Clinical trial results:
A phase II, open, multi-center study to evaluate the long-term anti-body persistence at 1 year, 3 years and 5 years after the administration of one or two doses of GlaxoSmithKline (GSK) Biologicals' meningococcal serogroups A, C, W-135, Y-tetanus toxoid conjugate (MenACWY-TT) vaccine in healthy toddlers at 9-12 months of age, and to evaluate the safety and immunogenicity of a booster dose of MenACWY-TT administered 5 years post-primary vaccination and of a primary vaccination of MenACWY-TT in a newly enrolled group, aged 5-6 years, as a naïve control.

Summary

EudraCT number	2012-002719-24
Trial protocol	Outside EU/EEA
Global end of trial date	28 March 2014

Results information

Result version number	v1
This version publication date	10 March 2016
First version publication date	02 July 2015

Trial information

Trial identification

Sponsor protocol code	112021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00718666
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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	15 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 November 2013
Global end of trial reached?	Yes
Global end of trial date	28 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To evaluate the long-term persistence of the immunogenicity induced by one or two doses of MenACWY-TT vaccine administered at 12 months or 9 and 12 months of age in terms of the percentage of subjects with N. meningitidis serogroup A (MenA), N. meningitidis serogroup C (MenC), N. meningitidis serogroup W-135 (MenW-135), and N. meningitidis serogroup Y (MenY) antibody titers >= 1:8 as measured by a serum bactericidal assay using human complement (hSBA).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 October 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 387
Worldwide total number of subjects	387
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)	0
Children (2-11 years)	387
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

Period 1 title	Persistence Phase Year 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix 1 Group Y1

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One intramuscular injection in the deltoid of non-dominant arm.

Arm title	Nimenrix 2 Group Y1

Arm description: -

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

Dosage and administration details:

One intramuscular injection in the deltoid of non-dominant arm.

Number of subjects in period 1[1]	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1
Started	118	130
Completed	118	130

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: 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.

Period 2

Period 2 title	Persistence Phase Year 3
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 Y3

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One intramuscular injection in the deltoid of non-dominant arm.

Arm title	Nimenrix 2 Group Y3

Arm description: -

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

Dosage and administration details:

One intramuscular injection in the deltoid of non-dominant arm.

Number of subjects in period 2[2]	Nimenrix 1 Group Y3	Nimenrix 2 Group Y3
Started	98	104
Completed	98	104

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.

Period 3

Period 3 title	Persistence Phase Year 5
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 Y5

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One intramuscular injection in the deltoid of non-dominant arm.

Arm title	Nimenrix 2 Group Y5

Arm description: -

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

Dosage and administration details:

One intramuscular injection in the deltoid of non-dominant arm.

Number of subjects in period 3[3]	Nimenrix 1 Group Y5	Nimenrix 2 Group Y5
Started	70	82
Completed	70	82

Notes:

[3] - 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.

Period 4

Period 4 title	Booster Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Nimenrix 1 Booster Group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: One intramuscular injection in the deltoid of non-dominant arm.	
Arm title	Nimenrix 2 Booster Group
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: One intramuscular injection in the deltoid of non-dominant arm.	
Arm title	Nimenrix Naive Group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: One intramuscular injection in the deltoid of non-dominant arm.	

Number of subjects in period 4	Nimenrix 1 Booster Group	Nimenrix 2 Booster Group	Nimenrix Naive Group
Started	38	46	68
Completed	36	46	94
Not completed	2	0	6
Consent withdrawn by subject	-	-	1
Lost to follow-up	1	-	4
Request no active participation but phone calls ok	-	-	1
Declined v-4 serology	1	-	-
Joined	0	0	32
Harmonization of subject numbers between periods	-	-	32

Baseline characteristics

Reporting groups	
Reporting group title	Nimenrix 1 Group Y1
Reporting group description: -	
Reporting group title	Nimenrix 2 Group Y1
Reporting group description: -	

Reporting group values	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1	Total
Number of subjects	118	130	248
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: months			
arithmetic mean	24.5	24.6	
standard deviation	± 0.97	± 1	-
Gender categorical Units: Subjects			
Female	56	66	122
Male	62	64	126

End points

End points reporting groups

Reporting group title	Nimenrix 1 Group Y1
Reporting group description: -	
Reporting group title	Nimenrix 2 Group Y1
Reporting group description: -	
Reporting group title	Nimenrix 1 Group Y3
Reporting group description: -	
Reporting group title	Nimenrix 2 Group Y3
Reporting group description: -	
Reporting group title	Nimenrix 1 Group Y5
Reporting group description: -	
Reporting group title	Nimenrix 2 Group Y5
Reporting group description: -	
Reporting group title	Nimenrix 1 Booster Group
Reporting group description: -	
Reporting group title	Nimenrix 2 Booster Group
Reporting group description: -	
Reporting group title	Nimenrix Naive Group
Reporting group description: -	

Primary: Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values.

End point title	Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values.[1]

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8.

End point type	Primary

End point timeframe:

At Year 1 after primary vaccination.

Notes:

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

End point values	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	120		
Units: Subjects				
hSBA-MenA, M12, ≥ 1:8 (N=102; 108)	21	28		
hSBA-MenC, M12 ≥ 1:8 (N=104; 113)	91	103		
hSBA-MenW-135, M12 ≥ 1:8 (N=104; 112)	93	111		
hSBA-MenY, M12 ≥ 1:8 (N=110; 120)	88	111		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values.

End point title	Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values.[2]

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8.

End point type	Primary

End point timeframe:

At Year 3 after primary vaccination.

Notes:

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

End point values	Nimenrix 1 Group Y3	Nimenrix 2 Group Y3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	97		
Units: Subjects				
hSBA-MenA, M36, ≥ 1:8 (N=82; 96)	14	16		
hSBA-MenC, M36 ≥ 1:8 (N=81; 94)	57	68		
hSBA-MenW-135, M36 ≥ 1:8 (N=86; 97)	54	82		
hSBA-MenY, M36 ≥ 1:8 (N=85; 95)	53	59		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values.

End point title	Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values.[3]

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8.

End point type	Primary

End point timeframe:

At Year 5 after primary vaccination.

Notes:

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

End point values	Nimenrix 1 Group Y5	Nimenrix 2 Group Y5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	72		
Units: Subjects				
hSBA-MenA, M60, ≥ 1:8 (N=63; 71)	20	27		
hSBA-MenC, M60 ≥ 1:8 (N=60; 71)	45	53		
hSBA-MenW-135, M60 ≥ 1:8 (N=61; 72)	40	62		
hSBA-MenY, M60 ≥ 1:8 (N=50; 63)	32	49		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY titers equal to or above the cut-off values.

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY titers equal to or above the cut-off values.

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:4.

End point type	Secondary

End point timeframe:

At Year 1 after primary vaccination.

End point values	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	120		
Units: Subjects				
hSBA-MenA, M12, ≥ 1:4 (N=102; 108)	23	29		
hSBA-MenC, M12 ≥ 1:4 (N=104; 113)	91	103		
hSBA-MenW-135, M12 ≥ 1:4 (N=104; 112)	93	111		
hSBA-MenY, M12 ≥ 1:4 (N=110; 120)	89	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY titers equal to or above the cut-off values.

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY titers equal to or above the cut-off values.

End point description:

End point type	Secondary

End point timeframe:

At Year 3 after primary vaccination.

End point values	Nimenrix 1 Group Y3	Nimenrix 2 Group Y3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	97		
Units: Subjects				
hSBA-MenA, M36, ≥ 1:4 (N=82; 96)	14	19		
hSBA-MenC, M36 ≥ 1:4 (N=81; 94)	59	69		
hSBA-MenW-135, M36 ≥ 1:4 (N=86; 97)	54	82		
hSBA-MenY, M36 ≥ 1:4 (N=85; 95)	53	59		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY titers equal to or above the cut-off values.

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY titers equal to or above the cut-off values.

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:4.

End point type	Secondary

End point timeframe:

At Year 5 after primary vaccination.

End point values	Nimenrix 1 Group Y5	Nimenrix 2 Group Y5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	72		
Units: Subjects				
hSBA-MenA, M60, ≥ 1:4 (N=63; 71)	20	27		
hSBA-MenC, M60 ≥ 1:4 (N=60; 71)	47	56		
hSBA-MenW-135, M60 ≥ 1:4 (N=61; 72)	40	62		
hSBA-MenY, M60 ≥ 1:4 (N=50; 63)	32	49		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers.

End point title	hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers.

End point description:

End point type	Secondary

End point timeframe:

At Year 1 after primary vaccination.

End point values	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	120		
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA, M12 (N=102; 108)	3.7 (2.9 to 4.8)	4.1 (3.2 to 5.2)		
hSBA-MenC, M12 (N=104; 113)	70.5 (50.4 to 98.5)	72.4 (53.3 to 98.4)		
hSBA-MenW-135, M12 (N=104; 112)	127.9 (87.3 to 187.3)	204.6 (163.6 to 255.9)		
hSBA-MenY, M12 (N=110; 120)	55.6 (38.1 to 81.1)	86.2 (65.8 to 112.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers.

End point title	hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY

	antibody titers.

End point description:

End point type	Secondary

End point timeframe:

At Year 3 after primary vaccination.

End point values	Nimenrix 1 Group Y3	Nimenrix 2 Group Y3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	97		
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA, M36 (N=82; 96)	3.5 (2.6 to 4.6)	3.4 (2.7 to 4.3)		
hSBA-MenC, M36 (N=81; 94)	31.2 (18.9 to 51.6)	29.8 (18.9 to 47)		
hSBA-MenW-135, M36 (N=86; 97)	29 (18 to 46.9)	63.9 (44 to 92.8)		
hSBA-MenY, M36 (N=85; 95)	22 (14 to 34.5)	20.5 (13.6 to 30.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers.

End point title	hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers.

End point description:

End point type	Secondary

End point timeframe:

At Year 5 after primary vaccination.

End point values	Nimenrix 1 Group Y5	Nimenrix 2 Group Y5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	72		
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA, M60 (N=63; 71)	4.6 (3.3 to 6.3)	6.6 (4.5 to 9.8)		
hSBA-MenC, M60 (N=60; 71)	40.7 (22.7 to 73.1)	38.2 (22.5 to 64.9)		

hSBA-MenW-135, M60 (N=61; 72)	24.2 (14.4 to 40.7)	53.7 (35.8 to 80.4)		
hSBA-MenY, M60 (N=50; 63)	26 (14.1 to 47.8)	37.9 (24.3 to 59.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with titers ≥ 1:8 and ≥ 1:128 for meningococcal polysaccharides A , C, W-135 and Y serum bactericidal antibodies, using baby rabbit complement for assay (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY).

End point title	Number of subjects with titers ≥ 1:8 and ≥ 1:128 for meningococcal polysaccharides A , C, W-135 and Y serum bactericidal antibodies, using baby rabbit complement for assay (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY).

End point description:

rSBA antibody titers were assessed for the rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8 and 1:128.

End point type	Secondary

End point timeframe:

At Year 1 persistence.

End point values	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	114		
Units: Subjects				
rSBA-MenA, M12 ≥ 1:8 (N=95; 104)	90	101		
rSBA-MenA, M12 ≥ 1:128 (N=95; 104)	71	80		
rSBA-MenC, M12 ≥ 1:8 (N=95; 112)	83	96		
rSBA-MenC, M12 ≥ 1:128 (N=95; 112)	46	54		
rSBA-MenW-135, M12 ≥ 1:8 (N=101;114)	97	114		
rSBA-MenW-135, M12 ≥ 1:128 (N=101;114)	82	89		
rSBA-MenY, M12 ≥ 1:8 (N=101; 113)	96	113		
rSBA-MenY, M12 ≥ 1:128 (N=101; 113)	85	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with titers ≥ 1:8 and ≥ 1:128 for meningococcal polysaccharides A , C, W-135 and Y serum bactericidal antibodies, using baby rabbit complement for assay (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY).

End point title	Number of subjects with titers ≥ 1:8 and ≥ 1:128 for meningococcal polysaccharides A , C, W-135 and Y serum

	bactericidal antibodies, using baby rabbit complement for assay (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY).

End point description:

rSBA antibody titers were assessed for the rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8 and 1:128.

End point type	Secondary

End point timeframe:

At Year 3 persistence.

End point values	Nimenrix 1 Group Y3	Nimenrix 2 Group Y3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	89		
Units: Subjects				
rSBA-MenA, M36 ≥ 1:4 (N=69;84)	65	82		
rSBA-MenA, M36 ≥ 1:128 (N=69;84)	51	65		
rSBA-MenC, M36 ≥ 1:4 (N=68;89)	60	75		
rSBA-MenC, M36 ≥ 1:128 (N=68;89)	32	40		
rSBA-MenW-135, M36 ≥ 1:4 (N=72;88)	68	88		
rSBA-MenW-135, M36 ≥ 1:128 (N=72;88)	56	69		
rSBA-MenY, M36 ≥ 1:4 (N=73;89)	69	89		
rSBA-MenY, M36 ≥ 1:128 (N=73;89)	62	78		

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA antibody titers.

End point title	rSBA antibody titers.

End point description:

End point type	Secondary

End point timeframe:

At Year 1 persistence.

End point values	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	114		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA, M12 (N=95; 104)	259.7 (191.4 to 352.3)	237.2 (187 to 301)		

rSBA-MenC, M12 (N=95; 112)	94.1 (67.1 to 131.9)	90.3 (65.5 to 124.4)		
rSBA-MenW-135, M12 (N=101; 114)	385.2 (286.4 to 518.1)	345.3 (280.1 to 425.8)		
rSBA-MenY, M12 (N=101; 113)	364.5 (273.7 to 485.4)	342.2 (284.5 to 411.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA antibody titers.

End point title	rSBA antibody titers.

End point description:

End point type	Secondary

End point timeframe:

At Year 3 persistence.

End point values	Nimenrix 1 Group Y3	Nimenrix 2 Group Y3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	89		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA, M36 (N=69; 84)	247.9 (173.8 to 353.7)	241.8 (185.6 to 315)		
rSBA-MenC, M36 (N=68; 89)	87 (59.3 to 127.8)	76.4 (53.5 to 109)		
rSBA-MenW-135, M36 (N=72; 88)	353.3 (240 to 520.1)	358 (282.8 to 453.3)		
rSBA-MenY, M36 (N=73; 89)	360.5 (253.4 to 512.9)	341.4 (276.9 to 421.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY titers equal to or above the cut-off values.

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY titers equal to or above the cut-off values.

End point description:

rSBA antibody titers were assessed for the rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8 and 1:128 (PHE laboratory assay).

End point type	Secondary

End point timeframe:

At Year 3 post-primary vaccination.

End point values	Nimenrix 1 Group Y3	Nimenrix 2 Group Y3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	98		
Units: Subjects				
rSBA-MenA, M36, ≥ 1:8 (N=83; 97)	38	44		
rSBA-MenA, M36, ≥ 1:128 (N=83; 97)	23	24		
rSBA-MenC, M36, ≥ 1:8 (N=83; 97)	27	30		
rSBA-MenC, M36, ≥ 1:128 (N=83; 97)	18	15		
rSBA-MenW-135, M36, ≥ 1:8 (N=83; 95)	36	35		
rSBA-MenW-135, M36, ≥ 1:128 (N=83; 95)	24	23		
rSBA-MenY, M36, ≥ 1:8 (N=83; 98)	39	45		
rSBA-MenY, M36, ≥ 1:128 (N=83; 98)	21	24		

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY antibody titers.

End point title	rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY antibody titers.

End point description:

Titers are given as geometric mean titers (GMTs) for the serogroups rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY respectively.

End point type	Secondary

End point timeframe:

At Year 3 post-primary vaccination.

End point values	Nimenrix 1 Group Y3	Nimenrix 2 Group Y3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	98		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA, M36 (N=83; 97)	18.4 (12 to 28.3)	16.6 (11.3 to 24.3)		
rSBA-MenC, M36 (N=83; 97)	13.2 (8.6 to 20.2)	10.6 (7.4 to 15)		
rSBA-MenW-135, M36 (N=83; 95)	19.4 (12.3 to 30.6)	14.6 (9.7 to 21.8)		

rSBA-MenY, M36 (N=83; 98)	19.6 (12.7 to 30.1)	16.7 (11.5 to 24.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody to Polysacccharide N. meningitidis Serogroup A, C, W-135 and Y (anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY) antibody concentrations.

End point title	Antibody to Polysacccharide N. meningitidis Serogroup A, C, W-135 and Y (anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY) antibody concentrations.

End point description:

End point type	Secondary

End point timeframe:

At Year 1 post-primary vaccination.

End point values	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	120		
Units: µg/ml				
geometric mean (confidence interval 95%)				
Anti-PSA, M12 (N=103; 120)	0.45 (0.36 to 0.58)	0.33 (0.28 to 0.4)		
Anti-PSC, M12 (N=102; 114)	0.27 (0.22 to 0.32)	0.25 (0.22 to 0.3)		
Anti-PSW-135, M12 (N=99; 113)	0.96 (0.74 to 1.25)	1.2 (1 to 1.44)		
Anti-PSY, M12 (N=98; 117)	1.41 (1.07 to 1.85)	1.7 (1.43 to 2.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY above the cut-off values.

End point title	Number of subjects with anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY above the cut-off values.

End point description:

End point type	Secondary

End point timeframe:

At Year 1 post-primary vaccination.

End point values	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	120		
Units: Subjects				
Anti-PSA, M12, ≥0.3 µg/ml (N=103; 120)	60	59		
Anti-PSA, M12, ≥2.0 µg/ml (N=103; 120)	12	6		
Anti-PSC, M12, ≥0.3 µg/ml (N=102; 114)	36	39		
Anti-PSC, M12, ≥2.0 µg/ml (N=102; 114)	3	4		
Anti-PSW-135, M12, ≥0.3 µg/ml (N=99; 113)	78	104		
Anti-PSW-135, M12, ≥2.0 µg/ml (N=99; 113)	28	29		
Anti-PSY, M12, ≥0.3 µg/ml (N=98; 117)	84	114		
Anti-PSY, M12, ≥2.0 µg/ml (N=98; 117)	45	50		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY titers above the cut-off values.

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY titers above the cut-off values.

End point description:

End point type	Secondary

End point timeframe:

At Year 5 pre-vaccination (naïve control group - Month 60)

End point values	Nimenrix Naive Group			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Subjects				
hSBA-MenA, PRE(M60), ≥ 1:4	16			
hSBA-MenA, PRE(M60), ≥ 1:8	16			
hSBA-MenC, PRE(M60), ≥ 1:4	28			
hSBA-MenC, PRE(M60), ≥ 1:8	24			
hSBA-MenW-135, PRE(M60), ≥ 1:4	28			

hSBA-MenW-135, PRE(M60), ≥ 1:8	28			
hSBA-MenY, PRE(M60), ≥ 1:4	29			
hSBA-MenY, PRE(M60), ≥ 1:8	29			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY titers.

End point title	hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY titers.

End point description:

End point type	Secondary

End point timeframe:

At Year 5 pre-vaccination (naïve control group - Month 60)

End point values	Nimenrix Naive Group			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA, PRE(M60)	3.3 (2.6 to 4.1)			
hSBA-MenC, PRE(M60)	5.3 (3.9 to 7.3)			
hSBA-MenW-135, PRE(M60)	7 (4.7 to 10.4)			
hSBA-MenY, PRE(M60)	9.5 (5.9 to 15.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY titers above the cut-off values.

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY titers above the cut-off values.

End point description:

End point type	Secondary

End point timeframe:

At Year 5, 1 month post-primary vaccination (naïve control group) and booster vaccination.

End point values	Nimenrix 1 Booster Group	Nimenrix 2 Booster Group	Nimenrix Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	38	79	
Units: Subjects				
rSBA-MenA, PRE[M60], ≥1:4 (N=32; 35; 79)	11	10	16	
rSBA-MenA, PRE[M60], ≥1:8 (N=32; 35; 79)	11	10	16	
rSBA-MenA, POST[M61], ≥1:4 (N=31; 38; 79)	31	38	62	
rSBA-MenA, POST[M61], ≥1:8 (N=31; 38; 79)	31	38	62	
rSBA-MenC, PRE[M60], ≥1:4 (N=30; 35; 71)	24	29	28	
rSBA-MenC, PRE[M60], ≥1:8 (N=30; 35; 71)	23	28	24	
rSBA-MenC, POST[M61], ≥1:4 (N=32; 37; 77)	32	37	68	
rSBA-MenC, POST[M61], ≥1:8 (N=32; 37; 77)	32	37	66	
rSBA-MenW-135, PRE[M60], ≥1:4 (N=31; 35; 77)	21	31	28	
rSBA-MenW-135, PRE[M60], ≥1:8 (N=31; 35; 77)	21	31	28	
rSBA-MenW-135, POST[M61], ≥1:4 (N=32; 38; 78)	32	38	70	
rSBA-MenW-135, POST[M61], ≥1:8 (N=32; 38; 78)	32	38	70	
rSBA-MenY, PRE[M60], ≥1:4 (N=26; 31; 69)	17	25	29	
rSBA-MenY, PRE[M60], ≥1:8 (N=26; 31; 69)	17	25	29	
rSBA-MenY, POST[M61], ≥1:4 (N=32; 38; 70)	32	38	66	
rSBA-MenY, POST[M61], ≥1:8 (N=32; 38; 70)	32	38	66	

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY titers.

End point title	hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY titers.

End point description:

End point type	Secondary

End point timeframe:

1 month post primary (naïve control group) and booster vaccination.

End point values	Nimenrix 1 Booster Group	Nimenrix 2 Booster Group	Nimenrix Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	38	79	
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA, PIM61 (N=0;0;79)	0 (0 to 0)	0 (0 to 0)	38.3 (25.4 to 57.9)	
hSBA-MenA, PIIM61 (N=31;0;0)	1395.9 (926 to 2104.4)	0 (0 to 0)	0 (0 to 0)	
hSBA-MenA, PIIIM61 (N=0;38;0)	0 (0 to 0)	1590.1 (1157.4 to 2184.6)	0 (0 to 0)	
hSBA-MenC, PIM61 (N=0;0;77)	0 (0 to 0)	0 (0 to 0)	95.3 (56.5 to 160.9)	
hSBA-MenC, PIIM61 (N=32;0;0)	8185.7 (4736.9 to 14145.4)	0 (0 to 0)	0 (0 to 0)	
hSBA-MenC, PIIIM61 (N=0;37;0)	0 (0 to 0)	12881.2 (8549.1 to 19408.4)	0 (0 to 0)	
hSBA-MenW-135, PIM61 (N=0;0;78)	0 (0 to 0)	0 (0 to 0)	98.1 (65.8 to 146)	
hSBA-MenW-135, PIIM61 (N=32;0;0)	15800.9 (12975.8 to 19241)	0 (0 to 0)	0 (0 to 0)	
hSBA-MenW-135, PIIIM61 (N=0;38;0)	0 (0 to 0)	20495.9 (16080.2 to 26124.3)	0 (0 to 0)	
hSBA-MenY, PIM61 (N=0;0;70)	0 (0 to 0)	0 (0 to 0)	198.7 (137.6 to 287)	
hSBA-MenY, PIIM61 (N=32;0;0)	8809.1 (6926.3 to 11203.9)	0 (0 to 0)	0 (0 to 0)	
hSBA-MenY, PIIIM61 (N=0;38;0)	0 (0 to 0)	10513.8 (7933.6 to 13933.2)	0 (0 to 0)	

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.

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers.

End point description:

For initially seronegative subjects (pre-vaccination titer < 1:4): hSBA post-vaccination antibody titers ≥ 1:8 and for seropositive subjects (pre-vaccination titers ≥ 1:4): hSBA antibody titers at least four times the pre-vaccination antibody titers, 1 month after vaccination).

End point type	Secondary

End point timeframe:

1 month post primary (naïve control group) and booster vaccination.

End point values	Nimenrix 1 Booster Group	Nimenrix 2 Booster Group	Nimenrix Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	35	77	
Units: Subjects				
hSBA-MenA, (N=31; 35; 77)	31	35	56	
hSBA-MenC, (N=30; 34; 68)	28	31	48	
hSBA-MenW-135, (N=31; 35; 74)	31	35	48	
hSBA-MenY, (N=26; 31; 61)	26	31	48	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited local symptom.

End point title	Number of subjects reporting any solicited local symptom.

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-primary (naïve control group) and booster vaccination.

End point values	Nimenrix 1 Booster Group	Nimenrix 2 Booster Group	Nimenrix Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	45	89	
Units: Subjects				
Any Pain	18	21	46	
Any Redness	10	15	22	
Any Swelling	8	9	21	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited general symptom.

End point title	Number of subjects reporting any solicited general symptom.

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-primary (naïve control group) and booster vaccination.

End point values	Nimenrix 1 Booster Group	Nimenrix 2 Booster Group	Nimenrix Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	45	89	
Units: Subjects				
Any Fatigue	10	7	18	
Any Gastrointestinal	4	5	7	
Any Headache	4	5	11	
Any Fever (Axillary)	1	2	5	

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 the 31-day (Days 0-30) post-primary (naïve control group) and booster vaccination.

End point values	Nimenrix 1 Booster Group	Nimenrix 2 Booster Group	Nimenrix Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	46	100	
Units: Subjects				
Any AE(s)	9	6	29	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

Days 0-180 post-primary (naïve control group) and booster vaccination.

End point values	Nimenrix 1 Booster Group	Nimenrix 2 Booster Group	Nimenrix Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	46	100	
Units: Subjects				
Any SAE(s)	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any specific AEs of new onset of chronic illnesses (NOCIs).

End point title	Number of subjects reporting any specific AEs of new onset of chronic illnesses (NOCIs).

End point description:

End point type	Secondary

End point timeframe:

Days 0-180 post-primary (naïve control group) and booster vaccination.

End point values	Nimenrix 1 Booster Group	Nimenrix 2 Booster Group	Nimenrix Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	46	100	
Units: Subjects				
Any NOCI(s)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local an general symptoms: During the 4-day (Days 0-3) post-vaccination period;
Unsolicited adverse events (AEs): During the 31-day (Days 0-30) post vaccination period;
Serious adverse events (SAEs): During the entire study period;

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Nimenrix 1 Group Y1
Reporting group description: -	
Reporting group title	Nimenrix 2 Group Y1
Reporting group description: -	
Reporting group title	Nimenrix Naive Group

Reporting group description: -

Serious adverse events	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1	Nimenrix Naive Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	0 / 46 (0.00%)	1 / 100 (1.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 38 (0.00%)	0 / 46 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Nimenrix 1 Group Y1	Nimenrix 2 Group Y1	Nimenrix Naive Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 38 (47.37%)	21 / 46 (45.65%)	46 / 100 (46.00%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			

subjects affected / exposed	18 / 38 (47.37%)	21 / 46 (45.65%)	46 / 100 (46.00%)
occurrences (all)	18	21	46
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 38 (26.32%)	15 / 46 (32.61%)	22 / 100 (22.00%)
occurrences (all)	10	15	22
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 38 (21.05%)	9 / 46 (19.57%)	21 / 100 (21.00%)
occurrences (all)	8	9	21
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 38 (26.32%)	7 / 46 (15.22%)	18 / 100 (18.00%)
occurrences (all)	10	7	18
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 38 (10.53%)	5 / 46 (10.87%)	7 / 100 (7.00%)
occurrences (all)	4	5	7
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 38 (10.53%)	5 / 46 (10.87%)	11 / 100 (11.00%)
occurrences (all)	4	5	11
Fever (Axillary)			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 38 (2.63%)	2 / 46 (4.35%)	5 / 100 (5.00%)
occurrences (all)	1	2	5
Injection site bruising			
subjects affected / exposed	2 / 38 (5.26%)	1 / 46 (2.17%)	2 / 100 (2.00%)
occurrences (all)	2	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 November 2010	A new cohort of subjects (naïve control group), aged 5-6 years, will be administered a dose of MenACWY-TT vaccine at the same time as the booster vaccination given to ACWY1 and ACWY2 groups to allow for evaluation of the safety and immunogenicity of a primary (naïve control group) and a booster dose (groups ACWY1 and ACWY2) within the same study.
14 December 2011	The primary objective of this study is to evaluate the antibody persistence at approximately 1 year, 3 years and 5 years post-administration of one or two doses of MenACWY-TT conjugate vaccine when given to healthy toddlers at 9-12 months of age. This study will generate antibody persistence data following administration of MenACWY-TT. In addition, the safety and immunogenicity of a booster dose of MenACWY-TT, administered at 5 years post-primary vaccination will be evaluated. Another cohort of subjects (naïve control group) 5-6 years of age will be administered a dose of MenACWY-TT vaccine at the same time to allow for evaluation of a primary (naïve control group) and booster dose within the same study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported