Clinical trial results:
A Phase III, open, randomized, controlled, multicenter study to assess the safety and immunogenicity of GlaxoSmithKline's Biologicals' (GSK Biologicals) Neisseria meningitidis serogroups A, C, W-135, Y-tetanus toxoid conjugate (MenACWY-TT) vaccine as compared to GSK Biologicals' Haemophilus influenzae type b and Neisseria meningitidis serogroups C and Y-tetanus toxoid conjugate vaccine combined (Hib-MenCY-TT) in healthy toddlers 12-15 months of age who were primed at 2, 4 and 6 months of age with Hib-MenCY-TT and Pediarix®, and to assess the safety and immunogenicity of MenACWY-TT co-administered with Infanrix® in healthy toddlers 15-18 months of age who were primed with HibMenCY-TT and Pediarix® at 2, 4, and 6 months of age as compared to the administration of Infanrix® alone in healthy toddlers 15-18 months of age who were primed with ActHIB® and Pediarix® at 2, 4 and 6 months of age

Summary

EudraCT number	2012-002401-22
Trial protocol	Outside EU/EEA
Global end of trial date	17 September 2009

Results information

Result version number	v1 (current)
This version publication date	20 November 2018
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	110870,110871

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00614614
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 Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 November 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2009
Global end of trial reached?	Yes
Global end of trial date	17 September 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• Immunogenicity of a booster dose of MenACWY-TT at 12–15 months of age
• Immunogenicity of a booster dose of MenACWY-TT co-administered with Infanrix® at 15-18 months of age
• Non-inferiority of the antibody responses to diphtheria and tetanus toxoid when Infanrix® is co-administered with MenACWY-TT at 15-18 months of age compared to Infanrix® administered alone at 15-18 months of age
• Non-inferiority of the antibody responses to pertussis toxoid, filamentous hemagglutinin, and pertactin when Infanrix® is co-administered with MenACWY-TT at 15-18 months of age compared to Infanrix® administered alone
• Non-inferiority of a booster dose of MenACWY-TT com-pared to HibMenCY administered at 12–15 months of age
• Non-inferiority of a booster dose of MenACWY-TT co-administered with Infanrix® at 15-18 months of age com-pared to HibMenCY when administered at 12–15 months of age

Protection of trial subjects:

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 February 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
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: 1558

Worldwide total number of subjects	1558
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)	1558
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following was performed: informed consent was obtained and signed from parents or guardians of subjects, check for inclusion/exclusion criteria and contraindications/precautions was performed, and medical history of subjects was collected. Prior to vaccination, subjects' pre-vaccination body temperature was evaluated.

Pre-assignment period milestones

Number of subjects started	1558
Number of subjects completed	1554

Pre-assignment subject non-completion reasons

Reason: Number of subjects	No vaccination received : 4

Period 1

Period 1 title	Primary Vaccination Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

In a single-blind trial, the investigator and/or his staff are aware of the treatment assignment but the subject is not.

Arms

Are arms mutually exclusive?	Yes
Arm title	Menhibrix 1 Group

Arm description:

Subjects received 3 doses of Menhibrix + 3 doses of Pediarix® (at 2, 4 and 6 months of age)

Arm type	Experimental
Investigational medicinal product name	Menhibrix
Investigational medicinal product code	
Other name	GSK Biologicals' Hib-meningococcal vaccine GSK 792014
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses in the priming phase and at 2, 4 and 6 months of age

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

Dosage and administration details:

Three doses in the priming phase as intramuscular injection at 2, 4 and 6 months of age

Arm title	ActHIB- Infanrix Group

Arm description:	
Subjects received 3 doses of ActHIB vaccine and 3 doses of Pediarix vaccine at 2, 4 and 6 months of age	
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:	
Three doses in the priming phase as intramuscular injection at 2, 4 and 6 months of age	
Investigational medicinal product name	Pediarix®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Three doses in the priming phase as intramuscular injection at 2, 4 and 6 months of age	

Number of subjects in period 1[1]	Menhibrix 1 Group	ActHIB- Infanrix Group
Started	1272	282
Completed	1182	265
Not completed	90	17
Consent withdrawn by subject	90	17

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: A total of 1558 subjects (1276 in the Menhibrix 1 Group and 282 in ActHIB- Infanrix Group) were enrolled; however, 4 of these subjects never received the vaccine. Thus, 1554 subjects (1272 in the Menhibrix 1 Group and 282 in ActHIB- Infanrix Group) were vaccinated during primary vaccination phase.

Period 2

Period 2 title	Booster Vaccination Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix 1 Group
Arm description:	
Subjects received 1 dose of Nimenrix™ at 12-15 months of age and 1 dose of Infanrix® at 15-18 months of age	
Arm type	Experimental

Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	GSK Biologicals' Meningococcal vaccine GSK134612
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose in the booster phase as intramuscular injection at 12-15 months of age

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

Dosage and administration details:

One dose as intramuscular injection at 15-18 months of age

Arm title	Menhibrix 2 Group

Arm description:

Subjects received a fourth dose of Menhibrix at 12-15 months of age and 1 dose of Infanrix® at 15-18 months of age

Arm type	Active comparator
Investigational medicinal product name	Menhibrix
Investigational medicinal product code	
Other name	GSK Biologicals' Hib-meningococcal vaccine GSK 792014
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose as intramuscular injection at 12-15 months of age

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

Dosage and administration details:

One dose as intramuscular injection at 15-18 months of age

Arm title	Nimenrix 2 Group

Arm description:

Subjects received 1 dose of Nimenrix co-administered with 1 dose of Infanrix®, at 15-18 months of age

Arm type	Active comparator
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	GSK Biologicals' Meningococcal vaccine GSK134612
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose in the booster phase as intramuscular injection at 15-18 months of age

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

Dosage and administration details:

One dose as intramuscular injection at 15-18 months of age

Arm title	Infanrix Group

Arm description:

Subjects received 1 booster dose of ActHIB vaccine vaccine at 15-18 months of age.

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

Dosage and administration details:

One dose in the booster phase as intramuscular injection at 15-18 months of age

Number of subjects in period 2[2]	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group
Started	432	229	409
Completed	405	210	396
Not completed	27	19	13
Consent withdrawn by subject	26	18	13
Adverse event, non-fatal	1	1	-

Number of subjects in period 2[2]	Infanrix Group
Started	233
Completed	227
Not completed	6
Consent withdrawn by subject	6
Adverse event, non-fatal	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all study participants returned in time for every study visit, but they were allowed to continue the study nonetheless. The number of participants who started each study period depends on the actual rate of return of the subjects.

Baseline characteristics

Reporting groups	
Reporting group title	Menhibrix 1 Group
Reporting group description:	
Subjects received 3 doses of Menhibrix + 3 doses of Pediarix® (at 2, 4 and 6 months of age)	

Reporting group title	ActHIB- Infanrix Group
Reporting group description:	
Subjects received 3 doses of ActHIB vaccine and 3 doses of Pediarix vaccine at 2, 4 and 6 months of age	

Reporting group values	Menhibrix 1 Group	ActHIB- Infanrix Group	Total
Number of subjects	1272	282	1554
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: weeks			
arithmetic mean	8.6	8.7	
standard deviation	± 1.25	± 1.25	-
Gender categorical Units: Subjects			
Female	606	150	756
Male	666	132	798

End points

End points reporting groups

Reporting group title	Menhibrix 1 Group
Reporting group description:	
Subjects received 3 doses of Menhibrix + 3 doses of Pediarix® (at 2, 4 and 6 months of age)	

Reporting group title	ActHIB- Infanrix Group
Reporting group description:	
Subjects received 3 doses of ActHIB vaccine and 3 doses of Pediarix vaccine at 2, 4 and 6 months of age	

Reporting group title	Nimenrix 1 Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ at 12-15 months of age and 1 dose of Infanrix® at 15-18 months of age	

Reporting group title	Menhibrix 2 Group
Reporting group description:	
Subjects received a fourth dose of Menhibrix at 12-15 months of age and 1 dose of Infanrix® at 15-18 months of age	

Reporting group title	Nimenrix 2 Group
Reporting group description:	
Subjects received 1 dose of Nimenrix co-administered with 1 dose of Infanrix®, at 15-18 months of age	

Reporting group title	Infanrix Group
Reporting group description:	
Subjects received 1 booster dose of ActHIB vaccine vaccine at 15-18 months of age.	

Primary: Number of subjects with serum bactericidal activity using human complement (hSBA) antibody titers for N.meningitidis serogroups MenA, MenW-135, MenC and MenY greater than or equal to (≥) 1:8

End point title	Number of subjects with serum bactericidal activity using human complement (hSBA) antibody titers for N.meningitidis serogroups MenA, MenW-135, MenC and MenY greater than or equal to (≥) 1:8
End point description:	

End point type	Primary
End point timeframe:	
One month post vaccination at 12-15 months of age (Month 11)	

End point values	Nimenrix 1 Group	Menhibrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	291	157		
Units: Subjects				
hSBA-MenA [N=257;131]	254	1		
hSBA-MenC [N=286;155]	286	155		
hSBA-MenW-135 [N=273;137]	270	129		
hSBA-MenY [N=291;157]	291	157		

Statistical analyses

Statistical analysis title	Difference in % for hSBA-MenC antibodies
Comparison groups	Nimenrix 1 Group v Menhibrix 2 Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≥ 10
Method	t-test, 2-sided
Parameter estimate	Difference in % for hSBA-MenC antibodies
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	2.42

Statistical analysis title	Difference in % for hSBA-MenY antibodies
Comparison groups	Nimenrix 1 Group v Menhibrix 2 Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≥ 10
Method	t-test, 2-sided
Parameter estimate	Difference in % for hSBA-MenY antibodies
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	2.39

Primary: Number of subjects with hSBA-MenA, hSBA-MenW-135, hSBA-MenC and hSBA-MenY antibody titers ≥ 1:8

End point title	Number of subjects with hSBA-MenA, hSBA-MenW-135, hSBA-MenC and hSBA-MenY antibody titers ≥ 1:8

End point description:

End point type	Primary

End point timeframe:

One month post vaccination at 15-18 months of age (Month 14)

End point values	Menhibrix 2 Group	Nimenrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	303		
Units: Subjects				
hSBA-MenA [N=139;258]	1	248		
hSBA-MenC [N=147;293]	147	293		
hSBA-MenW-135 [N=140;283]	113	279		
hSBA-MenY [N=151;303]	150	303		

Statistical analyses

Statistical analysis title	Difference in % for hSBA-MenC antibodies
Comparison groups	Menhibrix 2 Group v Nimenrix 2 Group
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in % for hSBA-MenC antibodies
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	2.42

Statistical analysis title	Difference in % for hSBA-MenY antibodies
Comparison groups	Menhibrix 2 Group v Nimenrix 2 Group
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in % for hSBA-MenY antibodies
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.25
upper limit	2.39

Primary: Antibody titers for hSBA-MenC and hSBA-MenY

End point title	Antibody titers for hSBA-MenC and hSBA-MenY

End point description:

End point type	Primary

End point timeframe:

One month post vaccination at 12-15 months of age (Month 11)

End point values	Nimenrix 1 Group	Menhibrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	291	157		
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenC [N=286;155]	3845 (3310.8 to 4465.4)	2676.1 (2131.8 to 3359.5)		
hSBA-MenY [N=291;157]	4800.9 (4162 to 5537.9)	2227.7 (1881.9 to 2637)		

Statistical analyses

Statistical analysis title	Difference in % for hSBA-MenC antibodies
Comparison groups	Nimenrix 1 Group v Menhibrix 2 Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in % for hSBA-MenC antibodies
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	2.42

Statistical analysis title	Difference in % for hSBA-MenY antibodies
Comparison groups	Nimenrix 1 Group v Menhibrix 2 Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in % for hSBA-MenY antibodies
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	2.39

Primary: Antibody titers for hSBA-MenC and hSBA-MenY

End point title	Antibody titers for hSBA-MenC and hSBA-MenY

End point description:

End point type	Primary

End point timeframe:

One month post vaccination at 15-18 months of age (Month 14)

End point values	Menhibrix 2 Group	Nimenrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	303		
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenC [N=143;293]	580.4 (460.9 to 730.9)	7230.5 (6244.1 to 8372.8)		
hSBA-MenY [N=151;303]	786.7 (657.3 to 941.7)	7487.6 (6604.4 to 8488.9)		

Statistical analyses

Statistical analysis title	Difference in % for hSBA-MenC antibodies
Comparison groups	Menhibrix 2 Group v Nimenrix 2 Group
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in % for hSBA-MenC antibodies
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	2.42

Statistical analysis title	Difference in % for hSBA-MenY antibodies
Comparison groups	Menhibrix 2 Group v Nimenrix 2 Group
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in % for hSBA-MenY antibodies
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.25
upper limit	2.39

Primary: Number of subjects with Anti-Diptheria (Anti-D) and anti-Tetanus (Anti-T) antibody concentrations ≥ 1.0 International Units per milliliter (IU/mL)

End point title	Number of subjects with Anti-Diptheria (Anti-D) and anti-Tetanus (Anti-T) antibody concentrations ≥ 1.0 International Units per milliliter (IU/mL)

End point description:

End point type	Primary

End point timeframe:

One month post vaccination at 15-18 months of age (Month 14)

End point values	Nimenrix 2 Group	Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	254	146		
Units: Subjects				
Anti-D [N=254;146]	253	146		
Anti-T [N=253;146]	253	145		

Statistical analyses

Statistical analysis title	Difference in % for Anti-T antibodies
Comparison groups	Nimenrix 2 Group v Infanrix Group
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in % for Anti-T antibodies
Point estimate	0.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	3.78

Statistical analysis title	Difference in % for Anti-D antibodies
Comparison groups	Nimenrix 2 Group v Infanrix Group
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in % for Anti-T antibodies
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	2.18

Primary: Number of subjects with hSBA-MenC and hSBA-MenY antibody titers ≥ 1:8

End point title	Number of subjects with hSBA-MenC and hSBA-MenY antibody titers ≥ 1:8
End point description:	
End point type	Primary
End point timeframe:	
One month post vaccination at 12-15 months of age (Month 11)	

End point values	Nimenrix 1 Group	Menhibrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	291	157		
Units: Subjects				
hSBA-MenC [N=286;155]	285	155		
hSBA-MenY [N=291;157]	291	157		

Statistical analyses

Statistical analysis title	Difference in % for hSBA-MenC antibodies
Comparison groups	Menhibrix 2 Group v Nimenrix 1 Group

Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≥ 10
Method	t-test, 2-sided
Parameter estimate	Difference in % for hSBA-MenC antibodies
Confidence interval	
sides	2-sided
lower limit	-1.33
upper limit	2.42

Statistical analysis title	Difference in % for hSBA-MenY antibodies
Comparison groups	Menhibrix 2 Group v Nimenrix 1 Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≥ 10
Method	t-test, 2-sided
Parameter estimate	Difference in % for hSBA-MenY antibodies
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	2.39

Primary: Antibody concentrations for Anti-PT (pertusis toxoid), anti-FHA (filamentous hemagglutinin) and anti-PRN (pertactin)

End point title	Antibody concentrations for Anti-PT (pertusis toxoid), anti-FHA (filamentous hemagglutinin) and anti-PRN (pertactin)

End point description:

End point type	Primary

End point timeframe:

One month after vaccination at 15-18 months of age (Month 14)

End point values	Nimenrix 2 Group	Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	254	146		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT [N=254;146]	67.7 (62 to 73.9)	91 (81.7 to 101.4)		

Anti-FHA [N=253;146] Anti-PRN [N=253;146]	353.2 (320.8 to 388.9) 189.2 (167.2 to 214.1)	422.9 (369 to 484.6) 315.1 (274.2 to 362.1)		

Statistical analyses

Statistical analysis title	Geometric mean concentration ratio for Anti-PT
Comparison groups	Nimenrix 2 Group v Infanrix Group
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≥ 0.67
Method	t-test, 2-sided
Parameter estimate	GMC ratio
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.86

Statistical analysis title	Geometric mean concentration ratio for Anti-FHA
Comparison groups	Nimenrix 2 Group v Infanrix Group
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≥ 0.67
Method	t-test, 2-sided
Parameter estimate	GMC ratio
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.98

Statistical analysis title	Geometric mean concentration ratio for Anti-PRN
Comparison groups	Nimenrix 2 Group v Infanrix Group
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≥ 0.67
Method	t-test, 2-sided
Parameter estimate	GMC ratio

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.73

Secondary: Number of subjects with hSBA-MenC and hSBA-MenY antibody titers ≥ 1:4

End point title	Number of subjects with hSBA-MenC and hSBA-MenY antibody titers ≥ 1:4

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination at 12-15 months of age (Month 11)

End point values	Nimenrix 1 Group	Menhibrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	291	157		
Units: Subjects				
hSBA-MenC [N=286;155]	286	155		
hSBA-MenY [N=291;157]	291	157		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA and hSBA MenW-135 antibody titers ≥ 1:4

End point title	Number of subjects with hSBA-MenA and hSBA MenW-135 antibody titers ≥ 1:4

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination at 12-15 months of age (Month 11)

End point values	Nimenrix 1 Group			
Subject group type	Reporting group			
Number of subjects analysed	257			
Units: Subjects				
hSBA-MenA [N=257]	256			
hSBA-MenW-135 [N=273]	270			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers for hSBA-MenA and hSBA MenW-135

End point title	Antibody titers for hSBA-MenA and hSBA MenW-135

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination at 12-15 months of age (Month 11)

End point values	Nimenrix 1 Group			
Subject group type	Reporting group			
Number of subjects analysed	273			
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA [N=257]	94.8 (84.1 to 106.9)			
hSBA-MenW-135 [N=273]	923.9 (776 to 1099.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers for hSBA-MenC and hSBA-MenY

End point title	Antibody titers for hSBA-MenC and hSBA-MenY

End point description:

End point type	Secondary

End point timeframe:

Prior to vaccination at 15-18 months of age (Month 13)

End point values	Nimenrix 2 Group			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenC [N=268]	67.6 (55.5 to 82.3)			
hSBA-MenY [N=268]	142.3 (121.1 to 167.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenC and hSBA-MenY antibody titers ≥ 1:4 and ≥ 1:8

End point title	Number of subjects with hSBA-MenC and hSBA-MenY antibody titers ≥ 1:4 and ≥ 1:8

End point description:

End point type	Secondary

End point timeframe:

Prior to vaccination at 15-18 months of age (Month 13)

End point values	Nimenrix 2 Group			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: Subjects				
hSBA-MenC ≥ 1:4 [N=268]	243			
hSBA-MenC ≥ 1:8 [N=268]	241			
hSBA-MenY ≥ 1:4 [N=268]	258			
hSBA-MenY ≥ 1:8 [N=268]	258			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D and Anti-T geometric mean antibody concentrations

End point title	Anti-D and Anti-T geometric mean antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination with Infanrix at 15-18 months of age (Month 14) ≥ 1:4

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	252	132	254	146
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D [N=252;132;254;146]	7.214 (6.592 to 7.895)	7.36 (6.508 to 8.323)	7.458 (6.82 to 8.155)	8.259 (7.347 to 9.285)
Anti-T [N=252;132;253;146]	7.4 (6.9 to 7.936)	8.458 (7.762 to 9.215)	11.715 (10.818 to 12.765)	5.5 (4.877 to 6.204)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-D and Anti-T antibody concentrations ≥ 0.1 international units per millilitre (IU/mL)

End point title	Number of subjects with Anti-D and Anti-T antibody concentrations ≥ 0.1 international units per millilitre (IU/mL)

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination with Infanrix at 15-18 months of age (Month 14)

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	252	132	254	146
Units: Subjects				
Anti-D [N=252;132;254;146]	252	132	254	146
Anti-T [N=252;132;253;146]	252	132	253	146

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-PT, Anti-FHA and Anti-PRN concentrations to ≥ 5 enzyme-linked immunosorbent assay units per milliliter (EL.U/mL)

End point title	Number of subjects with Anti-PT, Anti-FHA and Anti-PRN concentrations to ≥ 5 enzyme-linked immunosorbent assay units per milliliter (EL.U/mL)

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination with Infanrix at 15-18 months of age (Month 14)

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	252	132	254	146
Units: Subjects				
Anti-PT [N=252;130;254;146]	252	130	254	146
Anti-FHA [N=252;132;253; 146]	252	132	253	146
Anti-PRN [N=252;132;253; 146]	251	132	253	146

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for Anti-PT, anti-FHA and anti-PRN

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

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination at 15-18 months of age (Month 14)

End point values	Nimenrix 1 Group	Menhibrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	252	132		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT [N=252;130]	73.7 (66.7 to 80.5)	86.9 (75.7 to 99.8)		
Anti-FHA [N=252;132]	321.6 (289.9 to 356.7)	371.7 (321.5 to 429.7)		

Anti-PRN [N=252;132]	203.8 (178.7 to 232.5)	220.2 (183.7 to 264)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-D and Anti-T antibody concentrations ≥ 1.0 IU/mL

End point title	Number of subjects with Anti-D and Anti-T antibody concentrations ≥ 1.0 IU/mL

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination at 15-18 months of age (Month 14)

End point values	Nimenrix 1 Group	Menhibrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	252	132		
Units: Subjects				
Anti-D [N=252;132]	250	132		
Anti-T [N=252;132]	250	132		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers ≥ 1:4

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers ≥ 1:4

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination at 15-18 months of age (Month 14)

End point values	Nimenrix 2 Group			
Subject group type	Reporting group			
Number of subjects analysed	303			
Units: Subjects				
hSBA-MenA [N= 258]	253			
hSBA-MenC [N= 293]	293			
hSBA-MenW-135 [N= 283]	279			
hSBA-MenY [N= 303]	303			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers for hSBA-MenA and hSBA-MenW-135

End point title	Antibody titers for hSBA-MenA and hSBA-MenW-135

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination with Infanrix at 15-18 months of age (Month 14)

End point values	Nimenrix 2 Group			
Subject group type	Reporting group			
Number of subjects analysed	283			
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA [N= 258]	92.4 (80.6 to 105.9)			
hSBA-MenW-135 [N= 283]	1582.9 (1321.8 to 1895.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local adverse events (AEs) following each dose with Nimenrix or Menhibrix vaccine

End point title	Number of subjects reporting any and grade 3 solicited local adverse events (AEs) following each dose with Nimenrix or Menhibrix vaccine

End point description:

End point type	Secondary

End point timeframe:

During the 8-day follow-up period (Day 0-7) after vaccination in the booster phase

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	408	217	386	
Units: Subjects				
Any pain	156	104	170	
Grade 3 pain	7	4	2	
Any redness	171	90	169	
Grade 3 redness	3	1	5	
Any swelling	97	54	105	
Grade 3 swelling	3	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general AEs in the booster phase, Dose 4

End point title	Number of subjects reporting any, grade 3 and related solicited general AEs in the booster phase, Dose 4

End point description:

End point type	Secondary

End point timeframe:

During the 8-day follow-up period (Day 0-7) after dose 4 vaccination

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	408	217	384	209
Units: Subjects				
Any drowsiness, Dose 4 [N=408;217;384; 209]	171	97	161	79
Grade3 drowsiness, Dose 4 [N=408;217;384; 209]	7	6	8	1
Related drowsiness, Dose 4 [N=408;217;384; 209]	148	80	132	62
Any fever, Dose4 [N=408;217;384; 209]	46	23	37	14
Grade3 fever, Dose 4 [N=408;217;384; 209]	2	2	1	0
Related fever, Dose 4 [N=408;217;384; 209]	32	16	23	7

Any irritability, Dose 4 [N=408;217;384; 209]	230	128	218	114
Grade3 irritability, Dose 4 [N=408;217;384; 209]	13	11	12	7
Related irritability, Dose4 [N=408;217;384; 209]	202	106	188	90
Any loss of appetite, Dose4 [N=408;217;384; 209]	144	73	138	55
Grade3 loss of appetite, Dose4 [N=408;217;384;209]	7	5	7	3
Related loss of apetite, Dose4 [N=408;217;384;209]	115	55	105	42

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general AEs in the booster phase, Dose 5

End point title	Number of subjects reporting any, grade 3 and related solicited general AEs in the booster phase, Dose 5

End point description:

End point type	Secondary

End point timeframe:

During the 8-day follow-up period (Day 0-7) after dose 5 vaccination

End point values	Nimenrix 1 Group	Menhibrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	197		
Units: Subjects				
Any drowsiness, Dose 5 [N=384;197]	132	67		
Grade3 drowsiness, Dose 5 [N=384;197]	7	6		
Related drowsiness, Dose 5 [N=384;197]	114	60		
Any fever, Dose 5 [N=384;197]	34	16		
Grade 3 fever, Dose 5 [N=384;197]	0	0		
Related fever, Dose 5 [N=384;197]	23	12		
Any irritability, Dose 5 [N=384;197]	195	103		
Grade 3 irritabity, Dose 5 [N=384;197]	12	8		
Related irritability, Dose 5 [N=384;197]	171	99		
Any loss of appetite, Dose 5 [N=384;197]	117	62		
Grade 3 loss of appetite, Dose 5 [N=384;197]	2	5		
Related loss of appetite, Dose 5 [N=384;197]	86	53		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rash

End point title	Number of subjects reporting any rash

End point description:

End point type	Secondary

End point timeframe:

From the first booster phase visit up to six months after the last vaccination (Month 10-13 up to Month 19-22)

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	432	229	409	233
Units: Subjects				
Any rash	93	54	83	40

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local adverse events (AEs) following vaccination with Infanrix vaccine

End point title	Number of subjects reporting any and grade 3 solicited local adverse events (AEs) following vaccination with Infanrix vaccine

End point description:

End point type	Secondary

End point timeframe:

During the 8-day follow-up period (Day 0-7) after vaccination in the booster phase

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	384	197	374	210
Units: Subjects				
Any pain	145	99	156	99
Grade 3 pain	5	2	4	4
Any redness	175	102	171	121
Grade 3 redness	9	5	2	4
Any swelling	114	73	113	80
Grade 3 swelling	6	5	2	5

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any New Onset of Chronic Illness (NOCI) and any Emergency Room (ER) visits

End point title	Number of subjects reporting any New Onset of Chronic Illness (NOCI) and any Emergency Room (ER) visits

End point description:

End point type	Secondary

End point timeframe:

From the first booster phase visit up to six months after the last vaccination (Month 10-13 up to Month 19-22)

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	432	229	409	233
Units: Subjects				
Any NOCI(s)	19	11	18	13
Any ER visit(s)	73	49	76	29

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any New Onset of Chronic Illness (NOCI) and any Emergency Room (ER) visits

End point title	Number of subjects reporting any New Onset of Chronic Illness (NOCI) and any Emergency Room (ER) visits

End point description:

End point type	Secondary

End point timeframe:

From the first primary study dose up to/excluding the first booster study dose (Month 0 up to Month 10-13)

End point values	Menhibrix 1 Group	ActHIB-Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1272	282		
Units: Subjects				
Any NOCI(s)	128	29		
Any ER visit(s)	293	55		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

During a 31-day follow-up period (Day 0-30) after booster vaccination

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	432	229	409	233
Units: Subjects				
Any AE(s)	194	105	182	101

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited AEs

End point title	Number of subjects reporting any unsolicited AEs

End point description:

End point type	Secondary

End point timeframe:

During the 31-day follow-up period (Day 0-30) after the second booster vaccination

End point values	Nimenrix 1 Group	Menhibrix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	432	229		
Units: Subjects				
Any AE(s)	167	79		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting any and related serious adverse events (SAEs)

End point description:

End point type	Secondary

End point timeframe:

From the first primary study dose up to/excluding the first booster study dose (Month 0 up to Month 10-13).

End point values	Menhibrix 1 Group	ActHIB-Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1272	282		
Units: Subjects				
Any SAE(s)	58	14		
Related SAE(s)	1	0		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting any and related serious adverse events (SAEs)

End point description:

End point type	Secondary

End point timeframe:

From the first booster phase visit up to 6 months after the last vaccination (Month 10-13 up to Month 19-22)

End point values	Nimenrix 1 Group	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	432	229	409	233
Units: Subjects				
Any SAE(s)	15	3	9	2
Related SAE(s)	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local, general AE(s) during (Days 0-7) and unsolicited AE(s) the 31-day period after the first booster phase vaccination at 12-15 months and single booster phase vaccination at 15-18 months. SAE(s) during the primary phase and the booster phase

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Menhibrix 1 Group

Reporting group description:

Subjects received 3 doses of Menhibrix + 3 doses of Pediarix® (at 2, 4 and 6 months of age)

Reporting group title	ActHIB- Infanrix Group

Reporting group description:

Subjects received 3 doses of ActHIB vaccine and 3 doses of Pediarix vaccine at 2, 4 and 6 months of age

Reporting group title	Nimenrix™ 1 Group

Reporting group description:

Subjects received 1 dose of Nimenrix™ (at 12-15 months of age) and 1 dose of Infanrix® (at 15-18 months of age)

Reporting group title	Menhibrix 2 Group

Reporting group description:

Subjects received a fourth dose of Menhibrix (at 12-15 months of age) and 1 dose of Infanrix® (at 15-18 months of age)

Reporting group title	Nimenrix 2 Group

Reporting group description:

Subjects received 1 dose of Nimenrix co-administered with 1 dose of Infanrix® (at 15-18 months of age)

Reporting group title	Infanrix Group

Reporting group description:

Subjects received 1 booster dose of ActHIB vaccine vaccine at 15-18 months of age.

Serious adverse events	Menhibrix 1 Group	ActHIB- Infanrix Group	Nimenrix™ 1 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	58 / 1272 (4.56%)	14 / 282 (4.96%)	15 / 432 (3.47%)
number of deaths (all causes)	4	0	0
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Leukaemia			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	3 / 1272 (0.24%)	1 / 282 (0.35%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden infant death syndrome			
subjects affected / exposed	2 / 1272 (0.16%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	2 / 1272 (0.16%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apparent life threatening event			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			

subjects affected / exposed	1 / 1272 (0.08%)	3 / 282 (1.06%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	2 / 1272 (0.16%)	1 / 282 (0.35%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status asthmaticus			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 1272 (0.00%)	1 / 282 (0.35%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			

subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	1 / 1272 (0.08%)	2 / 282 (0.71%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic brain injury			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cyanosis			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	3 / 1272 (0.24%)	1 / 282 (0.35%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 1272 (0.00%)	1 / 282 (0.35%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonia			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			

subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic uraemic syndrome			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 1272 (0.08%)	1 / 282 (0.35%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric volvulus			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin burning sensation			
subjects affected / exposed	0 / 1272 (0.00%)	1 / 282 (0.35%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Obstructive uropathy			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Floppy infant			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Beta haemolytic streptococcal infection			
subjects affected / exposed[1]	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			

subjects affected / exposed	9 / 1272 (0.71%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 1272 (0.00%)	1 / 282 (0.35%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	3 / 1272 (0.24%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			
subjects affected / exposed	4 / 1272 (0.31%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis viral			

subjects affected / exposed	0 / 1272 (0.00%)	1 / 282 (0.35%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	1 / 1272 (0.08%)	3 / 282 (1.06%)	2 / 432 (0.46%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	2 / 1272 (0.16%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 1272 (0.08%)	2 / 282 (0.71%)	3 / 432 (0.69%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 1272 (0.00%)	1 / 282 (0.35%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			

subjects affected / exposed	4 / 1272 (0.31%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	2 / 1272 (0.16%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	2 / 1272 (0.16%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 1272 (0.08%)	1 / 282 (0.35%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes oesophagitis			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative respiratory distress			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	7 / 1272 (0.55%)	2 / 282 (0.71%)	5 / 432 (1.16%)
occurrences causally related to treatment / all	0 / 7	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	1 / 1272 (0.08%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 229 (1.31%)	9 / 409 (2.20%)	2 / 233 (0.86%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Leukaemia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden infant death syndrome			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apparent life threatening event			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	1 / 233 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
subjects affected / exposed	1 / 229 (0.44%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			

subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status asthmaticus			
subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic brain injury			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Cyanosis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	2 / 229 (0.87%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Leukocytosis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 229 (0.44%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric volvulus			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Skin burning sensation			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Obstructive uropathy			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Floppy infant			
subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Beta haemolytic streptococcal infection			
subjects affected / exposed[1]	0 / 229 (0.00%)	0 / 408 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis viral			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis			

subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			

subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			
subjects affected / exposed	1 / 229 (0.44%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			

subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes oesophagitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	1 / 233 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative respiratory distress			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 229 (0.44%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 229 (0.00%)	1 / 409 (0.24%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 229 (0.00%)	2 / 409 (0.49%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	1 / 229 (0.44%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

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

Non-serious adverse events	Menhibrix 1 Group	ActHIB- Infanrix Group	Nimenrix™ 1 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	230 / 432 (53.24%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	20 / 432 (4.63%)
occurrences (all)	0	0	20
Injection site nodule			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences (all)	0	0	0
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[2]	0 / 1272 (0.00%)	0 / 282 (0.00%)	145 / 385 (37.66%)
occurrences (all)	0	0	145
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[3]	0 / 1272 (0.00%)	0 / 282 (0.00%)	175 / 385 (45.45%)
occurrences (all)	0	0	175
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	0 / 1272 (0.00%)	0 / 282 (0.00%)	114 / 385 (29.61%)
occurrences (all)	0	0	114
Drowsiness Dose 4			
alternative assessment type: Systematic			
subjects affected / exposed[5]	0 / 1272 (0.00%)	0 / 282 (0.00%)	171 / 408 (41.91%)
occurrences (all)	0	0	171
Fever Dose 4			
alternative assessment type: Systematic			
subjects affected / exposed[6]	0 / 1272 (0.00%)	0 / 282 (0.00%)	46 / 408 (11.27%)
occurrences (all)	0	0	46
Irritability Dose 4			

subjects affected / exposed[7]	0 / 1272 (0.00%)	0 / 282 (0.00%)	230 / 408 (56.37%)
occurrences (all)	0	0	230
Loss of appetite Dose 4			
subjects affected / exposed[8]	0 / 1272 (0.00%)	0 / 282 (0.00%)	144 / 408 (35.29%)
occurrences (all)	0	0	144
Drowsiness Dose 5			
subjects affected / exposed[9]	0 / 1272 (0.00%)	0 / 282 (0.00%)	132 / 384 (34.38%)
occurrences (all)	0	0	132
Fever Dose 5			
alternative assessment type: Systematic			
subjects affected / exposed[10]	0 / 1272 (0.00%)	0 / 282 (0.00%)	34 / 384 (8.85%)
occurrences (all)	0	0	34
Irritability Dose 5			
alternative assessment type: Systematic			
subjects affected / exposed[11]	0 / 1272 (0.00%)	0 / 282 (0.00%)	195 / 384 (50.78%)
occurrences (all)	0	0	195
Loss of appetite Dose 5			
subjects affected / exposed[12]	0 / 1272 (0.00%)	0 / 282 (0.00%)	117 / 384 (30.47%)
occurrences (all)	0	0	117
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	12 / 432 (2.78%)
occurrences (all)	0	0	12
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	20 / 432 (4.63%)
occurrences (all)	0	0	20
Teething			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	19 / 432 (4.40%)
occurrences (all)	0	0	19
vomiting			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	7 / 432 (1.62%)
occurrences (all)	0	0	7
Respiratory, thoracic and mediastinal disorders			

Rhinorrhoea			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	13 / 432 (3.01%)
occurrences (all)	0	0	13
Cough			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	19 / 432 (4.40%)
occurrences (all)	0	0	19
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Otitis media			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	54 / 432 (12.50%)
occurrences (all)	0	0	54
Upper respiratory tract			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	34 / 432 (7.87%)
occurrences (all)	0	0	34
Viral infection			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	12 / 432 (2.78%)
occurrences (all)	0	0	12
Rhinitis			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 1272 (0.00%)	0 / 282 (0.00%)	0 / 432 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Menhibrix 2 Group	Nimenrix 2 Group	Infanrix Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	128 / 229 (55.90%)	218 / 409 (53.30%)	121 / 233 (51.93%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 229 (1.31%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	3	0	0

Injection site nodule			
subjects affected / exposed	4 / 229 (1.75%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	4	0	0
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[2]	99 / 197 (50.25%)	156 / 374 (41.71%)	99 / 210 (47.14%)
occurrences (all)	99	156	99
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[3]	102 / 197 (51.78%)	171 / 374 (45.72%)	121 / 210 (57.62%)
occurrences (all)	102	171	121
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	73 / 197 (37.06%)	113 / 374 (30.21%)	80 / 210 (38.10%)
occurrences (all)	73	113	80
Drowsiness Dose 4			
alternative assessment type: Systematic			
subjects affected / exposed[5]	97 / 217 (44.70%)	161 / 384 (41.93%)	79 / 209 (37.80%)
occurrences (all)	97	161	79
Fever Dose 4			
alternative assessment type: Systematic			
subjects affected / exposed[6]	23 / 217 (10.60%)	37 / 384 (9.64%)	14 / 209 (6.70%)
occurrences (all)	23	37	14
Irritability Dose 4			
subjects affected / exposed[7]	128 / 217 (58.99%)	218 / 384 (56.77%)	114 / 209 (54.55%)
occurrences (all)	128	218	114
Loss of appetite Dose 4			
subjects affected / exposed[8]	73 / 217 (33.64%)	138 / 384 (35.94%)	55 / 209 (26.32%)
occurrences (all)	73	138	55
Drowsiness Dose 5			
subjects affected / exposed[9]	67 / 197 (34.01%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	67	0	0
Fever Dose 5			
alternative assessment type: Systematic			

subjects affected / exposed[10]	16 / 197 (8.12%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	16	0	0
Irritability Dose 5			
alternative assessment type: Systematic			
subjects affected / exposed[11]	103 / 197 (52.28%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	103	0	0
Loss of appetite Dose 5			
subjects affected / exposed[12]	62 / 197 (31.47%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	62	0	0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 229 (3.93%)	20 / 409 (4.89%)	8 / 233 (3.43%)
occurrences (all)	9	20	8
Teething			
subjects affected / exposed	8 / 229 (3.49%)	18 / 409 (4.40%)	10 / 233 (4.29%)
occurrences (all)	8	18	10
vomiting			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	11 / 229 (4.80%)	13 / 409 (3.18%)	7 / 233 (3.00%)
occurrences (all)	11	13	7
Cough			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	9 / 229 (3.93%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	9	0	0
Infections and infestations			

Otitis media			
subjects affected / exposed	24 / 229 (10.48%)	36 / 409 (8.80%)	11 / 233 (4.72%)
occurrences (all)	24	36	11
Upper respiratory tract			
subjects affected / exposed	22 / 229 (9.61%)	36 / 409 (8.80%)	11 / 233 (4.72%)
occurrences (all)	22	36	11
Viral infection			
subjects affected / exposed	0 / 229 (0.00%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	3 / 229 (1.31%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	3	0	0
Nasopharyngitis			
subjects affected / exposed	5 / 229 (2.18%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	5	0	0
Gastroenteritis			
subjects affected / exposed	4 / 229 (1.75%)	0 / 409 (0.00%)	0 / 233 (0.00%)
occurrences (all)	4	0	0

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their

symptom sheets completed.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 June 2008	Amendment 1 • To allow for increase in enrollment up to approximately 1548 subjects, due to revised assumptions on the percentage of subjects that will be unevaluable or will withdraw. It is planned to monitor the number of evaluable subjects on an ongoing basis throughout the study. If the assumptions for the sample size are found to be inaccurate, the enrollment may be adjusted accordingly. • To remove the PedvaxHIB® booster from the study, in line with CDC recommendations to defer the booster due to a shortage of Hib vaccine in the US, and alter the study design, objectives and endpoints accordingly. • To eliminate testing of samples by rSBA and anti-capsular polysaccharide ELISA. • To specify that subjects in the Control group will be offered the opportunity to receive a dose of Menactra once they reach 2 years of age. This will occur outside of the study, however Menactra will be supplied for these subjects. • To change the primary endpoint from hSBA titers 1:4 to hSBA titers 1:8, in line with FDA-recommended revisions in the Hib-MenCY-TT program. • To revise the criteria for demonstrating immunogenicity of MenACWY as compared to HibMenCY with respect to Neisseria meningitidis serogroups C and Y, in line with FDA recommendations for the HibMenCY program. • To specify that the first booster vaccination at Visit 4 should be given to subjects between 12 and 15 months of age, independent of the time since the last primary vaccination and to collect all SAEs prior to Visit 4 in the primary phase. • To specify that the second booster vaccination at Visit 6 must be given to subjects who are between 15 and 18 months of age and >30 days since the last booster vaccination at Visit 4. Both the criterion with respect to subject age and time since first booster vaccination (when applicable, i.e. in the HibMenCY and MenACWY groups) must be met.
20 June 2008	Amendment 1 • To specify that the interval for post-vaccination blood draw visits 5 and 7 can be 21-48 days following vaccination, although returning after 30 days is strongly encouraged. • To allow injection of vaccines in the booster phase in the arm or the leg. • To specify that subjects will be informed retrospectively what their treatment group assignment was in the primary phase after completion of the primary phase of the study (at Visit 4 or at the ESFU contact for the primary phase). • To remove checking for elimination criteria at the ESFU contacts. • To add exclusion criteria for entry into the booster phase. • To adjust wording allowing for diluent for Hib-MenCY-TT to be in supplied either in a monodose vial or a syringe. • To add in an exploratory analysis comparing the ratio of post-booster hSBA GMTs at Visit 7 for the Infanrix co-ad group (where MenACWY-TT is co-administered with Infanrix) and at Visit 5 for the MenACWY group. • To clarify in the study design when concomitant vaccinations can be administered. To clarify in the table of study procedures for the booster phase which concomitant medications/vaccinations must be recorded in the eCRF.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported