Clinical trial results:
A Phase II, open (partially double-blind), randomized, controlled dose-range study to evaluate the immunogenicity, reactogenicity and safety of four different formulations of GlaxoSmithKline (GSK) Biologicals' new generations meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate (MenACWY-TT) vaccine versus MENINGITEC™ or MENCEVAX™ ACWY when given as one dose to children aged 12 to 14 months and 3 to 5 years old.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2005-001288-73
Trial protocol	AT DE
Global end of trial date	13 February 2008

Results information

Result version number	v2 (current)
This version publication date	10 June 2016
First version publication date	05 June 2015
Version creation reason	• Correction of full data set Data correction due to a system error in EudraCT – Results.

Trial information

Trial identification

Sponsor protocol code	104703, 104704

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00126984
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	Interim
Date of interim/final analysis	13 April 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 February 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Based on the immune response induced one month post vaccination, to select the best of four different formulations of GSK Biologicals' new generations MenACWY-TT conjugate vaccine when given as one single dose to healthy children aged 12-14 months and 3-5 years.

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	26 July 2005
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	16 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 110
Country: Number of subjects enrolled	Germany: 398
Worldwide total number of subjects	508
EEA total number of subjects	508

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	240

months)	
Children (2-11 years)	268
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	Primary study
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

The 4 different formulations of MenACWY-TT vaccine were administered in a double-blind manner, while the control vaccines, MenC and MenACWY were given to the subjects in an open manner.

Arms

Are arms mutually exclusive?	Yes
Arm title	12-14 months of age Formulation 1 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:

1 dose of Nimenrix™ vaccine Formulation 1 at Day 0, intramuscularly in the left deltoid.

Investigational medicinal product name	DTPa/Hib
Investigational medicinal product code	
Other name	GSK Biologicals' combined diphtheria, tetanus, acellular pertussis vaccine mixed with Haemophilus influenzae type
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose 1 months after the administration of Nimenrix, injected intramuscularly into the left anterolateral thigh or into the left deltoid according to local requirements.

Arm title	12-14 months of age Formulation 2 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:

1 dose of Nimenrix™ vaccine Formulation 2 at Day 0, intramuscularly in the left deltoid.

Investigational medicinal product name	DTPa/Hib
Investigational medicinal product code	
Other name	GSK Biologicals' combined diphtheria, tetanus, acellular pertussis vaccine mixed with Haemophilus influenzae type
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose 1 months after the administration of Nimenrix, injected intramuscularly into the left anterolateral thigh or into the left deltoid according to local requirements.

Arm title	12-14 months of age Formulation 3 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:

1 dose of Nimenrix™ vaccine Formulation 3 at Day 0, intramuscularly in the left deltoid.

Investigational medicinal product name	DTPa/Hib
Investigational medicinal product code	
Other name	GSK Biologicals' combined diphtheria, tetanus, acellular pertussis vaccine mixed with Haemophilus influenzae type
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose 1 months after the administration of Nimenrix, injected intramuscularly into the left anterolateral thigh or into the left deltoid according to local requirements.

Arm title	12-14 months of age Formulation 4 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:

1 dose of Nimenrix™ vaccine Formulation 4 at Day 0, intramuscularly in the left deltoid.

Investigational medicinal product name	DTPa/Hib
Investigational medicinal product code	
Other name	GSK Biologicals' combined diphtheria, tetanus, acellular pertussis vaccine mixed with Haemophilus influenzae type
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose 1 months after the administration of Nimenrix, injected intramuscularly into the left anterolateral thigh or into the left deltoid according to local requirements.

Arm title	12-14 months of age Control Group

Arm description: -

Arm type	Active comparator

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

Dosage and administration details:

1 dose of Meningitec™ at Day 0, intramuscularly into the left deltoid.

Investigational medicinal product name	DTPa/Hib
Investigational medicinal product code	
Other name	GSK Biologicals' combined diphtheria, tetanus, acellular pertussis vaccine mixed with Haemophilus influenzae type
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose 1 months after the administration of Nimenrix, injected intramuscularly into the left anterolateral thigh or into the left deltoid according to local requirements.

Arm title	3-5 years of age Formulation 1 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:

1 dose of Nimenrix™ vaccine Formulation 1 at Day 0.

Arm title	3-5 years of age Formulation 2 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:

1 dose of Nimenrix™ vaccine Formulation 2 at Day 0.

Arm title	3-5 years of age Formulation 3 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:

1 dose of Nimenrix™ vaccine Formulation 3 at Day 0.

Arm title	3-5 years of age Formulation 4 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:

1 dose of Nimenrix™ vaccine Formulation 4 at Day 0.

Arm title	3-5 years of age Control Group

Arm description: -

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

Dosage and administration details:

1 dose of Meningitec™ at Day 0.

Number of subjects in period 1	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group
Started	48	48	48
Completed at Visit 2	0 [1]	0 [2]	0 [3]
Completed at Visit 3	48	45	48
Completed	48	45	48
Not completed	0	3	0
Other	-	3	-

Number of subjects in period 1	12-14 months of age Formulation 4 Group	12-14 months of age Control Group	3-5 years of age Formulation 1 Group
Started	48	48	54
Completed at Visit 2	0 [4]	0 [5]	53
Completed at Visit 3	47	47	0 [6]
Completed	47	47	53
Not completed	1	1	1
Other	1	1	1

Number of subjects in period 1	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group	3-5 years of age Formulation 4 Group
Started	53	54	54
Completed at Visit 2	53	54	54
Completed at Visit 3	0 [7]	0 [8]	0 [9]
Completed	53	54	54
Not completed	0	0	0
Other	-	-	-

Number of subjects in period 1	3-5 years of age Control Group
Started	53
Completed at Visit 2	53
Completed at Visit 3	0 [10]
Completed	53
Not completed	0
Other	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The children (3-5 years) groups completed the study at Visit 2, while the toddlers (12-14 months) groups completed it at Visit 3.

Period 2	
Period 2 title	Persistence/challenge study
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	12-14 months of age Challenge Group

Arm description: -

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

Dosage and administration details:

1/5 of a dose of Mencevax™ ACWY at Month 15

Arm title	12-14 months of age Control Group

Arm description: -

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

Dosage and administration details:

The subjects in the toddler age stratum vaccinated with the selected MenACWY-TT formulation or with the control vaccine were given 1/5 of a dose of MenACWY at Month 15. MenACWY-TT vaccines were administered intramuscularly in the left deltoid.

Arm title	3-5 years of age Challenge Group

Arm description: -

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	3-5 years of age Control Group

Arm description: -

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2[11]	12-14 months of age Challenge Group	12-14 months of age Control Group	3-5 years of age Challenge Group
Started	42	43	50
Completed	42	42	50
Not completed	0	1	0
Other	-	1	-

Number of subjects in period 2	3-5 years of age Control Group

[11]	
Started	50
Completed	50
Not completed	0
Other	-

Notes:

[11] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects not returning for a specific visit were not withdrawn and could participate in the subsequent follow-up phase. Actual enrollment differed depending on the rate of return for the follow-up phase, so not all enrolled subjects came to each visit.

Baseline characteristics

Reporting groups	
Reporting group title	12-14 months of age Formulation 1 Group
Reporting group description: -	
Reporting group title	12-14 months of age Formulation 2 Group
Reporting group description: -	
Reporting group title	12-14 months of age Formulation 3 Group
Reporting group description: -	
Reporting group title	12-14 months of age Formulation 4 Group
Reporting group description: -	
Reporting group title	12-14 months of age Control Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 1 Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 2 Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 3 Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 4 Group
Reporting group description: -	
Reporting group title	3-5 years of age Control Group
Reporting group description: -	

Reporting group values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group
Number of subjects	48	48	48
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: months			
arithmetic mean	12.6	12.5	12.7
standard deviation	± 0.79	± 0.8	± 0.84
Gender categorical Units: Subjects			
Female	20	25	25
Male	28	23	23

Reporting group values	12-14 months of age Formulation 4 Group	12-14 months of age Control Group	3-5 years of age Formulation 1 Group
Number of subjects	48	48	54
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: months			
arithmetic mean	12.4	12.6	47.1
standard deviation	± 0.71	± 0.77	± 7.7
Gender categorical			
Units: Subjects			
Female	29	27	18
Male	19	21	36

Reporting group values	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group	3-5 years of age Formulation 4 Group
Number of subjects	53	54	54
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: months			
arithmetic mean	45.9	47.4	46.7
standard deviation	± 7.93	± 6.91	± 6.66
Gender categorical			
Units: Subjects			
Female	27	29	27
Male	26	25	27

Reporting group values	3-5 years of age Control Group	Total	
Number of subjects	53	508	

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	47.8		
standard deviation	± 7.47	-	
Gender categorical Units: Subjects			
Female	28	255	
Male	25	253	

End points

End points reporting groups

Reporting group title	12-14 months of age Formulation 1 Group
Reporting group description: -	
Reporting group title	12-14 months of age Formulation 2 Group
Reporting group description: -	
Reporting group title	12-14 months of age Formulation 3 Group
Reporting group description: -	
Reporting group title	12-14 months of age Formulation 4 Group
Reporting group description: -	
Reporting group title	12-14 months of age Control Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 1 Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 2 Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 3 Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 4 Group
Reporting group description: -	
Reporting group title	3-5 years of age Control Group
Reporting group description: -	
Reporting group title	12-14 months of age Challenge Group
Reporting group description: -	
Reporting group title	12-14 months of age Control Group
Reporting group description: -	
Reporting group title	3-5 years of age Challenge Group
Reporting group description: -	
Reporting group title	3-5 years of age Control Group
Reporting group description: -	

Primary: Number of subjects with an immune response to the serum bactericidal assay meningococcal serogroup A using rabbit complement (rSBA-MenA), rSBA-MenC, rSBA-MenW-135, rSBA-MenY

End point title	Number of subjects with an immune response to the serum bactericidal assay meningococcal serogroup A using rabbit complement (rSBA-MenA), rSBA-MenC, rSBA-MenW-135, rSBA-MenY[1]

End point description:

End point type	Primary

End point timeframe:

One month 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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	41	42	41
Units: Subjects				
rSBA-MenA (N=36,35,36,35,31,34,37,40,36,31)	36	35	35	34
rSBA-MenC (N=43,40,41,41,45,47,47,47,49,32)	42	39	40	39
rSBA-MenW-135 (N=43,41,42,40,44,47,47,47,49,32)	43	39	41	40
rSBA-MenY (N=43,41,40,41,44,46,47,48,50,34)	42	40	35	39

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	47	47	48
Units: Subjects				
rSBA-MenA (N=36,35,36,35,31,34,37,40,36,31)	3	31	34	37
rSBA-MenC (N=43,40,41,41,45,47,47,47,49,32)	41	46	46	44
rSBA-MenW-135 (N=43,41,42,40,44,47,47,47,49,32)	6	46	47	47
rSBA-MenY (N=43,41,40,41,44,46,47,48,50,34)	5	43	42	48

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	34		
Units: Subjects				
rSBA-MenA (N=36,35,36,35,31,34,37,40,36,31)	36	25		
rSBA-MenC (N=43,40,41,41,45,47,47,47,49,32)	43	26		
rSBA-MenW-135 (N=43,41,42,40,44,47,47,47,49,32)	43	31		
rSBA-MenY (N=43,41,40,41,44,46,47,48,50,34)	49	27		

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 ≥ 1:8

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

End point description:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after (M1) the first vaccine dose

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	41	43	42
Units: Subjects				
rSBA-MenA, PRE (N=37,35,37,35,37,34,39,40,36,31)	10	13	19	18
rSBA-MenA, M1 (N=44,41,42,42,39,48,46,49,50,33)	44	41	42	42
rSBA-MenC, PRE (N=44,40,42,41,45,47,47,47,49,32)	7	9	3	4
rSBA-MenC, M1 (N=44,41,42,42,46,48,48,49,50,34)	43	41	42	42
rSBA-MenW-135,PRE(N=44,41,42,40,45,47,47,47,45	17	8	15	13
rSBA-MenW-135,M1 (N=44,41,43,42,45,48,48,49,50,34)	44	41	43	42
rSBA-MenY, PRE (N=44,41,41,41,45,46,47,48,50,34)	24	16	24	20
rSBA-MenY, M1 (N=44,41,42,42,45,48,48,49,50,34)	44	41	42	42

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	48	49
Units: Subjects				
rSBA-MenA, PRE (N=37,35,37,35,37,34,39,40,36,31)	7	30	38	32
rSBA-MenA, M1 (N=44,41,42,42,39,48,46,49,50,33)	14	48	46	49
rSBA-MenC, PRE (N=44,40,42,41,45,47,47,47,49,32)	4	11	11	11
rSBA-MenC, M1 (N=44,41,42,42,46,48,48,49,50,34)	45	48	48	49

rSBA-MenW-135,PRE(N=44,41,42,40,45,47,47,47,45	14	27	25	24
rSBA-MenW-135,M1 (N=44,41,43,42,45,48,48,49,50,34)	15	47	48	49
rSBA-MenY, PRE (N=44,41,41,41,45,46,47,48,50,34)	20	33	29	33
rSBA-MenY, M1 (N=44,41,42,42,45,48,48,49,50,34)	21	48	48	49

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	34		
Units: Subjects				
rSBA-MenA, PRE (N=37,35,37,35,37,34,39,40,36,31)	31	22		
rSBA-MenA, M1 (N=44,41,42,42,39,48,46,49,50,33)	50	33		
rSBA-MenC, PRE (N=44,40,42,41,45,47,47,47,49,32)	10	11		
rSBA-MenC, M1 (N=44,41,42,42,46,48,48,49,50,34)	50	33		
rSBA-MenW-135,PRE(N=44,41,42,40,45,47,47,47,45	20	17		
rSBA-MenW-135,M1 (N=44,41,43,42,45,48,48,49,50,34)	50	34		
rSBA-MenY, PRE (N=44,41,41,41,45,46,47,48,50,34)	30	22		
rSBA-MenY, M1 (N=44,41,42,42,45,48,48,49,50,34)	50	34		

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 ≥ 1:128.

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers ≥ 1:128.

End point description:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after (M1) the first vaccine dose

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	41	43	42
Units: Subjects				
rSBA-MenA, PRE (N=37,35,37,35,37,34,39,40,36,31)	6	10	18	16
rSBA-MenA, M1 (N=44,41,42,42,39,48,46,49,50,33)	44	41	42	42
rSBA-MenC, PRE (N=44,40,42,41,45,47,47,47,49,32)	2	2	1	3
rSBA-MenC, M1 (N=44,41,42,42,46,48,48,49,50,34)	40	38	40	37
rSBA-MenW-135,PRE (N=44,41,42,40,45,47,47,47,45,32	3	3	4	5
rSBA-MenW-135,M1 (N=44,41,43,42,45,48,48,49,50,34)	44	41	43	42
rSBA-MenY, PRE (N=44,41,41,41,45,46,47,48,50,34)	12	12	14	11
rSBA-MenY, M1(N=44,41,42,42,45,48,48,49,50,34)	44	40	42	42

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	48	49
Units: Subjects				
rSBA-MenA, PRE (N=37,35,37,35,37,34,39,40,36,31)	7	26	38	32
rSBA-MenA, M1 (N=44,41,42,42,39,48,46,49,50,33)	14	48	46	49
rSBA-MenC, PRE (N=44,40,42,41,45,47,47,47,49,32)	1	4	5	9
rSBA-MenC, M1 (N=44,41,42,42,46,48,48,49,50,34)	40	47	48	48
rSBA-MenW-135,PRE (N=44,41,42,40,45,47,47,47,45,32	5	9	14	12
rSBA-MenW-135,M1 (N=44,41,43,42,45,48,48,49,50,34)	10	47	48	49
rSBA-MenY, PRE (N=44,41,41,41,45,46,47,48,50,34)	10	21	22	25
rSBA-MenY, M1(N=44,41,42,42,45,48,48,49,50,34)	15	48	48	49

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	45		

Units: Subjects				
rSBA-MenA, PRE (N=37,35,37,35,37,34,39,40,36,31)	30	22		
rSBA-MenA, M1 (N=44,41,42,42,39,48,46,49,50,33)	50	33		
rSBA-MenC, PRE (N=44,40,42,41,45,47,47,47,49,32)	7	6		
rSBA-MenC, M1 (N=44,41,42,42,46,48,48,49,50,34)	48	30		
rSBA-MenW-135,PRE (N=44,41,42,40,45,47,47,47,45,32	13	8		
rSBA-MenW-135,M1 (N=44,41,43,42,45,48,48,49,50,34)	50	34		
rSBA-MenY, PRE (N=44,41,41,41,45,46,47,48,50,34)	22	17		
rSBA-MenY, M1(N=44,41,42,42,45,48,48,49,50,34)	50	33		

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:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after (M1) the first vaccine dose

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	41	43	42
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA, PRE (N=37,35,37,35,37,34,39,40,36,31)	11.2 (6.2 to 20.1)	17.1 (8.5 to 34.5)	44.1 (19.5 to 99.6)	41.2 (18.2 to 93)
rSBA-MenA, M1 (N=44,41,42,42,39,48,46,49,50,33)	4050.6 (3087.4 to 5314.3)	6060.2 (4447 to 8258.6)	5665.2 (4086 to 7854.9)	4859.8 (3488.7 to 6769.8)
rSBA-MenC, PRE (N=44,40,42,41,45,47,47,47,49,32)	6.4 (4.6 to 8.9)	7.8 (5.2 to 11.9)	5.4 (3.8 to 7.8)	6 (4 to 9)
rSBA-MenC, M1 (N=44,41,42,42,46,48,48,49,50,34)	536.8 (365.8 to 787.7)	1075.3 (744.4 to 1553.2)	983.5 (718.7 to 1345.9)	543.9 (380.9 to 776.8)
rSBA-MenW-135,PRE (N=44,41,42,40,45,47,47,47,45,32	12.6 (7.8 to 20.3)	7.9 (5 to 12.4)	12 (7.4 to 19.4)	11.4 (6.9 to 18.9)

rSBA-MenW-135,M1 (N=44,41,43,42,45,48,48,49,50,34)	3389.6 (2581.6 to 4450.4)	2665.9 (1985.9 to 3578.8)	3975.2 (3065.7 to 5154.5)	3240.7 (2375.9 to 4420.4)
rSBA-MenY, PRE (N=44,41,41,41,45,46,47,48,50,34)	27 (15.1 to 48.3)	19.4 (10 to 37.7)	42.1 (21.2 to 83.8)	23.9 (12.5 to 46)
rSBA-MenY, M1(N=44,41,42,42,45,48,48,49,50,34)	2010.3 (1458.8 to 2770.3)	2196.3 (1510 to 3194.5)	2295.1 (1701.5 to 3095.8)	2006.5 (1477 to 2725.9)

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	48	49
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA, PRE (N=37,35,37,35,37,34,39,40,36,31)	9.1 (5.1 to 16.3)	236.6 (129.6 to 432.2)	441.3 (317.6 to 613.2)	192.8 (100.1 to 371.4)
rSBA-MenA, M1 (N=44,41,42,42,39,48,46,49,50,33)	20.5 (9.7 to 43.3)	7223.8 (5905 to 8837.1)	9287.4 (7177.6 to 12017.4)	8299.4 (6734.2 to 10228.4)
rSBA-MenC, PRE (N=44,40,42,41,45,47,47,47,49,32)	5.3 (4 to 7)	8.2 (5.4 to 12.4)	8.8 (5.5 to 13.9)	10.1 (6.1 to 16.9)
rSBA-MenC, M1 (N=44,41,42,42,46,48,48,49,50,34)	372.5 (257.7 to 538.4)	1325.4 (954.9 to 1839.7)	1951.1 (1402 to 2715.1)	1577.8 (1123.5 to 2215.9)
rSBA-MenW-135,PRE (N=44,41,42,40,45,47,47,47,45,32	10.8 (6.7 to 17.4)	25.2 (15.4 to 41.4)	27.7 (15.6 to 49.3)	22.9 (13.3 to 39.4)
rSBA-MenW-135,M1 (N=44,41,43,42,45,48,48,49,50,34)	14.6 (8 to 26.6)	4736.7 (3302 to 6794.9)	6400.6 (5037.9 to 8132)	5987.2 (4846.9 to 7395.7)
rSBA-MenY, PRE (N=44,41,41,41,45,46,47,48,50,34)	21 (11.3 to 39)	73.1 (38.8 to 137.5)	62.8 (31.4 to 125.4)	80.3 (42.5 to 151.7)
rSBA-MenY, M1(N=44,41,42,42,45,48,48,49,50,34)	27.8 (14 to 55.3)	4456.2 (3489.7 to 5690.4)	4670.4 (3541.9 to 6158.4)	6433 (4921 to 8409.6)

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	45		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA, PRE (N=37,35,37,35,37,34,39,40,36,31)	277.2 (147 to 522.7)	139 (56.7 to 341.1)		
rSBA-MenA, M1 (N=44,41,42,42,39,48,46,49,50,33)	9980.3 (8019.4 to 12420.7)	3798.4 (2888.9 to 4994.2)		
rSBA-MenC, PRE (N=44,40,42,41,45,47,47,47,49,32)	9.3 (5.5 to 15.6)	14.1 (7.1 to 28.1)		

rSBA-MenC, M1 (N=44,41,42,42,46,48,48,49,50,34)	1495.8 (1093.4 to 2046.3)	445.4 (263.3 to 753.3)		
rSBA-MenW-135,PRE (N=44,41,42,40,45,47,47,47,45,32	20.8 (11.6 to 37.4)	24.4 (12.6 to 47.2)		
rSBA-MenW-135,M1 (N=44,41,43,42,45,48,48,49,50,34)	7123.1 (5960.2 to 8512.9)	1811.1 (1233.3 to 2659.5)		
rSBA-MenY, PRE (N=44,41,41,41,45,46,47,48,50,34)	52.3 (27.2 to 100.4)	61 (27.5 to 135.2)		
rSBA-MenY, M1(N=44,41,42,42,45,48,48,49,50,34)	6042.4 (4720.2 to 7734.9)	1435.5 (972.6 to 2118.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti-PSW-135 and anti- PSY antibody concentrations ≥ 0.3 µg/mL

End point title	Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti- PSY antibody concentrations ≥ 0.3 µg/mL

End point description:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after (M1) the first vaccine dose

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	40	43	41
Units: Subjects				
Anti-PSA, PRE (N=43,36,37,38,43,42,42,46,46,30)	1	3	2	0
Anti-PSC, PRE (N=43,36,38,41,43,44,43,47,47,30)	0	1	0	1
Anti-PSW-135, PRE(N=39,35,35,37,39,42,41,44,47,29)	1	2	0	0
Anti-PSY, PRE (N=42,38,39,40,42,45,45,45,49,31)	2	0	0	2
Anti-PSA, M1 (N=46,39,43,40,43,48,47,49,49,34)	46	39	43	40
Anti-PSC, M1 (N=46,40,43,41,45,46,47,49,50,34)	46	40	43	41
Anti-PSW-135, M1 (N=44,38,40,39,40,44,45,48,48,33)	43	37	40	39
Anti-PSY, M1 (N=44,40,39,41,42,47,46,49,49,34)	43	39	39	41

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	48	46	49
Units: Subjects				
Anti-PSA, PRE (N=43,36,37,38,43,42,42,46,46,30)	2	7	8	6
Anti-PSC, PRE (N=43,36,38,41,43,44,43,47,47,30)	2	2	0	2
Anti-PSW-135, PRE(N=39,35,35,37,39,42,41,44,47,29)	0	1	1	0
Anti-PSY, PRE (N=42,38,39,40,42,45,45,45,49,31)	1	0	1	1
Anti-PSA, M1 (N=46,39,43,40,43,48,47,49,49,34)	3	47	47	49
Anti-PSC, M1 (N=46,40,43,41,45,46,47,49,50,34)	44	46	47	49
Anti-PSW-135, M1 (N=44,38,40,39,40,44,45,48,48,33)	0	43	44	48
Anti-PSY, M1 (N=44,40,39,41,42,47,46,49,49,34)	3	46	46	49

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	34		
Units: Subjects				
Anti-PSA, PRE (N=43,36,37,38,43,42,42,46,46,30)	7	5		
Anti-PSC, PRE (N=43,36,38,41,43,44,43,47,47,30)	4	5		
Anti-PSW-135, PRE(N=39,35,35,37,39,42,41,44,47,29)	1	0		
Anti-PSY, PRE (N=42,38,39,40,42,45,45,45,49,31)	3	2		
Anti-PSA, M1 (N=46,39,43,40,43,48,47,49,49,34)	49	34		
Anti-PSC, M1 (N=46,40,43,41,45,46,47,49,50,34)	50	34		
Anti-PSW-135, M1 (N=44,38,40,39,40,44,45,48,48,33)	48	33		
Anti-PSY, M1 (N=44,40,39,41,42,47,46,49,49,34)	49	34		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti-PSW-135 and anti- PSY antibody concentrations ≥ 2.0 µg/mL

End point title	Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti- PSY antibody concentrations ≥ 2.0 µg/mL

End point description:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after (M1) the first vaccine dose

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	40	43	41
Units: Subjects				
Anti-PSA, PRE (N=43,36,37,38,43,42,42,46,46,30)	0	0	0	0
Anti-PSC, PRE (N=43,36,38,41,43,44,43,47,47,30)	0	1	0	0
Anti-PSW-135, PRE(N=39,35,35,37,39,42,41,44,47,29)	0	0	0	0
Anti-PSY, PRE (N=42,38,39,40,42,45,45,45,49,31)	0	0	0	0
Anti-PSA, M1 (N=46,39,43,40,43,48,47,49,49,34)	45	39	43	40
Anti-PSC, M1 (N=46,40,43,41,45,46,47,49,50,34)	45	40	42	41
Anti-PSW-135, M1 (N=44,38,40,39,40,44,45,48,48,33)	31	28	36	36
Anti-PSY, M1 (N=44,40,39,41,42,47,46,49,49,34)	36	35	37	40

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	48	47	49
Units: Subjects				
Anti-PSA, PRE (N=43,36,37,38,43,42,42,46,46,30)	0	2	3	2
Anti-PSC, PRE (N=43,36,38,41,43,44,43,47,47,30)	0	1	0	1
Anti-PSW-135, PRE(N=39,35,35,37,39,42,41,44,47,29)	0	0	0	0
Anti-PSY, PRE (N=42,38,39,40,42,45,45,45,49,31)	0	0	0	0

Anti-PSA, M1 (N=46,39,43,40,43,48,47,49,49,34)	1	45	47	49
Anti-PSC, M1 (N=46,40,43,41,45,46,47,49,50,34)	42	42	47	49
Anti-PSW-135, M1 (N=44,38,40,39,40,44,45,48,48,33)	0	31	29	39
Anti-PSY, M1 (N=44,40,39,41,42,47,46,49,49,34)	1	39	40	44

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	34		
Units: Subjects				
Anti-PSA, PRE (N=43,36,37,38,43,42,42,46,46,30)	3	1		
Anti-PSC, PRE (N=43,36,38,41,43,44,43,47,47,30)	2	1		
Anti-PSW-135, PRE(N=39,35,35,37,39,42,41,44,47,29)	1	0		
Anti-PSY, PRE (N=42,38,39,40,42,45,45,45,49,31)	1	1		
Anti-PSA, M1 (N=46,39,43,40,43,48,47,49,49,34)	49	32		
Anti-PSC, M1 (N=46,40,43,41,45,46,47,49,50,34)	50	33		
Anti-PSW-135, M1 (N=44,38,40,39,40,44,45,48,48,33)	45	28		
Anti-PSY, M1 (N=44,40,39,41,42,47,46,49,49,34)	48	33		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti-PSY antibody concentrations

End point title	Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti-PSY antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after (M1) the first vaccine dose

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	40	40	41
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA, PRE (N=43,36,37,38,43,42,42,46,46,30)	0.15 (0.15 to 0.16)	0.17 (0.14 to 0.21)	0.16 (0.14 to 0.18)	0.15 (0.15 to 0.15)
Anti-PSC, PRE (N=43,36,38,41,43,44,43,47,47,30)	0.15 (0.15 to 0.15)	0.16 (0.14 to 0.19)	0.15 (0.15 to 0.15)	0.15 (0.15 to 0.16)
Anti-PSW-135, PRE(N=39,35,35,37,39,42,41,44,47,29)	0.15 (0.15 to 0.16)	0.16 (0.14 to 0.19)	0.15 (0.15 to 0.15)	0.15 (0.15 to 0.15)
Anti-PSY, PRE (N=42,38,39,40,42,45,45,45,49,31)	0.16 (0.15 to 0.17)	0.15 (0.15 to 0.15)	0.15 (0.15 to 0.15)	0.16 (0.14 to 0.18)
Anti-PSA, M1 (N=46,39,43,40,43,48,47,49,49,34)	17.24 (12.8 to 23.21)	28.83 (20.85 to 39.86)	37.27 (29.31 to 47.4)	35.37 (27.39 to 45.68)
Anti-PSC, M1 (N=46,40,43,41,45,46,47,49,50,34)	10.49 (8.17 to 13.48)	18.88 (14.96 to 23.82)	20.66 (16.66 to 25.61)	13.26 (10.48 to 16.78)
Anti-PSW-135, M1 (N=44,38,40,39,40,44,45,48,48,33)	3.38 (2.49 to 4.57)	4.02 (2.91 to 5.56)	6.81 (5.07 to 9.14)	6.31 (4.9 to 8.13)
Anti-PSY, M1 (N=44,40,39,41,42,47,46,49,49,34)	6.64 (4.63 to 9.52)	6.12 (4.17 to 8.98)	10.89 (8.08 to 14.69)	9.61 (6.97 to 13.25)

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	48	47	49
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA, PRE (N=43,36,37,38,43,42,42,46,46,30)	0.16 (0.14 to 0.18)	0.2 (0.16 to 0.26)	0.24 (0.17 to 0.34)	0.19 (0.16 to 0.24)
Anti-PSC, PRE (N=43,36,38,41,43,44,43,47,47,30)	0.17 (0.14 to 0.19)	0.16 (0.14 to 0.19)	0.15 (0.15 to 0.15)	0.16 (0.14 to 0.19)
Anti-PSW-135, PRE(N=39,35,35,37,39,42,41,44,47,29)	0.15 (0.15 to 0.15)	0.15 (0.15 to 0.17)	0.16 (0.14 to 0.17)	0.15 (0.15 to 0.15)
Anti-PSY, PRE (N=42,38,39,40,42,45,45,45,49,31)	0.15 (0.15 to 0.16)	0.15 (0.15 to 0.15)	0.16 (0.14 to 0.18)	0.15 (0.15 to 0.16)
Anti-PSA, M1 (N=46,39,43,40,43,48,47,49,49,34)	0.17 (0.14 to 0.2)	18.15 (12.2 to 27)	29.71 (22.82 to 38.68)	29.25 (22.57 to 37.9)
Anti-PSC, M1 (N=46,40,43,41,45,46,47,49,50,34)	8.01 (6.01 to 10.67)	7.43 (5.71 to 9.68)	10.81 (8.89 to 13.14)	13.12 (10.27 to 16.76)
Anti-PSW-135, M1 (N=44,38,40,39,40,44,45,48,48,33)	0.15 (0.15 to 0.15)	3.88 (2.69 to 5.58)	3.24 (2.25 to 4.65)	4.07 (3.16 to 5.23)
Anti-PSY, M1 (N=44,40,39,41,42,47,46,49,49,34)	0.18 (0.14 to 0.23)	5.48 (3.96 to 7.59)	6.52 (4.67 to 9.12)	9.15 (6.77 to 12.37)

End point values	3-5 years of age Formulation 4	3-5 years of age Control Group		

	Group			
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	34		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA, PRE (N=43,36,37,38,43,42,42,46,46,30)	0.22 (0.16 to 0.3)	0.2 (0.14 to 0.3)		
Anti-PSC, PRE (N=43,36,38,41,43,44,43,47,47,30)	0.19 (0.15 to 0.24)	0.22 (0.16 to 0.3)		
Anti-PSW-135, PRE(N=39,35,35,37,39,42,41,44,47,29)	0.16 (0.14 to 0.19)	0.15 (0.15 to 0.15)		
Anti-PSY, PRE (N=42,38,39,40,42,45,45,45,49,31)	0.17 (0.14 to 0.21)	0.17 (0.14 to 0.21)		
Anti-PSA, M1 (N=46,39,43,40,43,48,47,49,49,34)	39.4 (30.83 to 50.36)	11.43 (7.73 to 16.89)		
Anti-PSC, M1 (N=46,40,43,41,45,46,47,49,50,34)	11.09 (8.87 to 13.87)	11.44 (8.35 to 15.67)		
Anti-PSW-135, M1 (N=44,38,40,39,40,44,45,48,48,33)	7.03 (5.33 to 9.27)	6.68 (4.3 to 10.38)		
Anti-PSY, M1 (N=44,40,39,41,42,47,46,49,49,34)	15.06 (10.65 to 21.28)	14.07 (8.9 to 22.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-tetanus (anti-T) antibody titers ≥ 0.1 IU/mL

End point title	Number of subjects with anti-tetanus (anti-T) antibody titers ≥ 0.1 IU/mL

End point description:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after (M1) the first vaccine dose

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	41	43	42
Units: Subjects				
Anti-T, PRE (N=46,41,43,42,45,46,48,48,51,33)	45	37	39	38
Anti-T, M1 (N=46,41,43,41,44,48,48,49,50,34)	46	41	43	41

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	48	48	49
Units: Subjects				
Anti-T, PRE (N=46,41,43,42,45,46,48,48,51,33)	41	41	43	42
Anti-T, M1 (N=46,41,43,41,44,48,48,49,50,34)	39	48	48	49

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	34		
Units: Subjects				
Anti-T, PRE (N=46,41,43,42,45,46,48,48,51,33)	49	28		
Anti-T, M1 (N=46,41,43,41,44,48,48,49,50,34)	50	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-tetanus (anti-T) antibody concentrations

End point title	Anti-tetanus (anti-T) antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after (M1) the first vaccine dose

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	41	43	42
Units: IU/mL				
geometric mean (confidence interval				

95%)				
Anti-T, PRE (N=46,41,43,42,45,46,48,48,51,33)	0.622 (0.457 to 0.847)	0.555 (0.385 to 0.799)	0.428 (0.307 to 0.596)	0.366 (0.26 to 0.514)
Anti-T, M1 (N=46,41,43,41,44,48,48,49,50,34)	6.026 (4.249 to 8.546)	6.358 (4.267 to 9.474)	6.456 (4.325 to 9.638)	3.553 (2.348 to 5.378)

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	48	48	49
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-T, PRE (N=46,41,43,42,45,46,48,48,51,33)	0.464 (0.329 to 0.654)	0.581 (0.395 to 0.854)	0.659 (0.449 to 0.967)	0.47 (0.335 to 0.659)
Anti-T, M1 (N=46,41,43,41,44,48,48,49,50,34)	0.423 (0.29 to 0.618)	11.786 (8.711 to 15.947)	18.722 (13.704 to 25.576)	16.696 (12.732 to 21.894)

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	34		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-T, PRE (N=46,41,43,42,45,46,48,48,51,33)	0.465 (0.357 to 0.605)	0.363 (0.238 to 0.555)		
Anti-T, M1 (N=46,41,43,41,44,48,48,49,50,34)	13.877 (10.424 to 18.474)	0.352 (0.239 to 0.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serum bactericidal assay using human complement (hSBA-MenA, hSBA-MenC ,hSBA-MenW-135, hSBA-MenY) titers ≥ 1:4

End point title	Number of subjects with serum bactericidal assay using human complement (hSBA-MenA, hSBA-MenC ,hSBA-MenW-135, hSBA-MenY) titers ≥ 1:4[2]

End point description:

The hSBA-MenA and hSBA-MenW-135 assays were performed using 2 bacterial strains. For the hSBA-MenA assay, strains
with an L10 and L11 immunotype were used. For the hSBA-MenW-135 assay, the 3193 and MP01240070 (referred to as MP)
strains were used.

End point type	Secondary

End point timeframe:

Prior to (PRE) and 1 month after (M1) the vaccine dose and 15 months after priming (M15)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint analysis was based only on subjects of the control groups and all subjects in the group that received Nimenrix formulation 3.

End point values	12-14 months of age Formulation 3 Group	12-14 months of age Control Group	3-5 years of age Formulation 3 Group	3-5 years of age Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	43	38	29
Units: Subjects				
hSBA-MenA L10, Pre (N=36,42,38,29)	2	3	6	4
hSBA-MenA L11, PRE (N=30,34,38,27)	0	1	0	0
hSBA-MenC, PRE (N=12,14,20,12)	1	1	5	7
hSBA-MenW-135 MP, PRE (N=34,40,34,23)	2	0	6	2
hSBA-MenW-135 3193, PRE (N=31,35,34,23)	0	0	3	1
hSBA-MenY, PRE (N=33,43,38,28)	2	4	7	7
hSBA-MenA L10, M1 (N=26,30,37,24)	24	4	31	10
hSBA-MenA L11, M1 (N=22,28,25,24)	21	1	19	7
hSBA-MenC, M1 (N=11,12,19,12)	11	10	18	11
hSBA-MenW-135 MP, M1 (N=24,28,30,16)	20	0	26	10
hSBA-MenW-135 3193, M1 (N=26,27,31,21)	15	0	18	10
hSBA-MenY, M1 (N=26,31,33,25)	20	2	30	14
hSBA-MenA, M15 (N=18,20,24,14)	4	1	5	1
hSBA-MenC, M15 (N=27,27,35,22)	26	18	33	17
hSBA-MenW-135, M15 (N=18,16,24,6)	18	0	23	2
hSBA-MenY, M15 (N=26,25,32,19)	25	3	29	12

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[3]

End point description:

End point type	Secondary

End point timeframe:

Prior to and 1 month after the vaccine dose and 15 months after priming

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint analysis was based only on subjects of the control groups and all subjects in the group that received Nimenrix formulation 3.

End point values	12-14 months of age Formulation 3 Group	12-14 months of age Control Group	3-5 years of age Formulation 3 Group	3-5 years of age Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	43	38	29
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA L10, Pre (N=36,42,38,29)	2.1 (1.9 to 2.4)	2.1 (2 to 2.3)	2.7 (2.1 to 3.4)	3.2 (2 to 5)
hSBA-MenA L11, PRE (N=30,34,38,27)	2 (2 to 2)	2.1 (1.9 to 2.2)	2 (2 to 2)	2 (2 to 2)
hSBA-MenC, PRE (N=12,14,20,12)	2.2 (1.8 to 2.7)	2.1 (1.9 to 2.5)	3.3 (2.1 to 5.1)	5.7 (2.6 to 12.4)
hSBA-MenW-135 MP, PRE (N=34,40,34,23)	2.1 (1.9 to 2.4)	2 (2 to 2)	4.9 (2.5 to 9.9)	3 (1.6 to 5.4)
hSBA-MenW-135 3193, PRE (N=31,35,34,23)	2 (2 to 2)	2 (2 to 2)	3 (1.9 to 4.6)	2.1 (1.9 to 2.4)
hSBA-MenY, PRE (N=33,43,38,28)	2.4 (1.8 to 3.2)	2.5 (1.9 to 3.1)	3.6 (2.3 to 5.6)	4 (2.4 to 6.8)
hSBA-MenA L10, M1 (N=26,30,37,24)	39 (23.2 to 65.5)	2.7 (2 to 3.7)	24.6 (15 to 40.6)	5.7 (3 to 10.8)
hSBA-MenA L11, M1 (N=22,28,25,24)	54.3 (32.7 to 90.3)	2.1 (1.9 to 2.3)	29.8 (14.4 to 61.6)	3.8 (2.3 to 6.3)
hSBA-MenC, M1 (N=11,12,19,12)	194.7 (152.4 to 248.7)	33.4 (11.6 to 96.6)	89.7 (44.5 to 180.8)	26.5 (11.4 to 61.5)
hSBA-MenW-135 MP, M1 (N=24,28,30,16)	134.6 (54.3 to 333.3)	2 (2 to 2)	247.3 (113.5 to 538.9)	53.5 (11.3 to 252.8)
hSBA-MenW-135 3193, M1 (N=26,27,31,21)	9.1 (4.9 to 17)	2 (2 to 2)	17.3 (8.3 to 36)	8 (3.7 to 17.4)
hSBA-MenY, M1 (N=26,31,33,25)	21.1 (10.4 to 42.7)	2.3 (1.9 to 2.8)	56.2 (33.8 to 93.3)	12.5 (5.8 to 26.9)
hSBA-MenA, M15 (N=18,20,24,14)	2.8 (2 to 3.9)	2.2 (1.8 to 2.6)	3.5 (2.2 to 5.7)	2.2 (1.8 to 2.7)
hSBA-MenC, M15 (N=27,27,35,22)	189.2 (111.9 to 319.9)	19.6 (9.6 to 39.9)	112.4 (70.2 to 180)	28.1 (12.9 to 61)
hSBA-MenW-135, M15 (N=18,16,24,21)	313.8 (182.6 to 539.2)	2 (2 to 2)	221.5 (136.8 to 358.7)	8.1 (0.8 to 79.7)
hSBA-MenY, M15 (N=26,25,32,19)	95.3 (56.7 to 160.4)	2.9 (1.8 to 4.6)	92.3 (48.6 to 175.1)	20.9 (7.4 to 58.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms in children

End point title	Number of subjects with solicited local symptoms in children[4]

End point description:

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) post-vaccination period after each dose and overall

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: These symptoms were only reported in children.

End point values	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group	3-5 years of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	53	54	54
Units: Subjects				
Any Pain	16	22	18	15
Any Redness	23	28	28	26
Any Swelling	15	19	18	18

End point values	3-5 years of age Control Group			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: Subjects				
Any Pain	23			
Any Redness	20			
Any Swelling	12			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms in toddlers

End point title	Number of subjects with solicited local symptoms in toddlers[5]

End point description:

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) post-vaccination period after each dose and overall

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint analysis was based only on subjects of the control groups and all subjects in the group that received Nimenrix formulation 3.

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	47	48	48
Units: Subjects				
Any Pain, Men Vac (N=48,47,48,48,47)	11	5	8	7
Any Pain, DTPa (N=46,45,48,47,47)	11	10	13	13
Any Redness, Men Vac (N=48,47,48,48,47)	19	20	20	27
Any Redness, DTPa (N=46,45,48,47,47)	20	17	23	26
Any Swelling, Men Vac (N=48,47,48,48,47)	10	8	10	10
Any Swelling, DTPa (N=46,45,48,47,47)	14	8	16	16

End point values	12-14 months of age Control Group			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: Subjects				
Any Pain, Men Vac (N=48,47,48,48,47)	8			
Any Pain, DTPa (N=46,45,48,47,47)	10			
Any Redness, Men Vac (N=48,47,48,48,47)	17			
Any Redness, DTPa (N=46,45,48,47,47)	18			
Any Swelling, Men Vac (N=48,47,48,48,47)	10			
Any Swelling, DTPa (N=46,45,48,47,47)	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms in children

End point title	Number of subjects with solicited general symptoms in

End point description:

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) post-vaccination period

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: These symptoms were only reported in children.

End point values	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group	3-5 years of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	53	54	54
Units: Subjects				
Any Drowsiness	11	16	12	16
Any Fever	4	9	9	7
Any Irritability	11	10	10	16
Any Loss of appetite	5	16	6	12

End point values	3-5 years of age Control Group			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: Subjects				
Any Drowsiness	14			
Any Fever	5			
Any Irritability	12			
Any Loss of appetite	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms in toddlers

End point title	Number of subjects with solicited general symptoms in

End point description:

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) post-vaccination period following each study dose

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: These symptoms were only reported in toddlers.

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	47	48	48
Units: Subjects				
Any Drowsiness, Men Vac (N=48,47,48,48,47)	19	16	17	20

Any Drowsiness, DTPa (N=46,45,48,47,47)	14	8	11	12
Any Fever, Men Vac (N=48,47,48,48,47)	9	15	12	12
Any Fever, DTPa (N=46,45,48,47,47)	15	16	16	14
Any Irritability, Men Vac (N=48,47,48,48,47)	22	16	16	21
Any Irritability, DTPa (N=46,45,48,47,47)	15	9	14	15
Any Loss of appetite, Men Vac (N=48,47,48,48,47)	9	10	11	9
Any Loss of appetite, DTPa (N=46,45,48,47,47)	9	7	8	12

End point values	12-14 months of age Control Group			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: Subjects				
Any Drowsiness, Men Vac (N=48,47,48,48,47)	18			
Any Drowsiness, DTPa (N=46,45,48,47,47)	17			
Any Fever, Men Vac (N=48,47,48,48,47)	16			
Any Fever, DTPa (N=46,45,48,47,47)	20			
Any Irritability, Men Vac (N=48,47,48,48,47)	19			
Any Irritability, DTPa (N=46,45,48,47,47)	14			
Any Loss of appetite, Men Vac (N=48,47,48,48,47)	11			
Any Loss of appetite, DTPa (N=46,45,48,47,47)	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited Adverse events (AEs)

End point title	Number of subjects with unsolicited Adverse events (AEs)

End point description:

End point type	Secondary

End point timeframe:

Within 31 days (Days 0-30) after the primary vaccination

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	48	48	48
Units: Subjects				
Any AEs	30	29	30	27

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	54	53	54
Units: Subjects				
Any AEs	29	21	22	21

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: Subjects				
Any AEs	22	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Number (%) of subjects with Serious Adverse Events (SAEs)

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

End point description:

End point type	Secondary

End point timeframe:

During the primary vaccination study

End point values	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group	12-14 months of age Formulation 4 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	48	48	48
Units: Subjects				
Any SAEs	1	1	1	3

End point values	12-14 months of age Control Group	3-5 years of age Formulation 1 Group	3-5 years of age Formulation 2 Group	3-5 years of age Formulation 3 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	54	53	54
Units: Subjects				
Any SAEs	1	1	1	0

End point values	3-5 years of age Formulation 4 Group	3-5 years of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: Subjects				
Any SAEs	0	0		

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 ≥ 1:8

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

End point description:

End point type	Secondary

End point timeframe:

15 months after priming

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The endpoint analysis was based only on subjects of the control groups and all subjects in the group that received Nimenrix formulation 3.

End point values	12-14 months of age Formulation 3 Group	12-14 months of age Control Group	3-5 years of age Formulation 3 Group	3-5 years of age Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	41	46	34
Units: Subjects				
rSBA-MenA L10 (N=40,36,45,29)	39	11	45	26
rSBA-MenA L11 (N=39,31,46,33)	38	25	46	32
rSBA-MenC (N=39,40,46,32)	36	24	46	19
rSBA-MenW-135 3193 (N=40,40,46,34)	39	17	46	32
rSBA-MenW-135 MP (N=40,41,46,32)	39	17	46	30
rSBA-MenY (N= 40,40,46,33)	39	30	46	26

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 ≥ 1:128.

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers ≥ 1:128.[9]

End point description:

End point type	Secondary

End point timeframe:

15 months after priming

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint analysis was based only on subjects of the control groups and all subjects in the group that received Nimenrix formulation 3.

End point values	12-14 months of age Formulation 3 Group	12-14 months of age Control Group	3-5 years of age Formulation 3 Group	3-5 years of age Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	41	46	34
Units: Subjects				
rSBA-MenA L10 (N=40,36,45,29)	37	10	44	24
rSBA-MenA L11 (N=39,31,46,33)	36	23	46	32
rSBA-MenC (N=39,40,46,32)	27	11	30	9
rSBA-MenW-135 3193 (N=40,40,46,34)	38	10	46	30
rSBA-MenW-135 MP (N=40,41,46,32)	36	11	46	30
rSBA-MenY (N= 40,40,46,33)	36	18	46	22

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[10]

End point description:

End point type	Secondary

End point timeframe:

15 months after priming

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint analysis was based only on subjects of the control groups and all subjects in the group that received Nimenrix formulation 3.

End point values	12-14 months of age Formulation 3 Group	12-14 months of age Control Group	3-5 years of age Formulation 3 Group	3-5 years of age Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	41	46	34
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA L10 (N=40,36,45,29)	573.7 (373.3 to 881.7)	14.3 (7.3 to 27.8)	891.1 (693.1 to 1145.8)	251.3 (137.4 to 459.8)
rSBA-MenA L11 (N=39,31,46,33)	1385.1 (820.5 to 2338.3)	184.6 (85.5 to 398.7)	2619.6 (2125.2 to 3229.1)	879.5 (579 to 1336)
rSBA-MenC (N=39,40,46,32)	172 (108.7 to 272.1)	28 (15 to 52.6)	187.6 (124.3 to 283.2)	28.6 (14.3 to 57.1)
rSBA-MenW-135 3193 (N=40,40,46,34)	528.2 (368.6 to 756.7)	18.6 (10.2 to 33.9)	961.6 (731.2 to 1264.6)	239.3 (157.1 to 364.7)
rSBA-MenW-135 MP (N=40,41,46,32)	692 (462.4 to 1035.6)	18.7 (10.1 to 34.7)	1564.1 (1174.6 to 2082.7)	365.9 (228.4 to 586.2)
rSBA-MenY (N= 40,40,46,33)	477.2 (321.3 to 708.6)	76.9 (41.2 to 143.5)	1287.4 (1001.8 to 1654.3)	139.4 (66.9 to 290.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti-PSY antibody concentrations

End point title	Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti-PSY antibody concentrations[11]

End point description:

End point type	Secondary

End point timeframe:

15 months after priming

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint analysis was based only on subjects of the control groups and all subjects in the group that received Nimenrix formulation 3.

End point values	12-14 months of age Formulation 3 Group	12-14 months of age Control Group	3-5 years of age Formulation 3 Group	3-5 years of age Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	32	32
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA (N=34,32,40,32)	0.65 (0.44 to 0.95)	0.16 (0.14 to 0.17)	1.04 (0.67 to 1.62)	2.71 (1.54 to 4.78)
Anti-PSC (N=36,37,46,31)	0.35 (0.25 to 0.49)	0.27 (0.2 to 0.36)	0.4 (0.27 to 0.6)	2.72 (1.68 to 4.42)
Anti-PSW-135 (N=34,34,41,31)	1.09 (0.78 to 1.53)	0.15 (0.15 to 0.15)	0.43 (0.34 to 0.54)	2.33 (1.29 to 4.2)
Anti-PSY (N=35,34,40,28)	1.5 (1.06 to 2.11)	0.15 (0.15 to 0.15)	0.71 (0.51 to 0.98)	4.46 (2.47 to 8.07)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti-PSW-135 and anti- PSY antibody concentrations ≥ 0.3 µg/mL

End point title	Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti- PSY antibody concentrations ≥ 0.3 µg/mL[12]

End point description:

End point type	Secondary

End point timeframe:

15 months after priming

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint analysis was based only on subjects of the control groups and all subjects in the group that received Nimenrix formulation 3.

End point values	12-14 months of age Formulation 3 Group	12-14 months of age Control Group	3-5 years of age Formulation 3 Group	3-5 years of age Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	41	32
Units: Subjects				
Anti-PSA (N=34,32,40,32)	25	1	33	29

Anti-PSC (N=36,37,46,31)	18	14	19	28
Anti-PSW-135 (N=34,34,41,31)	33	0	30	29
Anti-PSY (N=35,34,40,28)	33	0	33	26

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti-PSW-135 and anti- PSY antibody concentrations ≥ 2.0 µg/mL

End point title	Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti- PSY antibody concentrations ≥ 2.0 µg/mL[13]

End point description:

End point type	Secondary

End point timeframe:

15 months after priming

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint analysis was based only on subjects of the control groups and all subjects in the group that received Nimenrix formulation 3.

End point values	12-14 months of age Formulation 3 Group	12-14 months of age Control Group	3-5 years of age Formulation 3 Group	3-5 years of age Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	41	32
Units: Subjects				
Anti-PSA (N=34,32,40,32)	6	0	13	21
Anti-PSC (N=36,37,46,31)	3	1	6	21
Anti-PSW-135 (N=34,34,41,31)	7	0	1	16
Anti-PSY (N=35,34,40,28)	14	0	6	21

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms

End point description:

End point type	Secondary

End point timeframe:

During the 8-day follow-up period (Day 0-7) following the vaccine administration

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	42		
Units: Subjects				
Any Pain	7	8		
Any Redness	13	12		
Any Swelling	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms

End point description:

End point type	Secondary

End point timeframe:

During the 8-day follow-up period (Day 0-7) following the vaccine administration

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	42		
Units: Subjects				
Any Drowsiness	9	9		
Any Fever	9	5		
Any Irritability	7	5		
Any Loss of appetite	6	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited Adverse events (AEs)

End point title	Number of subjects with unsolicited Adverse events (AEs)

End point description:

End point type	Secondary

End point timeframe:

Within the 31-day follow-up period (Day 0-30) following the vaccine administration

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	43		
Units: Subjects				
Any AEs	14	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number (%) of subjects with Serious Adverse Events (SAEs)

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

End point description:

End point type	Secondary

End point timeframe:

Between completion of the primary phase and the start of the persistence/challenge phase

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group	3-5 years of age Challenge Group	3-5 years of age Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	43	50	50
Units: Subjects				
Any SAEs	0	1	1	2

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 ≥ 1:8

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-

	135 and rSBA-MenY titers ≥ 1:8

End point description:

End point type	Secondary

End point timeframe:

1 month after the administration of the challenge dose

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: Subjects				
rSBA-MenA L10 (N=25,30)	25	30		
rSBA-MenA L11 (N=18,29)	18	29		
rSBA-MenC (N=32,30)	32	30		
rSBA-MenW-135 3193 (N=32,30)	32	30		
rSBA-MenW-135 MP (N=32,30)	32	30		
rSBA-MenY (N=32,30)	32	29		

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 ≥ 1:128.

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers ≥ 1:128.

End point description:

End point type	Secondary

End point timeframe:

1 month after the administration of the challenge dose

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: Subjects				
rSBA-MenA L10 (N=25,30)	25	27		
rSBA-MenA L11 (N=18,29)	18	28		
rSBA-MenC (N=32,30)	32	30		
rSBA-MenW-135 3193 (N=32,30)	32	29		

rSBA-MenW-135 MP (N=32,30)	32	29		
rSBA-MenY (N=32,30)	32	28		

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:

End point type	Secondary

End point timeframe:

1 month after the administration of the challenge dose

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA L10 (N=25,30)	3321.9 (2294.2 to 4810)	514.1 (354.8 to 744.8)		
rSBA-MenA L11 (N=18,29)	4271.8 (3092.6 to 5900.8)	1349.4 (942.5 to 1932)		
rSBA-MenC (N=32.30)	5965.7 (4128.4 to 8620.7)	5265.2 (3437.3 to 8065.1)		
rSBA-MenW-135 3193 (N=32,30)	8677.4 (6501.9 to 11580.8)	1044.6 (694.7 to 1570.6)		
rSBA-MenW-135 MP (N=32,30)	11058.1 (8587.2 to 14239.9)	1386.1 (935.6 to 2053.6)		
rSBA-MenY (N=32,30)	5736.6 (4215.9 to 7806)	546.5 (324 to 921.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti-PSW-135 and anti- PSY antibody concentrations ≥ 0.3 µg/mL

End point title	Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti- PSY antibody concentrations ≥ 0.3 µg/mL

End point description:

End point type	Secondary

End point timeframe:

1 month after the administration of the challenge dose

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Subjects				
Anti-PSA (N=29,26)	29	25		
Anti-PSC (N=31,30)	31	30		
Anti-PSW-135 (N=30,28)	30	26		
Anti-PSY (N=29,30)	29	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti-PSW-135 and anti- PSY antibody concentrations ≥ 2.0 µg/mL

End point title	Number of subjects with Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti- PSY antibody concentrations ≥ 2.0 µg/mL

End point description:

End point type	Secondary

End point timeframe:

1 month after the administration of the challenge dose

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	30		
Units: Subjects				
Anti-PSA (N=29,26)	29	15		

Anti-PSC (N=31,30)	27	30		
Anti-PSW-135 (N=30,28)	30	16		
Anti-PSY (N=29,30)	29	23		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti-PSY antibody concentrations

End point title	Anti-polysaccharide A (PSA), anti-PSC, anti- PSW-135 and anti-PSY antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

1 month after the administration of the challenge dose

End point values	12-14 months of age Challenge Group	12-14 months of age Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	30		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA (N=29,26)	42.51 (29.65 to 60.94)	2.47 (1.38 to 4.41)		
Anti-PSC (N=31,30)	6.82 (4.9 to 9.48)	18.33 (14.36 to 23.4)		
Anti-PSW-135 (N=30,28)	122.17 (85.74 to 174.07)	2.08 (1.22 to 3.56)		
Anti-PSY (N=29,30)	130.17 (91.23 to 185.72)	4.64 (2.73 to 7.89)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 8-day (Days 0-7) post-vaccination period. Unsolicited AEs: within 31 days (Days 0-30) after each vaccination. SAEs: from the beginning of the primary study up to the end of the booster study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	12-14 months of age Formulation 1 Group
Reporting group description: -	
Reporting group title	12-14 months of age Formulation 2 Group
Reporting group description: -	
Reporting group title	12-14 months of age Formulation 3 Group
Reporting group description: -	
Reporting group title	12-14 months of age Formulation 4 Group
Reporting group description: -	
Reporting group title	12-14 months of age Control Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 1 Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 2 Group
Reporting group description: -	
Reporting group title	3-5 years of age Control Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 4 Group
Reporting group description: -	
Reporting group title	3-5 years of age Formulation 3 Group
Reporting group description: -	
Reporting group title	12-14 months of age Control Group
Reporting group description: -	
Reporting group title	12-14 months of age Challenge Group
Reporting group description: -	
Reporting group title	3-5 years of age Challenge Group
Reporting group description: -	
Reporting group title	3-5 years of age Control Group

Reporting group description: -

Serious adverse events	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 48 (2.08%)	1 / 48 (2.08%)	1 / 48 (2.08%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Nervous system disorders			
Facial paresis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (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
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (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			
Vomiting			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (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			
Gastroenteritis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (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 rotavirus			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (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 infection			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 48 (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
Mastoiditis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (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 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (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
Pseudocroup			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (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	12-14 months of age Formulation 4 Group	12-14 months of age Control Group	3-5 years of age Formulation 1 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 48 (6.25%)	1 / 48 (2.08%)	1 / 54 (1.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Facial paresis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Vomiting			

subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 54 (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
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 54 (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 rotavirus			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Mastoiditis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 / 48 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 / 48 (2.08%)	0 / 48 (0.00%)	0 / 54 (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
Otitis media			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Pseudocroup			

subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 54 (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	3-5 years of age Formulation 2 Group	3-5 years of age Control Group	3-5 years of age Formulation 4 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 53 (1.89%)	0 / 53 (0.00%)	0 / 54 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Facial paresis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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			
Vomiting			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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			
Gastroenteritis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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 rotavirus			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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 infection			

subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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
Mastoiditis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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	1 / 53 (1.89%)	0 / 53 (0.00%)	0 / 54 (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
Pseudocroup			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (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	3-5 years of age Formulation 3 Group	12-14 months of age Control Group	12-14 months of age Challenge Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 54 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Facial paresis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (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

Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (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			
Gastroenteritis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (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 rotavirus			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (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 infection			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Mastoiditis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (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 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (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	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (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 / 54 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
Pseudocroup			
subjects affected / exposed	0 / 54 (0.00%)	1 / 43 (2.33%)	0 / 42 (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

Serious adverse events	3-5 years of age Challenge Group	3-5 years of age Control Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 50 (2.00%)	2 / 50 (4.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Facial paresis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudocroup			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	12-14 months of age Formulation 1 Group	12-14 months of age Formulation 2 Group	12-14 months of age Formulation 3 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 48 (62.50%)	29 / 48 (60.42%)	30 / 48 (62.50%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	11 / 48 (22.92%)	5 / 47 (10.64%)	8 / 46 (17.39%)
occurrences (all)	11	5	8
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	19 / 48 (39.58%)	20 / 47 (42.55%)	20 / 48 (41.67%)
occurrences (all)	19	20	20
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	10 / 48 (20.83%)	8 / 47 (17.02%)	10 / 48 (20.83%)
occurrences (all)	10	8	10
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[4]	19 / 48 (39.58%)	16 / 47 (34.04%)	17 / 48 (35.42%)
occurrences (all)	19	16	17
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[5]	9 / 48 (18.75%)	15 / 47 (31.91%)	12 / 48 (25.00%)
occurrences (all)	9	15	12
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[6]	22 / 48 (45.83%)	16 / 47 (34.04%)	16 / 48 (33.33%)
occurrences (all)	22	16	16

Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[7]	9 / 48 (18.75%)	10 / 47 (21.28%)	11 / 48 (22.92%)
occurrences (all)	9	10	11
Pyrexia			
subjects affected / exposed	3 / 48 (6.25%)	4 / 48 (8.33%)	4 / 48 (8.33%)
occurrences (all)	3	4	4
Pain - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[8]	11 / 48 (22.92%)	10 / 45 (22.22%)	13 / 48 (27.08%)
occurrences (all)	11	10	13
Redness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[9]	20 / 48 (41.67%)	17 / 45 (37.78%)	23 / 48 (47.92%)
occurrences (all)	20	17	23
Swelling - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[10]	14 / 46 (30.43%)	8 / 45 (17.78%)	16 / 48 (33.33%)
occurrences (all)	14	8	16
Drowsiness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[11]	14 / 46 (30.43%)	8 / 45 (17.78%)	11 / 48 (22.92%)
occurrences (all)	14	8	11
Fever - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[12]	15 / 46 (32.61%)	16 / 45 (35.56%)	16 / 48 (33.33%)
occurrences (all)	15	16	16
Irritability - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[13]	15 / 46 (32.61%)	9 / 45 (20.00%)	14 / 48 (29.17%)
occurrences (all)	15	9	14
Loss of appetite - Booster Phase			
alternative assessment type: Systematic			

subjects affected / exposed[14]	9 / 46 (19.57%)	7 / 45 (15.56%)	8 / 48 (16.67%)
occurrences (all)	9	7	8
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Enteritis			
subjects affected / exposed	5 / 48 (10.42%)	3 / 48 (6.25%)	0 / 48 (0.00%)
occurrences (all)	5	3	0
Diarrhea			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	3 / 48 (6.25%)
occurrences (all)	2	0	3
Toothache			
subjects affected / exposed	0 / 48 (0.00%)	3 / 48 (6.25%)	0 / 48 (0.00%)
occurrences (all)	0	3	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	7 / 48 (14.58%)	8 / 48 (16.67%)	10 / 48 (20.83%)
occurrences (all)	7	8	10
Nasopharyngitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	2 / 48 (4.17%)	6 / 48 (12.50%)	3 / 48 (6.25%)
occurrences (all)	2	6	3
Bronchitis			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	5 / 48 (10.42%)
occurrences (all)	2	0	5
Rhinitis			
subjects affected / exposed	2 / 48 (4.17%)	3 / 48 (6.25%)	0 / 48 (0.00%)
occurrences (all)	2	3	0
Pharyngitis			

subjects affected / exposed	2 / 48 (4.17%)	4 / 48 (8.33%)	0 / 48 (0.00%)
occurrences (all)	2	4	0
Tonsillitis			
subjects affected / exposed	0 / 48 (0.00%)	3 / 48 (6.25%)	0 / 48 (0.00%)
occurrences (all)	0	3	0

Non-serious adverse events	12-14 months of age Formulation 4 Group	12-14 months of age Control Group	3-5 years of age Formulation 1 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 48 (56.25%)	29 / 48 (60.42%)	23 / 54 (42.59%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	7 / 48 (14.58%)	8 / 47 (17.02%)	16 / 53 (30.19%)
occurrences (all)	7	8	16
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	27 / 48 (56.25%)	17 / 47 (36.17%)	23 / 53 (43.40%)
occurrences (all)	27	17	23
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	10 / 48 (20.83%)	10 / 47 (21.28%)	15 / 53 (28.30%)
occurrences (all)	10	10	15
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[4]	20 / 48 (41.67%)	18 / 47 (38.30%)	11 / 53 (20.75%)
occurrences (all)	20	18	11
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[5]	12 / 48 (25.00%)	16 / 47 (34.04%)	4 / 53 (7.55%)
occurrences (all)	12	16	4
Irritability			

alternative assessment type: Systematic			
subjects affected / exposed[6]	21 / 48 (43.75%)	19 / 47 (40.43%)	11 / 53 (20.75%)
occurrences (all)	21	19	11
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[7]	9 / 48 (18.75%)	11 / 47 (23.40%)	5 / 53 (9.43%)
occurrences (all)	9	11	5
Pyrexia			
subjects affected / exposed	0 / 48 (0.00%)	3 / 48 (6.25%)	1 / 54 (1.85%)
occurrences (all)	0	3	1
Pain - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[8]	13 / 47 (27.66%)	10 / 47 (21.28%)	0 / 54 (0.00%)
occurrences (all)	13	10	0
Redness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[9]	26 / 47 (55.32%)	18 / 47 (38.30%)	0 / 54 (0.00%)
occurrences (all)	26	18	0
Swelling - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[10]	16 / 48 (33.33%)	11 / 47 (23.40%)	0 / 54 (0.00%)
occurrences (all)	16	11	0
Drowsiness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[11]	12 / 47 (25.53%)	17 / 47 (36.17%)	0 / 54 (0.00%)
occurrences (all)	12	17	0
Fever - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[12]	14 / 47 (29.79%)	20 / 47 (42.55%)	0 / 54 (0.00%)
occurrences (all)	14	20	0
Irritability - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[13]	15 / 47 (31.91%)	14 / 47 (29.79%)	0 / 54 (0.00%)
occurrences (all)	15	14	0

Loss of appetite - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[14]	12 / 47 (25.53%)	9 / 47 (19.15%)	0 / 54 (0.00%)
occurrences (all)	12	9	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 48 (4.17%)	3 / 48 (6.25%)	1 / 54 (1.85%)
occurrences (all)	2	3	1
Enteritis			
subjects affected / exposed	6 / 48 (12.50%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences (all)	6	0	0
Diarrhea			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences (all)	2	0	1
Toothache			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	8 / 48 (16.67%)	10 / 48 (20.83%)	3 / 54 (5.56%)
occurrences (all)	8	10	3
Nasopharyngitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	4 / 48 (8.33%)	5 / 48 (10.42%)	1 / 54 (1.85%)
occurrences (all)	4	5	1
Bronchitis			
subjects affected / exposed	2 / 48 (4.17%)	4 / 48 (8.33%)	1 / 54 (1.85%)
occurrences (all)	2	4	1
Rhinitis			

subjects affected / exposed	2 / 48 (4.17%)	3 / 48 (6.25%)	2 / 54 (3.70%)
occurrences (all)	2	3	2
Pharyngitis			
subjects affected / exposed	0 / 48 (0.00%)	3 / 48 (6.25%)	2 / 54 (3.70%)
occurrences (all)	0	3	2
Tonsillitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1

Non-serious adverse events	3-5 years of age Formulation 2 Group	3-5 years of age Control Group	3-5 years of age Formulation 4 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 53 (52.83%)	23 / 53 (43.40%)	26 / 54 (48.15%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 53 (0.00%)	3 / 53 (5.66%)	0 / 54 (0.00%)
occurrences (all)	0	3	0
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	22 / 53 (41.51%)	23 / 53 (43.40%)	15 / 54 (27.78%)
occurrences (all)	22	23	15
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	28 / 53 (52.83%)	20 / 53 (37.74%)	26 / 54 (48.15%)
occurrences (all)	28	20	26
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	19 / 53 (35.85%)	12 / 53 (22.64%)	18 / 54 (33.33%)
occurrences (all)	19	12	18
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[4]	16 / 53 (30.19%)	14 / 53 (26.42%)	16 / 54 (29.63%)
occurrences (all)	16	14	16
Fever			
alternative assessment type: Systematic			

subjects affected / exposed[5]	9 / 53 (16.98%)	5 / 53 (9.43%)	7 / 54 (12.96%)
occurrences (all)	9	5	7
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[6]	10 / 53 (18.87%)	12 / 53 (22.64%)	16 / 54 (29.63%)
occurrences (all)	10	12	16
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[7]	16 / 53 (30.19%)	7 / 53 (13.21%)	12 / 54 (22.22%)
occurrences (all)	16	7	12
Pyrexia			
subjects affected / exposed	3 / 53 (5.66%)	0 / 53 (0.00%)	4 / 54 (7.41%)
occurrences (all)	3	0	4
Pain - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[8]	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Redness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[9]	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Swelling - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[10]	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Drowsiness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[11]	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Fever - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[12]	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Irritability - Booster Phase			
alternative assessment type:			

Systematic			
subjects affected / exposed[13]	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Loss of appetite - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[14]	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 53 (5.66%)	1 / 53 (1.89%)	0 / 54 (0.00%)
occurrences (all)	3	1	0
Enteritis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Diarrhea			
subjects affected / exposed	0 / 53 (0.00%)	2 / 53 (3.77%)	0 / 54 (0.00%)
occurrences (all)	0	2	0
Toothache			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 53 (0.00%)	1 / 53 (1.89%)	3 / 54 (5.56%)
occurrences (all)	0	1	3
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 53 (3.77%)	1 / 53 (1.89%)	0 / 54 (0.00%)
occurrences (all)	2	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 53 (0.00%)	4 / 53 (7.55%)	0 / 54 (0.00%)
occurrences (all)	0	4	0
Otitis media			
subjects affected / exposed	2 / 53 (3.77%)	1 / 53 (1.89%)	0 / 54 (0.00%)
occurrences (all)	2	1	0
Bronchitis			

subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	2 / 54 (3.70%)
occurrences (all)	0	0	2
Rhinitis			
subjects affected / exposed	0 / 53 (0.00%)	2 / 53 (3.77%)	2 / 54 (3.70%)
occurrences (all)	0	2	2
Pharyngitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	3-5 years of age Formulation 3 Group	12-14 months of age Control Group	12-14 months of age Challenge Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 54 (51.85%)	12 / 43 (27.91%)	14 / 42 (33.33%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	18 / 54 (33.33%)	8 / 42 (19.05%)	7 / 42 (16.67%)
occurrences (all)	18	8	7
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	28 / 54 (51.85%)	12 / 42 (28.57%)	13 / 42 (30.95%)
occurrences (all)	28	12	13
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	18 / 54 (33.33%)	4 / 42 (9.52%)	4 / 42 (9.52%)
occurrences (all)	18	4	4
Drowsiness			
alternative assessment type: Systematic			

subjects affected / exposed[4]	12 / 54 (22.22%)	9 / 42 (21.43%)	9 / 42 (21.43%)
occurrences (all)	12	9	9
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[5]	9 / 54 (16.67%)	5 / 42 (11.90%)	9 / 42 (21.43%)
occurrences (all)	9	5	9
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[6]	10 / 54 (18.52%)	5 / 42 (11.90%)	7 / 42 (16.67%)
occurrences (all)	10	5	7
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[7]	6 / 54 (11.11%)	10 / 42 (23.81%)	6 / 42 (14.29%)
occurrences (all)	6	10	6
Pyrexia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Pain - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[8]	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Redness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[9]	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Swelling - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[10]	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Drowsiness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[11]	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Fever - Booster Phase			
alternative assessment type:			

Systematic			
subjects affected / exposed[12]	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Irritability - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[13]	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Loss of appetite - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[14]	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 54 (1.85%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Enteritis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 43 (2.33%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Diarrhea			
subjects affected / exposed	1 / 54 (1.85%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Toothache			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 54 (7.41%)	2 / 43 (4.65%)	0 / 42 (0.00%)
occurrences (all)	4	2	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	5 / 54 (9.26%)	2 / 43 (4.65%)	4 / 42 (9.52%)
occurrences (all)	5	2	4
Nasopharyngitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Otitis media			

subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	2 / 54 (3.70%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Pharyngitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	1 / 54 (1.85%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	1	1	0

Non-serious adverse events	3-5 years of age Challenge Group	3-5 years of age Control Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Drowsiness			

alternative assessment type: Systematic			
subjects affected / exposed[4]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[5]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[6]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[7]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Pain - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[8]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Redness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[9]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Swelling - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[10]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Drowsiness - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[11]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	

Fever - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[12]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Irritability - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[13]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Loss of appetite - Booster Phase			
alternative assessment type: Systematic			
subjects affected / exposed[14]	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Enteritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Diarrhea			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	

Otitis media			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	

Notes:

[1] - 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.

[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.
[13] - 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.
[14] - 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
11 July 2006	The study was planned to be done in two stages, with Stage 2 being done 12 months after vaccination in Stage 1; Stage 2 includes children part of the control groups and only those children part of the group with the selected MenACWY-TT formulation (selection being done based on Stage 1 data). Due to slow enrolment of the subjects in Stage 1 of the study, the interim analysis of the data pertaining to Stage 1 has been delayed. In order to allow for completion of the interim analysis, selection of the best dose and labelling and shipping of the vaccines, this amendment proposes that the start of Study Stage 2 be delayed by 3 months (i.e., children participating to Stage 2 will enter Stage 2 15 months after vaccination in Stage 1 instead of 12 months as initially planned). To further characterise the immune response induced by the vaccine, bactericidal assays using human complement source will be performed on a subset of subjects (i.e., those who received the selected formulation and the control groups). The protocol initially planned to use bactericidal assays using baby rabbit complement only. It was not clear in the original protocol which data (available up to 1 month or 2 months after primary vaccination) would be used to select the best MenACWY formulation. The protocol was amended to make clear that the data available up to 1 month after primary vaccination would be used.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported