicella titer equal to or above 1:40

End point title	Number of subjects with anti-varicella titer equal to or above 1:40

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-varicella antibody concentrations below 1:5 This analysis occurred on the cohort 1: Cohort 1 was to

include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	723	223		
Units: Subjects				
Anti-varicella	722	223		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-varicella antibody titers

End point title	Anti-varicella antibody titers

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-varicella antibody titers below 1:5 This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

42 days after fourth vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	723	223		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-varicella	407.1 (389.4 to 425.5)	394.1 (364.6 to 426)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-H1N1, anti-H3N2 and anti-influenza-B (anti B) antibody titers equal to or above 1:40

End point title	Number of subjects with anti-H1N1, anti-H3N2 and anti-influenza-B (anti B) antibody titers equal to or above 1:40

End point description:

Anti-H1N1, anti-H3N2 and anti-influenza-B (anti-B) antibody were measured by hemagglutination inhibition assay (HIA), in subjects who received 2 doses of influenza vaccine within the same influenza season of which at least one dose is concomitant with the study vaccine. For the purposes of this study, concomitant administration of influenza vaccine was defined as administration within 28 days before to 7 days after administration of study vaccines. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination and one month after the fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Subjects				
Anti-H1N1 pre-dose 4 (N=5;3)	0	0		
Anti-H1N1 post-dose 4 (N=4;4)	2	1		
Anti-H3N2 pre-dose 4 (N=5;3)	0	0		
Anti-H3N2 post-dose 4 (N=4;4)	3	1		
Anti-B pre-dose 4 (N=5;3)	0	0		
Anti-B post-dose 4 (N=4;4)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting fever above 39.5 degrees Celsius/103.1 degrees Fahrenheit

End point title	Number of subjects reporting fever above 39.5 degrees Celsius/103.1 degrees Fahrenheit

End point description:

Fever is defined as temperature (rectal or axillary/tympanic) above 39.5 degrees Celsius (°C) or 103.1 degrees Fahrenheit (°F).

End point type	Secondary

End point timeframe:

In the 4-day (Day 0-3) follow-up period after primary vaccination course

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3089	1015		
Units: Subjects				
Fever >39.5°C	46	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting fever above 39.5 degrees Celsius/103.1 degrees Fahrenheit

End point title	Number of subjects reporting fever above 39.5 degrees Celsius/103.1 degrees Fahrenheit

End point description:

Fever is defined as temperature (rectal or axillary/tympanic) above 39.5 degrees Celsius (°C) or 103.1 degrees Fahrenheit (°F).

End point type	Secondary

End point timeframe:

In the 4-day (Day0-3) follow-up period after the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2527	831		
Units: Subjects				
Fever >39.5°C	18	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local and general symptoms

End point title	Number of subjects reporting solicited local and general symptoms

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Solicited general symptoms assessed were fever, irritability/fussiness, drowsiness and loss of appetite. Fever is defined as temperature (rectal or axillary/tympanic) equal to or above 38.0°C.

End point type	Secondary

End point timeframe:

Within the 4 days (Day 0-3) following each dose of the primary vaccination course

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3089	1016		
Units: Subjects				
Pain Dose 1 (N=3056;1008)	1849	672		
Pain Dose 2 (N=2903;954)	1679	596		
Pain Dose 3 (N=2740;904)	1454	522		
Pain Across Doses (N=3088;1016)	2419	819		
Redness Dose 1 (N=3056;1008)	1152	401		
Redness Dose 2 (N=2903;954)	1455	483		
Redness Dose 3 (N=2740;904)	1409	495		
Redness Across Doses (N=3088;1016)	2052	691		
Swelling Dose 1 (N=3056;1008)	893	281		
Swelling Dose 2 (N=2903;954)	1091	350		
Swelling Dose 3 (N=2740;904)	1110	381		
Swelling Across Doses (N=3088;1016)	1707	568		
Drowsiness Dose 1 (N=3055;1008)	1864	655		
Drowsiness Dose 2 (N=2900;952)	1588	552		
Drowsiness Dose 3 (N=2736;905)	1260	444		
Drowsiness Across doses (N=3088;1015)	2418	804		
Temperature Dose 1 (N=3056;1008)	688	228		
Temperature Dose 2 (N=2900;951)	803	276		
Temperature Dose 3 (N=2736;905)	609	206		
Temperature Across doses (N=3089;1015)	1434	463		
Irritability Dose 1 (N=3055;1008)	2156	782		
Irritability Dose 2 (N=2900;952)	2074	708		
Irritability Dose 3 (N=2736;905)	1771	600		
Irritability Across doses (N=3088;1015)	2740	926		
Loss of appetite Dose 1 (N=3055;1008)	1024	375		
Loss of appetite Dose 2 (N=2900;952)	921	317		
Loss of appetite Dose 3 (N=2736;905)	828	285		
Loss of appetite Across doses (N=3088;1015)	1764	609		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local and general symptoms

End point title	Number of subjects reporting solicited local and general symptoms

End point description:

Solicited local symptoms assessed were pain, redness, swelling and an increase in limb circumference. Solicited general symptoms assessed were fever, irritability/fussiness, drowsiness and lost of appetite. Fever is defined as temperature (rectal or axillary/tympanic) equal to or above 38.0°C

End point type	Secondary

End point timeframe:

Within the 4 days (Day 0-3) post-vaccination period following the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2769	923		
Units: Subjects				
Pain (N=2528;832)	1319	494		
Redness (N=2528;833)	1213	463		
Swelling (N=2526;832)	936	334		
Increase in limb circumference (N=2769;923)	1489	503		
Drowsiness (N=2526;830)	1088	381		
Fever (N=2527;831)	341	134		
Irritability (N=2526;830)	1482	534		
Loss of appetite (N=2526;830)	825	287		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0-30) following the primary vaccination course

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3136	1044		
Units: Subjects				
AEs	1820	602		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0-30) following the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2769	923		
Units: Subjects				
AEs	1010	334		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting increased circumferential swelling at the injection limb(s)

End point title	Number of subjects reporting increased circumferential swelling at the injection limb(s)

End point description:

Increased circumferential swelling defined as either swelling with a diameter of >50 mm or a >50 mm increase in the circumference of the mid-limb when compared to the baseline (pre-vaccination) measurement, or any diffuse swelling that interferes with or prevents everyday activities (for example, active playing, eating, sleeping).

End point type	Secondary

End point timeframe:

Within 4 days (Day 0 to Day 3) after fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2769	923		
Units: Subjects				
Increase in circumference	1489	503		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting general symptoms specific to measles,

mumps, rubella and varicella vaccination	
End point title	Number of subjects reporting general symptoms specific to measles, mumps, rubella and varicella vaccination

End point description:

Symptoms assessed were fever, rash/exanthem, parotid/salivary gland swelling, and any suspected signs of meningism including febrile convulsions. Fever is defined as temperature (rectal or axillary/tympanic) equal to or above 38.0°C.

End point type	Secondary

End point timeframe:

Within 43 days (Day 0 through Day 42) after vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	545	175		
Units: Subjects				
Meningismus (N=541;173)	0	0		
Parotiditis (N=541;173)	0	0		
Rash (N=544;175)	59	19		
Fever (N=545;173)	211	70		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting Serious Adverse Events (SAEs)	
End point title	Number of subjects reporting Serious Adverse Events (SAEs)

End point description:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects.

End point type	Secondary

End point timeframe:

From Dose 0 through 6 months after the last primary dose or untill administration of the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3136	1044		
Units: Subjects				
SAEs	126	50		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting Serious Adverse Events (SAEs)

End point title	Number of subjects reporting Serious Adverse Events (SAEs)

End point description:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects.

End point type	Secondary

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2769	923		
Units: Subjects				
SAEs	47	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting new onset of chronic illness(es) (NOCIs)

End point title	Number of subjects reporting new onset of chronic illness(es) (NOCIs)

End point description:

NOCIs include autoimmune disorders, asthma, type I diabetes, allergies.

End point type	Secondary

End point timeframe:

From Dose 0 through 6 months after the last primary dose or until administration of the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3136	1044		
Units: Subjects				
Any NOCIs	163	52		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting new onset of chronic illness(es) (NOCIs)

End point title	Number of subjects reporting new onset of chronic illness(es) (NOCIs)

End point description:

NOCIs include autoimmune disorders, asthma, type I diabetes, allergies.

End point type	Secondary

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2769	923		
Units: Subjects				
Any NOCIs	85	33		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting rash

End point title	Number of subjects reporting rash

End point description:

Rash assessed was hives, idiopathic thrombocytopenic purpura, petechiae.

End point type	Secondary

End point timeframe:

From Dose 0 through 6 months after the last primary dose or until administration of the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3136	1044		
Units: Subjects				
Any rash(es)	470	154		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting rash

End point title	Number of subjects reporting rash

End point description:

Rash assessed was hives, idiopathic thrombocytopenic purpura, petechiae.

End point type	Secondary

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2769	923		
Units: Subjects				
Any rash(es)	265	94		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting adverse events resulting in emergency room (ER) visits

End point title	Number of subjects reporting adverse events resulting in emergency room (ER) visits

End point description:

Emergency room (ER) visits were not related to well-child care, vaccination, injury or common acute illness such as upper respiratory tract infections; otitis media, pharyngitis, gastroenteritis.

End point type	Secondary

End point timeframe:

From Dose 0 through 6 months after the last primary dose or until administration of the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3136	1044		
Units: Subjects				
Any AEs	217	72		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting adverse events resulting in physicians

(MD) office visits.

End point title	Number of subjects reporting adverse events resulting in physicians (MD) office visits.

End point description:

Physicians (MD) office visits were not related to well-child care, vaccination, injury or common acute illness such as upper respiratory tract infections; otitis media, pharyngitis, gastroenteritis.

End point type	Secondary

End point timeframe:

From Dose 0 through 6 months after the last primary dose or until administration of the fourth dose

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3136	1044		
Units: Subjects				
Any AEs	1336	433		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting adverse events resulting in emergency room (ER) visits

End point title	Number of subjects reporting adverse events resulting in emergency room (ER) visits

End point description:

Emergency room (ER) visits were not related to well-child care, vaccination, injury or common acute illness such as upper respiratory tract infections; otitis media, pharyngitis, gastroenteritis.

End point type	Secondary

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2769	923		
Units: Subjects				
Any AEs	137	54		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting adverse events resulting in physicians (MD) office visits

End point title	Number of subjects reporting adverse events resulting in physicians (MD) office visits

End point description:

Physicians (MD) office visits were not related to well-child care, vaccination, injury or common acute illness such as upper respiratory tract infections; otitis media, pharyngitis, gastroenteritis.

End point type	Secondary

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2769	923		
Units: Subjects				
Any AEs	668	205		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter (µg/mL)

End point title	Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter (µg/mL)

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	341	112		
Units: Subjects				
Anti-PRP [pre-dose 4] (N=341;112)	227	52		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenC and hSBA-MenY antibody titer equal to or above 1:8

End point title	Number of subjects with hSBA-MenC and hSBA-MenY antibody titer equal to or above 1:8

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

End point type	Secondary

End point timeframe:

Prior to the fourth dose vaccination

End point values	Menhibrix Group	ActHIB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	329	104		
Units: Subjects				
hSBA-MenC [pre-dose 4] (N=329;104)	318	12		
hSBA-MenY [pre-dose 4] (N=329;103)	306	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: From Day 0 after Dose 1 through the day preceding the fourth dose; From the fourth dose phase through the end of the safety follow-up; AEs: within the 31-day (Day 0-30) post vaccination period; Solicited AEs: During the 4-day post vaccination period

Adverse event reporting additional description:

Results are presented for the primary phase and the fourth dose phase.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	Menhibrix Group

Reporting group description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Reporting group title	ActHIB Group

Reporting group description:

Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

Serious adverse events	Menhibrix Group	ActHIB Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	126 / 3136 (4.02%)	50 / 1044 (4.79%)	
number of deaths (all causes)	4	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	2 / 3136 (0.06%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroblastoma			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (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	5 / 3136 (0.16%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritability			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden infant death syndrome			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Hypersensitivity (primary)			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity (fourth dose)			
subjects affected / exposed[1]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory distress (primary)			
subjects affected / exposed	5 / 3136 (0.16%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma (primary)			

subjects affected / exposed	3 / 3136 (0.10%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity (primary)			
subjects affected / exposed	3 / 3136 (0.10%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	3 / 3136 (0.10%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apparent life threatening event			
subjects affected / exposed	2 / 3136 (0.06%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnoea			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stridor			

subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing (primary)			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma (fourth dose)			
subjects affected / exposed[2]	4 / 2769 (0.14%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity (fourth dose)			
subjects affected / exposed[3]	1 / 2769 (0.04%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress (fourth dose)			
subjects affected / exposed[4]	1 / 2769 (0.04%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing (fourth dose)			
subjects affected / exposed[5]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Aspiration bronchial			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injury, poisoning and procedural complications			
Respiratory syncytial virus bronchiolitis			

subjects affected / exposed	8 / 3136 (0.26%)	2 / 1044 (0.19%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Child maltreatment syndrome			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Foreign body trauma			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury (primary)			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury (fourth dose)			
subjects affected / exposed[6]	1 / 2769 (0.04%)	2 / 923 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental drug intake by child			
subjects affected / exposed[7]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental exposure			
subjects affected / exposed[8]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns first degree			
subjects affected / exposed[9]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			

subjects affected / exposed[10]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed[11]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Seroma			
subjects affected / exposed[12]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed[13]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed[14]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Coarctation of the aorta			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberous sclerosis			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular septal defect (primary)			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular septal defect (fourth dose)			

subjects affected / exposed[15]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion (primary)			
subjects affected / exposed	2 / 3136 (0.06%)	2 / 1044 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion (primary)			
subjects affected / exposed	2 / 3136 (0.06%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar ataxia			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotonia			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile spasms			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion (fourth dose)			
subjects affected / exposed[16]	2 / 2769 (0.07%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion (fourth dose)			
subjects affected / exposed[17]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Lymphoid tissue hyperplasia			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic thrombocytopenic purpura			
subjects affected / exposed[18]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed[19]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed[20]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed[21]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dacryostenosis acquired			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intussusception			
subjects affected / exposed	4 / 3136 (0.13%)	2 / 1044 (0.19%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vomiting (primary)			
subjects affected / exposed	2 / 3136 (0.06%)	2 / 1044 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain (primary)			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain (fourth dose)			
subjects affected / exposed[22]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting (fourth dose)			
subjects affected / exposed[23]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Erythema multiforme			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash papular			
subjects affected / exposed[24]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed[25]	1 / 2769 (0.04%)	0 / 923 (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			
Gastroenteritis (primary)			
subjects affected / exposed	19 / 3136 (0.61%)	7 / 1044 (0.67%)	
occurrences causally related to treatment / all	0 / 19	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchiolitis (primary)			
subjects affected / exposed	18 / 3136 (0.57%)	5 / 1044 (0.48%)	
occurrences causally related to treatment / all	0 / 18	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media (primary)			
subjects affected / exposed	8 / 3136 (0.26%)	4 / 1044 (0.38%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection (primary)			
subjects affected / exposed	11 / 3136 (0.35%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 11	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus (primary)			
subjects affected / exposed	8 / 3136 (0.26%)	2 / 1044 (0.19%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia (primary)			

subjects affected / exposed	8 / 3136 (0.26%)	2 / 1044 (0.19%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection (primary)			
subjects affected / exposed	8 / 3136 (0.26%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	4 / 3136 (0.13%)	4 / 1044 (0.38%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious (primary)			
subjects affected / exposed	2 / 3136 (0.06%)	3 / 1044 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 3136 (0.03%)	3 / 1044 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection (primary)			
subjects affected / exposed	4 / 3136 (0.13%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis (primary)			
subjects affected / exposed	2 / 3136 (0.06%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection (primary)			
subjects affected / exposed	2 / 3136 (0.06%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral (primary)			

subjects affected / exposed	2 / 3136 (0.06%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 3136 (0.03%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral skin infection			
subjects affected / exposed	2 / 3136 (0.06%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall abscess			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess (primary)			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acarodermatitis			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis viral			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			

subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral (primary)			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Group b streptococcus neonatal sepsis			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIV infection			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia (primary)			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			

subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pertussis			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection (primary)			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhoid fever			
subjects affected / exposed	0 / 3136 (0.00%)	1 / 1044 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval abscess			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis (fourth dose)			
subjects affected / exposed[26]	5 / 2769 (0.18%)	4 / 923 (0.43%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection (fourth dose)			
subjects affected / exposed[27]	5 / 2769 (0.18%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious (fourth dose)			

subjects affected / exposed[28]	4 / 2769 (0.14%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis (fourth dose)			
subjects affected / exposed[29]	2 / 2769 (0.07%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media (fourth dose)			
subjects affected / exposed[30]	1 / 2769 (0.04%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral (fourth dose)			
subjects affected / exposed[31]	1 / 2769 (0.04%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection (fourth dose)			
subjects affected / exposed[32]	2 / 2769 (0.07%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess (fourth dose)			
subjects affected / exposed[33]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed[34]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoviral upper respiratory infection			
subjects affected / exposed[35]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis (fourth dose)			

subjects affected / exposed[36]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis of male external genital organ			
subjects affected / exposed[37]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus (fourth dose)			
subjects affected / exposed[38]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed[39]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral (fourth dose)			
subjects affected / exposed[40]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia (fourth dose)			
subjects affected / exposed[41]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection (fourth dose)			
subjects affected / exposed[42]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node abscess			
subjects affected / exposed[43]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			

subjects affected / exposed[44]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia (fourth dose)			
subjects affected / exposed[45]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed[46]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed[47]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection (fourth dose)			
subjects affected / exposed[48]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection (fourth dose)			
subjects affected / exposed[49]	1 / 2769 (0.04%)	0 / 923 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection (fourth dose)			
subjects affected / exposed[50]	0 / 2769 (0.00%)	1 / 923 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration (primary)			
subjects affected / exposed	15 / 3136 (0.48%)	2 / 1044 (0.19%)	
occurrences causally related to treatment / all	0 / 15	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			

subjects affected / exposed	2 / 3136 (0.06%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acidosis			
subjects affected / exposed	1 / 3136 (0.03%)	0 / 1044 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration (fourth dose)			
subjects affected / exposed[51]	3 / 2769 (0.11%)	2 / 923 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

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

Non-serious adverse events	Menhibrix Group	ActHIB Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3034 / 3136 (96.75%)	998 / 1044 (95.59%)	
General disorders and administration site conditions			
Pyrexia (primary)			
subjects affected / exposed	176 / 3136 (5.61%)	73 / 1044 (6.99%)	
occurrences (all)	176	73	
Pyrexia (fourth dose)			
subjects affected / exposed[52]	176 / 2769 (6.36%)	64 / 923 (6.93%)	
occurrences (all)	176	64	
Pain (primary)			
subjects affected / exposed[53]	2419 / 3088 (78.34%)	819 / 1016 (80.61%)	
occurrences (all)	2419	819	
Redness (primary)			
subjects affected / exposed[54]	2052 / 3088 (66.45%)	691 / 1016 (68.01%)	
occurrences (all)	2052	691	
Swelling (primary)			

subjects affected / exposed[55]	1707 / 3088 (55.28%)	568 / 1016 (55.91%)	
occurrences (all)	1707	568	
Drowsiness (primary)			
subjects affected / exposed[56]	2418 / 3088 (78.30%)	804 / 1015 (79.21%)	
occurrences (all)	2418	804	
Fever (primary)			
subjects affected / exposed[57]	1434 / 3089 (46.42%)	463 / 1015 (45.62%)	
occurrences (all)	1434	463	
Irritability (primary)			
subjects affected / exposed[58]	2740 / 3088 (88.73%)	926 / 1015 (91.23%)	
occurrences (all)	2740	926	
Loss of appetite (primary)			
subjects affected / exposed[59]	1764 / 3088 (57.12%)	609 / 1015 (60.00%)	
occurrences (all)	1764	609	
Pain (fourth dose)			
subjects affected / exposed[60]	1319 / 2528 (52.18%)	494 / 832 (59.38%)	
occurrences (all)	1319	494	
Redness (fourth dose)			
subjects affected / exposed[61]	1213 / 2528 (47.98%)	463 / 833 (55.58%)	
occurrences (all)	1213	463	
Swelling (fourth dose)			
subjects affected / exposed[62]	936 / 2526 (37.05%)	334 / 832 (40.14%)	
occurrences (all)	936	334	
Increase in limb circumference			
subjects affected / exposed[63]	1489 / 2769 (53.77%)	503 / 923 (54.50%)	
occurrences (all)	1489	503	
Drowsiness (fourth dose)			
subjects affected / exposed[64]	1088 / 2526 (43.07%)	381 / 830 (45.90%)	
occurrences (all)	1088	381	
Fever (fourth dose)			
subjects affected / exposed[65]	341 / 2527 (13.49%)	134 / 831 (16.13%)	
occurrences (all)	341	134	
Irritability (fourth dose)			

subjects affected / exposed[66]	1482 / 2526 (58.67%)	534 / 830 (64.34%)	
occurrences (all)	1482	534	
Loss of appetite (fourth dose)			
subjects affected / exposed[67]	825 / 2526 (32.66%)	287 / 830 (34.58%)	
occurrences (all)	825	287	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	197 / 3136 (6.28%)	65 / 1044 (6.23%)	
occurrences (all)	197	65	
Diarrhoea			
subjects affected / exposed	185 / 3136 (5.90%)	57 / 1044 (5.46%)	
occurrences (all)	185	57	
Teething (primary)			
subjects affected / exposed	180 / 3136 (5.74%)	55 / 1044 (5.27%)	
occurrences (all)	180	55	
Teething (fourth dose)			
subjects affected / exposed[68]	115 / 2769 (4.15%)	46 / 923 (4.98%)	
occurrences (all)	115	46	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	163 / 3136 (5.20%)	50 / 1044 (4.79%)	
occurrences (all)	163	50	
Nasal congestion			
subjects affected / exposed	146 / 3136 (4.66%)	53 / 1044 (5.08%)	
occurrences (all)	146	53	
Infections and infestations			
Upper respiratory tract infection (primary)			
subjects affected / exposed	524 / 3136 (16.71%)	173 / 1044 (16.57%)	
occurrences (all)	524	173	
Otitis media (primary)			
subjects affected / exposed	335 / 3136 (10.68%)	104 / 1044 (9.96%)	
occurrences (all)	335	104	
Upper respiratory tract infection (fourth dose)			

subjects affected / exposed[69]	152 / 2769 (5.49%)	50 / 923 (5.42%)	
occurrences (all)	152	50	
Otitis media (fourth dose)			
subjects affected / exposed[70]	135 / 2769 (4.88%)	47 / 923 (5.09%)	
occurrences (all)	135	47	

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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 March 2006	The aims of this trial are to demonstrate the consistency of 3 manufacturing lots of GSK Biologicals' Hib-MenCY-TT candidate vaccine in terms of immunogenicity, the immunogenicity of Hib-MenCY-TT vaccine against N. meningitidis serogroups C and Y and the non-inferiority of GSK Biologicals' Hib-MenCY-TT vaccine with respect to immunogenicity and safety compared to the control vaccine (ActHIB) when each are co-administered with Pediarix to healthy infants at 2, 4, and 6 months of age. The study will also evaluate the safety of a booster dose of Hib-MenCY-TT vaccine at 12 to 15 months of age as compared to PedvaxHIB. Finally, immunogenicity of a booster dose of Hib-MenCY-TT vaccine at 12 to 15 months co-administered with M-M-R II and Varivax will be evaluated. The booster immunogenicity will be performed on data from 2 studies: the current study and a second study with the same design, the non-US study, Hib-MenCY-TT-007/008, which is being conducted under US Investigational New Drug (IND) application.
05 October 2006	The aims of this trial are to demonstrate the consistency of 3 manufacturing lots of GSK Biologicals' Hib-MenCY-TT candidate vaccine in terms of immunogenicity, the immunogenicity of Hib-MenCY-TT vaccine against N. meningitidis serogroups C and Y and the non-inferiority of GSK Biologicals' Hib-MenCY-TT vaccine with respect to immunogenicity and safety compared to the control vaccine (ActHIB) when each are co-administered with Pediarix to healthy infants at 2, 4, and 6 months of age. The study will also evaluate the safety of a fourth dose of Hib-MenCY-TT vaccine at 12 to 15 months of age as compared to PedvaxHIB. Finally, immunogenicity of a fourth dose of Hib-MenCY-TT vaccine at 12 to 15 months coadministered with M-M-R II and Varivax will be evaluated. The M-M-R II and Varivax co-administration analysis will be performed on data from 2 studies: the current study and a second study with the same design, the non-US study, Hib-MenCY-TT-007/008, which is being conducted under US Investigational New Drug (IND) application.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported