



Clinical trial results:

A phase IIIB open, multicountry, randomized, controlled study to demonstrate the non-inferiority of the immune response of GSK Biologicals' meningococcal serogroup A, C, W-135 and Y conjugate vaccine (MenACWY-TT)* when given intramuscularly at 2, 4 and 12 months of age or given at 2, 3, 4 and 12 months of age compared to two licensed MenC conjugate vaccine given intramuscularly at 2, 4 and 12 months of age

***MenACWY-TT has been divested to Pfizer as of 01 October 2015.**

Summary

EudraCT number	2009-016841-24
Trial protocol	ES DE EE
Global end of trial date	10 September 2013

Results information

Result version number	v2
This version publication date	17 July 2016
First version publication date	05 June 2015
Version creation reason	<ul style="list-style-type: none">• New data added to full data setData for secondary endpoints have been added.

Trial information

Trial identification

Sponsor protocol code	113369
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01144663
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)	Yes
EMA paediatric investigation plan number(s)	EMA-000429-PIP01-08

Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 June 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 June 2012
Global end of trial reached?	Yes
Global end of trial date	10 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate at 5 months of age (Visit 4) the non-inferiority of the 3-dose schedule of MenACWY-TT vaccine compared to the 2- dose schedule of the MenC-CRM or MenC-TT vaccines in terms of percentage of subjects with post-primary vaccination rSBA-MenC antibody titre $\geq 1:8$.
- To demonstrate at 5 months of age (Visit 4) the non-inferiority of the 2-dose schedule of MenACWY-TT vaccine compared to the 2- dose schedule of the MenC-CRM or MenC-TT vaccines in terms of percentage of subjects with post-primary vaccination rSBA-MenC antibody titre $\geq 1:8$.
- To demonstrate at 5 months of age (Visit 4) the immunogenicity of the 3-dose and the 2-dose schedule for MenACWY-TT for serogroups A, W-135 and Y.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 34
Country: Number of subjects enrolled	Spain: 1559
Country: Number of subjects enrolled	Germany: 502

Worldwide total number of subjects	2095
EEA total number of subjects	2095

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	2095
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

Period 1 title	Primary Vaccination
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix™ 3 Group

Arm description:

Subjects received 3 primary vaccination doses of MenACWY-TT vaccine at 2, 3 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	GSK134612A MenACWY-TT, GlaxoSmithKline (GSK) Biologicals' meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine.
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose intramuscular injection at 2, 3 and 4 months of age and 1 booster dose at 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2, 3, 4 and 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2, 3, 4 and 12 months of age.

Arm title	Nimenrix™ 2 Group
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Arm description:	
Subjects received 2 primary vaccination doses of MenACWY-TT vaccine at 2 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.	
Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	GSK134612A, MenACWY-TT, GlaxoSmithKline (GSK) Biologicals' meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 and 4 months of age and 1 booster dose at 12 months of age.	
Investigational medicinal product name	Infanrix™ hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 4 and 12 months of age.	
Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 4 and 12 months of age.	
Arm title	Menjugate® Group
Arm description:	
Subjects received 2 primary vaccination doses of MenC-CRM vaccine at 2 and 4 months of age and 1 booster dose of MenC-CRM vaccine at 12 months of age.	
Arm type	Active comparator
Investigational medicinal product name	Menjugate®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 and 4 months of age and 1 booster dose at 12 months of age.	
Investigational medicinal product name	Infanrix™ hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 4 and 12 months of age.	
Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 4 and 12 months of age.	

Arm title	NeisVac-C™ Group
Arm description:	
Subjects received 2 primary vaccination doses of MenC-TT vaccine at 2 and 4 months of age and 1 booster dose of MenC- TT vaccine at 12 months of age.	
Arm type	Active comparator
Investigational medicinal product name	NeisVac-CTM
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 and 4 months of age and 1 booster dose at 12 months of age.	
Investigational medicinal product name	Infanrix™ hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 4 and 12 months of age.	
Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 4 and 12 months of age.	

Number of subjects in period 1	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group
Started	528	524	516
Completed	508	517	508
Not completed	20	7	8
Adverse event, serious fatal	2	-	1
Consent withdrawn by subject	9	5	3
Others	-	1	-
Adverse event, non-fatal	1	-	-
Migrated/moved from study area	4	1	2
Lost to follow-up	2	-	1
Protocol deviation	2	-	1

Number of subjects in period 1	NeisVac-C™ Group
Started	527
Completed	509
Not completed	18
Adverse event, serious fatal	-

Consent withdrawn by subject	10
Others	2
Adverse event, non-fatal	1
Migrated/moved from study area	3
Lost to follow-up	2
Protocol deviation	-

Period 2

Period 2 title	Booster Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix™ 3 Booster Group

Arm description:

Subjects received 3 primary vaccination doses of MenACWY-TT vaccine at 2, 3 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	GSK134612A, MenACWY-TT, GlaxoSmithKline (GSK) Biologicals' meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose intramuscular injection at 2, 3 and 4 months of age and 1 booster dose at 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2, 3, 4 and 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2, 3, 4 and 12 months of age.

Arm title	Nimenrix™ 2 Booster Group
Arm description: Subjects received 2 primary vaccination doses of MenACWY-TT vaccine at 2 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.	
Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	GSK134612A, MenACWY-TT, GlaxoSmithKline (GSK) Biologicals' meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose intramuscular injection at 2 and 4 months of age and 1 booster dose at 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2 4 and 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2 4 and 12 months of age.

Arm title	Menjugate® Booster Group
Arm description: Subjects received 2 primary vaccination doses of MenC-CRM vaccine at 2 and 4 months of age and 1 booster dose of MenC-CRM vaccine at 12 months of age.	
Arm type	Active comparator
Investigational medicinal product name	Menjugate®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose intramuscular injection at 2 and 4 months of age and 1 booster dose at 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2 4 and 12 months of age.

Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose intramuscular injection at 2 4 and 12 months of age.	
Arm title	NeisVac-C™ Booster Group

Arm description:

Subjects received 2 primary vaccination doses of MenC-TT vaccine at 2 and 4 months of age and 1 booster dose of MenC- TT vaccine at 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2 and 4 months of age and 1 booster dose at 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2 4 and 12 months of age.

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

Dosage and administration details:

Single dose intramuscular injection at 2 4 and 12 months of age.

Number of subjects in period 2^[1]	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group
Started	497	511	503
Completed	494	509	498
Not completed	3	2	5
Consent withdrawn by subject	-	-	1
Migrated/moved from study area	1	1	1
Lost to follow-up	2	1	3

Number of subjects in period 2^[1]	NeisVac-C™ Booster Group
Started	506

Completed	505
Not completed	1
Consent withdrawn by subject	1
Migrated/moved from study area	-
Lost to follow-up	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all study participants returned in time for every study visit, but they were allowed to continue the study nonetheless. The number of participants who started each study period depends on the actual rate of return of the subjects.

Baseline characteristics

Reporting groups

Reporting group title	Nimenrix™ 3 Group
Reporting group description:	
Subjects received 3 primary vaccination doses of MenACWY-TT vaccine at 2, 3 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.	
Reporting group title	Nimenrix™ 2 Group
Reporting group description:	
Subjects received 2 primary vaccination doses of MenACWY-TT vaccine at 2 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.	
Reporting group title	Menjugate® Group
Reporting group description:	
Subjects received 2 primary vaccination doses of MenC-CRM vaccine at 2 and 4 months of age and 1 booster dose of MenC-CRM vaccine at 12 months of age.	
Reporting group title	NeisVac-C™ Group
Reporting group description:	
Subjects received 2 primary vaccination doses of MenC-TT vaccine at 2 and 4 months of age and 1 booster dose of MenC- TT vaccine at 12 months of age.	

Reporting group values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group
Number of subjects	528	524	516
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: weeks			
arithmetic mean	8.7	8.6	8.7
standard deviation	± 1.54	± 1.52	± 1.53
Gender categorical Units: Subjects			
Female	255	273	264
Male	273	251	252

Reporting group values	NeisVac-C™ Group	Total	
Number of subjects	527	2095	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks)		0 0	

Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: weeks			
arithmetic mean	8.6		
standard deviation	± 1.49	-	
Gender categorical			
Units: Subjects			
Female	251	1043	
Male	276	1052	

End points

End points reporting groups

Reporting group title	Nimenrix™ 3 Group
Reporting group description: Subjects received 3 primary vaccination doses of MenACWY-TT vaccine at 2, 3 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.	
Reporting group title	Nimenrix™ 2 Group
Reporting group description: Subjects received 2 primary vaccination doses of MenACWY-TT vaccine at 2 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.	
Reporting group title	Menjugate® Group
Reporting group description: Subjects received 2 primary vaccination doses of MenC-CRM vaccine at 2 and 4 months of age and 1 booster dose of MenC-CRM vaccine at 12 months of age.	
Reporting group title	NeisVac-C™ Group
Reporting group description: Subjects received 2 primary vaccination doses of MenC-TT vaccine at 2 and 4 months of age and 1 booster dose of MenC- TT vaccine at 12 months of age.	
Reporting group title	Nimenrix™ 3 Booster Group
Reporting group description: Subjects received 3 primary vaccination doses of MenACWY-TT vaccine at 2, 3 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.	
Reporting group title	Nimenrix™ 2 Booster Group
Reporting group description: Subjects received 2 primary vaccination doses of MenACWY-TT vaccine at 2 and 4 months of age and 1 booster dose of MenACWY-TT vaccine at 12 months of age.	
Reporting group title	Menjugate® Booster Group
Reporting group description: Subjects received 2 primary vaccination doses of MenC-CRM vaccine at 2 and 4 months of age and 1 booster dose of MenC-CRM vaccine at 12 months of age.	
Reporting group title	NeisVac-C™ Booster Group
Reporting group description: Subjects received 2 primary vaccination doses of MenC-TT vaccine at 2 and 4 months of age and 1 booster dose of MenC- TT vaccine at 12 months of age.	

Primary: Number of subjects with titers \geq 1:8 for meningococcal polysaccharides A , W-135 and Y serum bactericidal antibodies, using baby rabbit complement for assay (rSBA-MenA, rSBA-MenW-135 and rSBA-MenY)

End point title	Number of subjects with titers \geq 1:8 for meningococcal polysaccharides A , W-135 and Y serum bactericidal antibodies, using baby rabbit complement for assay (rSBA-MenA, rSBA-MenW-135 and rSBA-MenY) ^{[1][2]}
End point description: Antibody titers equal to or above (\geq) 1:8.	
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 end point was descriptive, no statistical hypothesis test was performed.

[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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	462	456		
Units: Subjects				
rSBA-MenA [N=462;456]	459	444		
rSBA-MenW-135 [N=461;455]	457	451		
rSBA-MenY [N=461;456]	429	448		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with titers $\geq 1:8$ for rSBA-MenC

End point title	Number of subjects with titers $\geq 1:8$ for rSBA-MenC
End point description:	
Antibody titers equal to or above (\geq) 1:8.	
End point type	Primary
End point timeframe:	
One month after primary vaccination	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	461	456	455	457
Units: Subjects				
rSBA-MenC [N=461;456;455;457]	459	450	453	457

Statistical analyses

Statistical analysis title	Difference in % of subjects with rSBA-MenC $\geq 1:8$
Statistical analysis description:	
To demonstrate the non-inferiority of the Nimenrix™ 3 Group compared to the Menjugate® Group, two-sided standardized asymptotic 95% CI for the groups difference [Nimenrix™ 3 Group minus Menjugate® Group] in the percentages of subjects with bactericidal vaccine response to MenC was computed.	
Comparison groups	Nimenrix™ 3 Group v Menjugate® Group

Number of subjects included in analysis	916
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Parameter estimate	Difference in % of subjects
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.17
upper limit	1.2

Notes:

[3] - The lower limit of the two-sided standardized asymptotic 95% Confidence Interval (CI) for the group difference (MenACWY-TT-3 minus MenC-CRM) in the percentage of subjects with post-primary vaccination rSBA-MenC titre $\geq 1:8$ is greater than or equal to the pre-defined clinical limit of -5%.

Statistical analysis title	Difference in % of subjects with rSBA-MenC $\geq 1:8$
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Statistical analysis description:

To demonstrate the non-inferiority of the Nimenrix™ 3 Group compared to the NeisVac-C Group, two-sided standardized asymptotic 95% CI for the groups difference [Nimenrix™ 3 Group minus NeisVac-C Group] in the percentages of subjects with bactericidal vaccine response to MenC was computed.

Comparison groups	Nimenrix™ 3 Group v NeisVac-C™ Group
Number of subjects included in analysis	918
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[4]
Parameter estimate	Difference in % of subjects
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.57
upper limit	0.4

Notes:

[4] - The lower limit of the two-sided standardized asymptotic 95% CI for the group difference (MenACWY-TT-3 minus MenC-TT) in the percentage of subjects with post-primary vaccination rSBA-MenC titre $\geq 1:8$ is greater than or equal to the pre-defined clinical limit of -5%.

Statistical analysis title	Difference in % of subjects with rSBA-MenC $\geq 1:8$
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Statistical analysis description:

To demonstrate the non-inferiority of the Nimenrix™ 2 Group compared to Menjugate Group, two-sided standardized asymptotic 95% CI for the groups difference [Nimenrix™ 2 Group minus Menjugate Group] in the percentages of subjects with bactericidal vaccine response to MenC was computed.

Comparison groups	Nimenrix™ 2 Group v Menjugate® Group
Number of subjects included in analysis	911
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[5]
Parameter estimate	Difference in % of subjects
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.45
upper limit	0.43

Notes:

[5] - The LL of the two-sided standardized asymptotic 95% CI for the group difference (MenACWY-TT-2 minus MenC-CRM) in the percentage of subjects with post-primary vaccination rSBA-MenC titre $\geq 1:8$ is greater than the pre-defined clinical limit of -5%

Statistical analysis title	Difference in % of subjects with rSBA-MenC $\geq 1:8$
Statistical analysis description:	
To demonstrate the non-inferiority of the Nimenrix™ 2 Group compared to NeisVac-C Group, two-sided standardized asymptotic 95% CI for the groups difference [Nimenrix™ 2 Group minus NeisVac-C Group] in the percentages of subjects with bactericidal vaccine response to MenC was computed.	
Comparison groups	Nimenrix™ 2 Group v NeisVac-C™ Group
Number of subjects included in analysis	913
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[6]
Parameter estimate	Difference in % of subjects
Point estimate	-1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.84
upper limit	-0.48

Notes:

[6] - The LL of the two-sided standardized asymptotic 95% CI for the group difference (MenACWY-TT-2 minus MenC-TT) in the percentage of subjects with post-primary vaccination rSBA-MenC titre $\geq 1:8$ is greater than the pre-defined clinical limit of -5%

Secondary: Number of subjects reporting any and grade 3 solicited local symptom.

End point title	Number of subjects reporting any and grade 3 solicited local symptom.
End point description:	
Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.	
End point type	Secondary
End point timeframe:	
Within 8 days (days 0 to 7) after each primary vaccine dose.	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	518	523	509	518
Units: Subjects				
Any Pain, D1 (N=518; 523; 509; 517)	247	243	243	233
Grade 3 Pain, D1 (N=518; 523; 509; 517)	32	33	28	34
Any Redness, D1 (N=518; 523; 509; 517)	241	229	236	230
Grade 3 Redness, D1 (N=518; 523; 509; 517)	9	5	9	5
Any Swelling, D1 (N=518; 523; 509; 517)	188	182	179	188
Grade 3 Swelling, D1 (N=518; 523; 509; 517)	6	4	14	6
Any Pain, D2 (N=511; 517; 509; 513)	212	210	230	214

Grade 3 Pain, D2 (N=511; 517; 509; 513)	23	37	23	29
Any Redness, D2 (N=511; 517; 509; 513)	261	271	283	284
Grade 3 Redness, D2 (N=511; 517; 509; 513)	3	5	10	2
Any Swelling, D2 (N=511; 517; 509; 513)	211	206	225	210
Grade 3 Swelling, D2 (N=511; 517; 509; 513)	3	6	14	10
Any Pain, D3 (N=505; 517; 507; 508)	168	180	180	193
Grade 3 Pain, D3 (N=505; 517; 507; 508)	13	18	15	22
Any Redness, D3 (N=505; 517; 507; 508)	247	265	308	274
Grade 3 Redness, D3 (N=505; 517; 507; 508)	9	6	13	9
Any Swelling, D3 (N=505; 517; 507; 508)	210	216	252	218
Grade 3 Swelling, D3 (N=505; 517; 507; 508)	8	6	11	13
Any Pain, Overall (N=518; 523; 509; 518)	319	332	344	327
Grade 3 Pain, Overall (N=518; 523; 509; 518)	54	67	48	69
Any Redness, Overall (N=518; 523; 509; 518)	363	369	391	371
Grade 3 Redness, Overall (N=518; 523; 509; 518)	18	15	24	15
Any Swelling, Overall (N=518; 523; 509; 518)	326	318	343	317
Grade 3 Swelling, Overall (N=518; 523; 509; 518)	15	11	27	24

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptom post meningococcal vaccination.

End point title	Number of subjects reporting any and grade 3 solicited local symptom post meningococcal vaccination.
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

Within 8 days (days 0 to 7) after each primary vaccine dose.

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	518	523	509	518
Units: Subjects				
Any Pain, D1 (N=518; 523; 509; 517)	161	155	158	157
Grade 3 Pain, D1 (N=518; 523; 509; 517)	18	17	12	24
Any Redness, D1 (N=518; 523; 509; 517)	132	128	138	140
Grade 3 Redness, D1 (N=518; 523; 509; 517)	2	1	2	1
Any Swelling, D1 (N=518; 523; 509; 517)	68	62	87	82
Grade 3 Swelling, D1 (N=518; 523; 509; 517)	1	0	3	0
Any Pain, D2 (N=510; 0; 0; 0)	125	0	0	0
Grade 3 Pain, D2 (N=510; 0; 0; 0)	9	0	0	0
Any Redness, D2 (N=510; 0; 0; 0)	131	0	0	0
Grade 3 Redness, D2 (N=510; 0; 0; 0)	0	0	0	0
Any Swelling, D2 (N=510; 0; 0; 0)	77	0	0	0
Grade 3 Swelling, D2 (N=510; 0; 0; 0)	0	0	0	0
Any Pain, D3 (N=505; 516; 507; 507)	106	124	130	142
Grade 3 Pain, D3 (N=505; 516; 507; 507)	7	11	9	12
Any Redness, D3 (N=505; 516; 507; 507)	162	169	214	197
Grade 3 Redness, D3 (N=505; 516; 507; 507)	0	0	0	1
Any Swelling, D3 (N=505; 516; 507; 507)	104	115	137	130
Grade 3 Swelling, D3 (N=505; 516; 507; 507)	0	1	0	4
Any Pain, Overall (N=518; 523; 509; 518)	229	202	213	212
Grade 3 Pain, Overall (N=518; 523; 509; 518)	29	26	19	33
Any Redness, Overall (N=518; 523; 509; 518)	233	206	255	233
Grade 3 Redness, Overall (N=518; 523; 509; 518)	2	1	2	2
Any Swelling, Overall (N=518; 523; 509; 518)	154	136	175	164
Grade 3 Swelling, Overall (N=518; 523; 509; 518)	1	1	3	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptom post vaccination with Infanrix hexa.

End point title	Number of subjects reporting any and grade 3 solicited local symptom post vaccination with Infanrix hexa.
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type Secondary

End point timeframe:

Within 8 days (days 0 to 7) after each primary vaccine dose.

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	518	523	509	517
Units: Subjects				
Any Pain, D1 (N=518; 523; 509; 517)	212	202	208	210
Grade 3 Pain, D1 (N=518; 523; 509; 517)	28	28	25	32
Any Redness, D1 (N=518; 523; 509; 517)	201	190	191	192
Grade 3 Redness, D1 (N=518; 523; 509; 517)	7	3	6	2
Any Swelling, D1 (N=518; 523; 509; 517)	148	148	128	147
Grade 3 Swelling, D1 (N=518; 523; 509; 517)	6	4	13	4
Any Pain, D2 (N=511; 517; 509; 513)	184	200	219	198
Grade 3 Pain, D2 (N=511; 517; 509; 513)	18	34	22	27
Any Redness, D2 (N=511; 517; 509; 513)	232	250	264	265
Grade 3 Redness, D2 (N=511; 517; 509; 513)	1	5	10	2
Any Swelling, D2 (N=511; 517; 509; 513)	182	185	208	195
Grade 3 Swelling, D2 (N=511; 517; 509; 513)	1	3	13	10
Any Pain, D3 (N=505; 517; 507; 508)	144	159	153	175
Grade 3 Pain, D3 (N=505; 517; 507; 508)	9	14	11	19
Any Redness, D3 (N=505; 517; 507; 508)	228	243	272	247
Grade 3 Redness, D3 (N=505; 517; 507; 508)	5	4	11	7
Any Swelling, D3 (N=505; 517; 507; 508)	191	200	227	197
Grade 3 Swelling, D3 (N=505; 517; 507; 508)	6	4	11	11
Any Pain, Overall (N=518; 523; 509; 518)	289	311	314	310
Grade 3 Pain, Overall (N=518; 523; 509; 518)	44	58	43	63
Any Redness, Overall (N=518; 523; 509; 518)	336	344	358	349
Grade 3 Redness, Overall (N=518; 523; 509; 518)	13	11	19	10
Any Swelling, Overall (N=518; 523; 509; 518)	297	292	308	294

Grade 3 Swelling, Overall (N=518; 523; 509; 518)	12	7	25	21
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptom post vaccination with Synflorix.

End point title	Number of subjects reporting any and grade 3 solicited local symptom post vaccination with Synflorix.
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

Within 8 days (days 0 to 7) after each primary vaccine dose.

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	518	523	509	518
Units: Subjects				
Any Pain, D1 (N=518; 523; 509; 517)	218	201	217	195
Grade 3 Pain, D1 (N=518; 523; 509; 517)	29	26	26	32
Any Redness, D1 (N=518; 523; 509; 517)	209	184	196	183
Grade 3 Redness, D1 (N=518; 523; 509; 517)	4	2	5	4
Any Swelling, D1 (N=518; 523; 509; 517)	135	136	130	120
Grade 3 Swelling, D1 (N=518; 523; 509; 517)	4	1	10	4
Any Pain, D2 (N=511; 517; 509; 513)	179	186	203	189
Grade 3 Pain, D2 (N=511; 517; 509; 513)	20	31	19	25
Any Redness, D2 (N=511; 517; 509; 513)	197	216	225	235
Grade 3 Redness, D2 (N=511; 517; 509; 513)	2	1	5	1
Any Swelling, D2 (N=511; 517; 509; 513)	154	162	156	155
Grade 3 Swelling, D2 (N=511; 517; 509; 513)	3	4	8	5
Any Pain, D3 (N=505; 517; 507; 508)	129	152	132	150
Grade 3 Pain, D3 (N=505; 517; 507; 508)	10	13	10	18
Any Redness, D3 (N=505; 517; 507; 508)	173	213	227	209

Grade 3 Redness, D3 (N=505; 517; 507; 508)	4	4	6	2
Any Swelling, D3 (N=505; 517; 507; 508)	136	152	164	146
Grade 3 Swelling, D3 (N=505; 517; 507; 508)	3	4	6	5
Any Pain, Overall (N=518; 523; 509; 518)	285	304	312	291
Grade 3 Pain, Overall (N=518; 523; 509; 518)	46	54	41	61
Any Redness, Overall (N=518; 523; 509; 518)	297	322	331	316
Grade 3 Redness, Overall (N=518; 523; 509; 518)	8	7	12	7
Any Swelling, Overall (N=518; 523; 509; 518)	247	259	262	237
Grade 3 Swelling, Overall (N=518; 523; 509; 518)	9	7	16	13

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptom post meningococcal vaccination.

End point title	Number of subjects reporting any and grade 3 solicited local symptom post meningococcal vaccination.
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

Within 8 days (days 0 to 7) after booster vaccination.

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	491	510	496	503
Units: Subjects				
Any Pain	191	203	203	181
Grade 3 Pain	24	23	31	18
Any Redness	186	221	213	228
Grade 3 Redness	3	6	5	4
Any Swelling	133	152	158	165
Grade 3 Swelling	1	2	2	5

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptom post vaccination with Infanrix hexa.

End point title	Number of subjects reporting any and grade 3 solicited local symptom post vaccination with Infanrix hexa.
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

Within 8 days (days 0 to 7) after booster vaccination.

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	491	510	495	504
Units: Subjects				
Any Pain	240	241	242	221
Grade 3 Pain	35	33	39	23
Any Redness	259	286	282	280
Grade 3 Redness	29	24	32	22
Any Swelling	212	226	244	240
Grade 3 Swelling	20	18	17	14

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptom post vaccination with Synflorix.

End point title	Number of subjects reporting any and grade 3 solicited local symptom post vaccination with Synflorix.
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

Within 8 days (days 0 to 7) after booster vaccination.

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	491	510	495	504
Units: Subjects				
Any Pain	212	215	227	205
Grade 3 Pain	36	33	33	26
Any Redness	219	243	242	251
Grade 3 Redness	14	9	20	9
Any Swelling	173	174	189	195
Grade 3 Swelling	5	5	4	10

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptom.

End point title	Number of subjects reporting any, grade 3 and related solicited general symptom.
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End point description:

Symptoms were abbreviated as follows: D=Drowsiness; I=Irritability/Fussiness; L=Loss of appetite ; T=Temperature, while vaccine doses were D1=Dose 1, D2 = Dose2, D3 = Dose 3 and Overall = Across doses.

End point type	Secondary
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End point timeframe:

Within 8 days (days 0 to 7) after each primary vaccine dose.

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	518	523	509	518
Units: Subjects				
Any D, D1 (N=518; 523; 508; 517)	298	282	285	297
Grade 3 D, D1 (N=518; 523; 508; 517)	22	22	17	34
Related D, D1 (N=518; 523; 508; 517)	163	167	163	178
Any I, D1 (N=518; 523; 508; 517)	329	337	355	364
Grade 3 I, D1 (N=518; 523; 508; 517)	54	41	45	54
Related I, D1 (N=518; 523; 508; 517)	199	206	213	235
Any L, D1 (N=518; 523; 508; 517)	188	208	196	219
Grade 3 L, D1 (N=518; 523; 508; 517)	12	11	9	8
Related L, D1 (N=518; 523; 508; 517)	95	106	111	117
Any T, D1 (N=518; 523; 508; 517)	166	162	170	183
Grade 3 T, D1 (N=518; 523; 508; 517)	0	0	0	0
Related T, D1 (N=518; 523; 508; 517)	128	119	122	144
Any D, D2 (N=511; 515; 509; 512)	232	210	231	211
Grade 3 D, D2 (N=511; 515; 509; 512)	20	20	17	12
Related D, D2 (N=511; 515; 509; 512)	133	123	137	132

Any I, D2 (N=511; 515; 509; 512)	328	312	319	320
Grade 3 I, D2 (N=511; 515; 509; 512)	52	35	44	48
Related I, D2 (N=511; 515; 509; 512)	208	198	194	212
Any L, D2 (N=511; 515; 509; 512)	164	185	183	179
Grade 3 L, D2 (N=511; 515; 509; 512)	10	6	6	7
Related L, D2 (N=511; 515; 509; 512)	95	103	93	106
Any T, D2 (N=511; 515; 509; 512)	146	145	158	144
Grade 3 T, D2 (N=511; 515; 509; 512)	1	0	1	1
Related T, D2 (N=511; 515; 509; 512)	107	105	116	110
Any D, D3 (N=505; 516; 505; 507)	181	194	197	193
Grade 3 D, D3 (N=505; 516; 505; 507)	21	7	13	14
Related D, D3 (N=505; 516; 505; 507)	112	115	109	112
Any I, D3 (N=505; 516; 505; 507)	259	279	271	262
Grade 3 I, D3 (N=505; 516; 505; 507)	37	30	32	39
Related I, D3 (N=505; 516; 505; 507)	165	178	164	174
Any L, D3 (N=505; 516; 505; 507)	149	176	159	154
Grade 3 L, D3 (N=505; 516; 505; 507)	14	11	10	9
Related L, D3 (N=505; 516; 505; 507)	88	94	83	90
Any T, D3 (N=505; 516; 505; 507)	106	127	112	114
Grade 3 T, D3 (N=505; 516; 505; 507)	0	2	2	1
Related T, D3 (N=505; 516; 505; 507)	71	88	79	89
Any D, Overall (N=518; 523; 509; 518)	376	365	370	377
Grade 3 D, Overall (N=518; 523; 509; 518)	45	41	40	47
Related D, Overall (N=518; 523; 509; 518)	235	231	235	237
Any I, Overall (N=518; 523; 509; 518)	419	436	439	441
Grade 3 I, Overall (N=518; 523; 509; 518)	109	83	86	104
Related I, Overall (N=518; 523; 509; 518)	302	304	311	325
Any L, Overall (N=518; 523; 509; 518)	295	325	307	312
Grade 3 L, Overall (N=518; 523; 509; 518)	28	23	22	22
Related L, Overall (N=518; 523; 509; 518)	180	194	186	182
Any T, Overall (N=518; 523; 509; 518)	272	274	277	275
Grade 3 T, Overall (N=518; 523; 509; 518)	1	2	3	2
Related T, Overall (N=518; 523; 509; 518)	203	208	208	220

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptom.

End point title	Number of subjects reporting any, grade 3 and related solicited general symptom.
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End point description:

End point type	Secondary
End point timeframe:	
Within 8 days (days 0 to 7) after booster vaccination.	

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	491	510	496	504
Units: Subjects				
Any Drowsiness	198	206	208	202
Grade 3 Drowsiness	14	13	21	18
Related Drowsiness	125	129	119	125
Any Irritability	284	296	284	297
Grade 3 Irritability	41	37	37	45
Related Irritability	180	197	181	186
Any Loss of appetite	189	193	198	195
Grade 3 Loss of appetite	12	21	23	27
Related Loss of appetite	118	114	114	121
Any Temperature (Rectally)	187	180	186	170
Grade 3 Temperature (Rectally)	2	2	3	7
Related Temperature (Rectally)	133	132	122	125

Statistical analyses

No statistical analyses for this end point

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

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

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary
End point timeframe:	
Within 31 days (days 0 to 30) after each primary vaccine dose.	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	528	524	516	527
Units: Subjects				
Any AE(s)	293	273	291	280

Statistical analyses

No statistical analyses for this end point

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

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

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary
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End point timeframe:

Within 31 days (days 0 to 30) after booster vaccination.

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	497	511	503	506
Units: Subjects				
Any AE(s)	179	185	164	167

Statistical analyses

No statistical analyses for this end point

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

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

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary
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End point timeframe:

Throughout the entire primary study (Day 0 - Month 16).

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	528	524	516	527
Units: Subjects				
Any SAE(s)	1	0	0	0

Statistical analyses

No statistical analyses for this end point

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

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

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary
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End point timeframe:

From Booster vaccination up to Extended safety follow-up (ESFU) contact

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	497	511	503	506
Units: Subjects				
Any SAE(s)	14	18	14	17

Statistical analyses

No statistical analyses for this end point

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

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

End point type	Secondary
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End point timeframe:

During the 31 days (Days 0-30) post-each primary vaccination dose.

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	528	524	516	527
Units: Subjects				
Any NOCI(s)	11	6	5	5

Statistical analyses

No statistical analyses for this end point

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

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

End point type	Secondary
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End point timeframe:

From booster vaccination up to ESFU contact.

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	497	511	503	506
Units: Subjects				
Any NOCI(s)	2	2	7	5

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 $\geq 1:8$ and $\geq 1:128$

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers $\geq 1:8$ and $\geq 1:128$
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End point description:

rSBA titres $\geq 1:8$ and $\geq 1:128$ at pre-vaccination: in a randomized subset of 50% of subjects for each of the four serogroups in the investigational vaccine groups, and in a randomized subset of 50% and 25% of subjects for MenC and MenAWY respectively in the control groups.

End point type	Secondary
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End point timeframe:

Pre-primary vaccination at Month 0

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	223	220	207	220
Units: Subjects				
rSBA-MenA ≥1:8 [N=223;219;97;110]	2	4	2	2
rSBA-MenA ≥1:128 [N=223;219;97;110]	1	0	0	0
rSBA-MenC ≥1:8 [N=223;220;207;220]	12	10	15	14
rSBA-MenC ≥1:128 [N=223;220;207;220]	2	1	6	5
rSBA-MenW-135 ≥1:8 [N=215;217;110;107]	8	12	5	3
rSBA-MenW-135 ≥1:128 [N=215;217;110;107]	0	1	1	1
rSBA-MenY ≥1:8 [N=215;219;111;107]	6	6	8	3
rSBA-MenY ≥1:128 [N=215;219;111;107]	0	3	1	1

Statistical analyses

No statistical analyses for this end point

Secondary: Titres of rSBA-MenA, rSBA-MenC, rSBA-MenW-135, rSBA-MenY antibody

End point title	Titres of rSBA-MenA, rSBA-MenC, rSBA-MenW-135, rSBA-MenY antibody
End point description:	
Antibody titers were measured in Geometric mean titers (GMTs).	
End point type	Secondary
End point timeframe:	
Pre-primary vaccination at Month 0	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	223	220	207	220
Units: Titre				
geometric mean (confidence interval 95%)				
rSBA-MenA [N=223;219;97;110]	4.1 (4 to 4.2)	4.1 (4 to 4.2)	4.1 (4 to 4.3)	4.1 (3.9 to 4.3)
rSBA-MenC [N=223;220;207;220]	4.4 (4.1 to 4.8)	4.3 (4.1 to 4.5)	4.9 (4.4 to 5.5)	4.7 (4.3 to 5.2)
rSBA-MenW-135 [N=215;217;110;107]	4.3 (4.1 to 4.5)	4.4 (4.1 to 4.6)	4.3 (3.9 to 4.8)	4.3 (3.9 to 4.7)
rSBA-MenY [N=215;219;111;107]	4.2 (4 to 4.4)	4.2 (4 to 4.5)	4.7 (4.2 to 5.2)	4.2 (3.9 to 4.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135, rSBA-MenY antibody titre $\geq 1:8$ and $\geq 1:128$

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135, rSBA-MenY antibody titre $\geq 1:8$ and $\geq 1:128$
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End point description:

rSBA titres $\geq 1:8$ and $\geq 1:128$ at pre-booster dose and one month post-booster dose, for each of the four serogroups in all subjects

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Booster Phase

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	432	438	423	439
Units: Subjects				
rSBA-MenA $\geq 1:8$ (PRE) [N=214;224;103;105]	2	3	1	2
rSBA-MenA $\geq 1:128$ (PRE) [N=214;224;103;105]	1	0	0	0
rSBA-MenA $\geq 1:8$ (PIII[M3]) [N=432;438;423;438]	420	426	7	3
rSBA-MenA $\geq 1:128$ (PIII[M3]) [N=432;438;423;438]	366	360	4	1
rSBA-MenC $\geq 1:8$ (PRE) [N=215;225;206;213]	11	11	17	14
rSBA-MenC $\geq 1:128$ (PRE) [N=215;225;206;213]	1	1	7	5
rSBA-MenC $\geq 1:8$ (PIII[M3]) [N=422;438;423;439]	420	432	421	439
rSBA-MenC $\geq 1:128$ (PIII[M3]) [N=422;438;423;439]	386	410	406	438
rSBA-MenW-135 $\geq 1:8$ (PRE) [N=202;217;102;111]	7	12	6	3
rSBA-MenW-135 $\geq 1:128$ (PRE) [N=202;217;102;111]	0	1	1	1
rSBA-MenW-135 $\geq 1:8$ (PIII[M3]) [N=422;437;421;438]	416	434	9	9
rSBA-MenW-135 $\geq 1:128$ (PIII[M3]) [N=422;437;421;438]	396	419	8	5
rSBA-MenY $\geq 1:8$ (PRE) [N=202;218;103;111]	3	5	8	3
rSBA-MenY $\geq 1:128$ (PRE) [N=202;218;103;111]	0	3	2	1

rSBA-MenY $\geq 1:8$ (PIII[M3]) [N=422;438;423;439]	393	431	13	13
rSBA-MenY $\geq 1:128$ (PIII[M3]) [N=422;438;423;439]	338	394	10	12

Statistical analyses

No statistical analyses for this end point

Secondary: Titres of rSBA-MenA, rSBA-MenC, rSBA-MenW-135, rSBA-MenY antibody

End point title	Titres of rSBA-MenA, rSBA-MenC, rSBA-MenW-135, rSBA-MenY antibody
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End point description:

Antibody titers were measured in Geometric mean titers (GMTs).

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	432	438	423	439
Units: Titre				
geometric mean (confidence interval 95%)				
rSBA-MenA (PRE) [N=214;224;103;105]	4.1 (4 to 4.2)	4.1 (4 to 4.2)	4.1 (3.9 to 4.2)	4.1 (4 to 4.2)
rSBA-MenA (PIII[M3]) [N=432;438;423;438]	243.7 (220.9 to 268.8)	206.1 (183.5 to 231.4)	4.2 (4 to 4.4)	4.1 (4 to 4.2)
rSBA-MenC (PRE) [N=215;225;206;213]	4.3 (4.1 to 4.6)	4.3 (4.1 to 4.5)	5.1 (4.5 to 5.7)	4.8 (4.3 to 5.3)
rSBA-MenC (PIII[M3]) [N=422;438;423;439]	386 (345.1 to 431.7)	598.8 (526.5 to 681.1)	949.7 (837.6 to 1076.7)	1169.2 (1061.2 to 1288.3)
rSBA-MenW-135 (PRE) [N=202;217;102;111]	4.3 (4.1 to 4.5)	4.4 (4.1 to 4.6)	4.5 (4 to 5)	4.3 (3.9 to 4.7)
rSBA-MenW-135 (PIII[M3]) [N=422;437;421;438]	1093.5 (944.3 to 1266.3)	1601.6 (1378.4 to 1860.9)	4.5 (4.1 to 4.8)	4.3 (4.1 to 4.6)
rSBA-MenY (PRE) [N=202;218;103;111]	4.1 (4 to 4.2)	4.2 (4 to 4.5)	4.8 (4.2 to 5.5)	4.2 (3.9 to 4.6)
rSBA-MenY (PIII[M3]) [N=422;438;423;439]	269.8 (227.1 to 320.6)	489.8 (424.9 to 564.6)	4.4 (4.2 to 4.7)	4.5 (4.2 to 4.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135,

hSBA-MenY antibody titre $\geq 1:4$ and $\geq 1:8$

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, hSBA-MenY antibody titre $\geq 1:4$ and $\geq 1:8$
End point description: The cut-off values for hSBA antibody titers were $\geq 1:4$ and $\geq 1:8$ at pre-vaccination, one month after the final priming vaccination, for each of the four serogroups in all subjects	
End point type	Secondary
End point timeframe: At Month 0 and Month 3 Primary Phase	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	214	218	205	226
Units: Subjects				
hSBA-MenA $\geq 1:4$ (PRE) [N=164;166;161;166]	34	31	41	34
hSBA-MenA $\geq 1:8$ (PRE) [N=164;166;161;166]	28	19	27	27
hSBA-MenA $\geq 1:4$ (PIII[M3]) [N=200;202;172;205]	197	195	21	18
hSBA-MenA $\geq 1:8$ (PIII[M3]) [N=200;202;172;205]	196	195	15	14
hSBA-MenC $\geq 1:4$ (PRE) [N=181;178;168;185]	43	35	50	44
hSBA-MenC $\geq 1:8$ (PRE) [N=181;178;168;185]	43	35	49	42
hSBA-MenC $\geq 1:4$ (PIII[M3]) [N=214;218;202;226]	213	215	202	226
hSBA-MenC $\geq 1:8$ (PIII[M3]) [N=214;218;202;226]	213	215	202	226
hSBA-MenW-135 $\geq 1:4$ (PRE) [N=182;184;190;187]	50	46	54	37
hSBA-MenW-135 $\geq 1:8$ (PRE) [N=182;184;190;187]	49	44	52	36
hSBA-MenW-135 $\geq 1:4$ (PIII[M3]) [N=201;217;205;204]	197	217	6	3
hSBA-MenW-135 $\geq 1:8$ (PIII[M3]) [N=201;217;205;204]	197	217	4	3
hSBA-MenY $\geq 1:4$ (PRE) [N=191;192;204;192]	73	73	71	78
hSBA-MenY $\geq 1:8$ (PRE) [N=191;192;204;192]	73	72	71	77
hSBA-MenY $\geq 1:4$ (PIII[M3]) [N=209;214;204;196]	187	209	11	5
hSBA-MenY $\geq 1:8$ (PIII[M3]) [N=209;214;204;196]	185	209	11	4

Statistical analyses

No statistical analyses for this end point

Secondary: Titres of hSBA-MenA, hSBA-MenC, hSBA-MenW-135, hSBA-MenY antibody

End point title	Titres of hSBA-MenA, hSBA-MenC, hSBA-MenW-135, hSBA-MenY antibody
End point description: Antibody titers were measured in Geometric mean titers (GMTs).	
End point type	Secondary
End point timeframe: At Month 0 and Month 3, Primary Phase	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	214	218	205	226
Units: Titre				
geometric mean (confidence interval 95%)				
hSBA-MenA (PRE) [N=164;166;161;166]	2.8 (2.5 to 3.2)	2.7 (2.4 to 3)	3 (2.7 to 3.4)	2.9 (2.6 to 3.3)
hSBA-MenA (PIII[M3]) [N=200;202;172;205]	240.9 (207.8 to 279.3)	157.2 (131.4 to 188.1)	2.5 (2.2 to 2.7)	2.3 (2.2 to 2.5)
hSBA-MenC (PRE) [N=181;178;168;185]	3.9 (3.2 to 4.7)	3.6 (3 to 4.4)	4.9 (3.9 to 6.2)	3.9 (3.2 to 4.7)
hSBA-MenC (PIII[M3]) [N=214;218;202;226]	765.6 (647.4 to 905.3)	1308.3 (1051.7 to 1627.4)	3188.1 (2645.8 to 3841.5)	2626.5 (2218.9 to 3109)
hSBA-MenW-135 (PRE) [N=182;184;190;187]	5 (3.9 to 6.3)	4.7 (3.8 to 6)	5 (4 to 6.3)	3.7 (3.1 to 4.6)
hSBA-MenW-135 (PIII[M3]) [N=201;217;205;204]	190.9 (160 to 227.8)	753.5 (643.8 to 881.8)	2.1 (2 to 2.3)	2.1 (2 to 2.3)
hSBA-MenY (PRE) [N=191;192;204;192]	8 (6.1 to 10.5)	8 (6.1 to 10.5)	7.1 (5.5 to 9.2)	8.1 (6.3 to 10.4)
hSBA-MenY (PIII[M3]) [N=209;214;204;196]	66.5 (53.7 to 82.2)	328.1 (275.8 to 390.2)	2.4 (2.1 to 2.7)	2.1 (2 to 2.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, hSBA-MenY antibody titre $\geq 1:4$ and $\geq 1:8$

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, hSBA-MenY antibody titre $\geq 1:4$ and $\geq 1:8$
End point description: The cut-off values for hSBA antibody titers were $\geq 1:4$ and $\geq 1:8$ at pre-booster dose and one month post-booster dose, for each of the four serogroups in all subjects	
End point type	Secondary
End point timeframe: At Month 0 and Month 3, Booster Phase	

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	199	214	195	211
Units: Subjects				
hSBA-MenA ≥1:4 (PRE) [N=155;167;159;160]	36	34	41	33
hSBA-MenA ≥1:8 (PRE) [N=155;167;159;160]	29	20	25	26
hSBA-MenA ≥1:4 (PIII[M3]) [N=188;199;159;190]	186	193	18	17
hSBA-MenA ≥1:8 (PIII[M3]) [N=188;199;159;190]	185	193	13	13
hSBA-MenC ≥1:4 (PRE) [N=172;180;169;179]	42	40	54	44
hSBA-MenC ≥1:8 (PRE) [N=172;180;169;179]	42	40	53	42
hSBA-MenC ≥1:4 (PIII[M3]) [N=199;214;190;211]	198	211	190	211
hSBA-MenC ≥1:8 (PIII[M3]) [N=199;214;190;211]	198	211	190	211
hSBA-MenW-135 ≥1:4 (PRE) [N=170;183;181;191]	44	51	55	38
hSBA-MenW-135 ≥1:8 (PRE) [N=170;183;181;191]	43	49	52	37
hSBA-MenW-135 ≥1:4 (PIII[M3]) [N=180;205;188;203]	176	205	6	3
hSBA-MenW-135 ≥1:8 (PIII[M3]) [N=180;205;188;203]	176	205	5	3
hSBA-MenY ≥1:4 (PRE) [N=178;191;195;197]	62	76	70	78
hSBA-MenY ≥1:8 (PRE) [N=178;191;195;197]	62	75	70	78
hSBA-MenY ≥1:4 (PIII[M3]) [N=189;201;184;193]	168	196	9	4
hSBA-MenY ≥1:8 (PIII[M3]) [N=189;201;184;193]	167	196	9	3

Statistical analyses

No statistical analyses for this end point

Secondary: Titres of hSBA-MenA, hSBA-MenC, hSBA-MenW-135, hSBA-MenY antibody

End point title	Titres of hSBA-MenA, hSBA-MenC, hSBA-MenW-135, hSBA-MenY antibody
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End point description:

Antibody titers were measured in Geometric mean titers (GMTs).

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Booster Phase

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	199	214	195	211
Units: Titre				
geometric mean (confidence interval 95%)				
hSBA-MenA ≥1:4 (PRE) [N=155;167;159;160]	2.9 (2.6 to 3.3)	2.8 (2.5 to 3)	3 (2.7 to 3.4)	2.9 (2.6 to 3.2)
hSBA-MenA ≥1:4 (PIII[M3]) [N=188;199;159;190]	236 (203.6 to 273.5)	164 (136.8 to 196.6)	2.4 (2.2 to 2.7)	2.3 (2.2 to 2.5)
hSBA-MenC ≥1:4 (PRE) [N=172;180;169;179]	3.7 (3.1 to 4.4)	3.9 (3.2 to 4.7)	5.2 (4.1 to 6.6)	4.1 (3.3 to 5)
hSBA-MenC ≥1:4 (PIII[M3]) [N=199;214;190;211]	720.6 (602.4 to 862.1)	1340.7 (1073.1 to 1675.2)	3301.2 (2728.6 to 3994)	2594.4 (2176 to 3093.1)
hSBA-MenW-135 ≥1:4 (PRE) [N=170;183;181;191]	4.7 (3.7 to 6)	5.2 (4.1 to 6.6)	5.5 (4.3 to 7)	3.8 (3.1 to 4.6)
hSBA-MenW-135 ≥1:4 (PIII[M3]) [N=180;205;188;203]	177.7 (146.7 to 215.2)	756.8 (641.4 to 893.1)	2.2 (2 to 2.4)	2.1 (2 to 2.3)
hSBA-MenY ≥1:4 (PRE) [N=178;191;195;197]	7.2 (5.5 to 9.4)	8.6 (6.5 to 11.4)	7.5 (5.8 to 9.8)	8 (6.2 to 10.4)
hSBA-MenY ≥1:4 (PIII[M3]) [N=189;201;184;193]	62.8 (50.3 to 78.4)	327.4 (273 to 392.7)	2.4 (2.1 to 2.6)	2.1 (2 to 2.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects for anti- pneumococcal (anti-P) ≥ 0.15 µg/mL and ≥ 0.35 µg/mL

End point title	Number of subjects for anti- pneumococcal (anti-P) ≥ 0.15 µg/mL and ≥ 0.35 µg/mL
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End point description:

Concentrations ≥ 0.15 µg/mL (seropositivity), ≥ 0.35 µg/mL and concentrations in a randomized subset of 25% of subjects, at prevaccination, one month after the final priming vaccination.

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Primary Phase

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	104	95	103
Units: Subjects				
Anti-1 ≥ 0.15 µg/mL (PRE) [N=98;92;90;97]	18	15	17	18

Anti-1 ≥ 0.15 µg/mL (PIII[M3]) [N=96;104;93;103]	96	102	93	103
Anti-1 ≥ 0.35 µg/mL (PRE) [N=98;92;90;97]	3	9	8	8
Anti-1 ≥ 0.35 µg/mL (PIII[M3]) [N=96;104;93;103]	93	95	89	91
Anti-4 ≥ 0.15 µg/mL (PRE) [N=98;93;92;95]	11	11	13	12
Anti-4 ≥ 0.15 µg/mL (PIII[M3]) [N=96;104;95;103]	96	102	95	103
Anti-4 ≥ 0.35 µg/mL (PRE) [N=98;93;92;95]	2	2	2	1
Anti-4 ≥ 0.35 µg/mL (PIII[M3]) [N=96;104;95;103]	94	99	93	99
Anti-5 ≥ 0.15 µg/mL (PRE) [N=97;92;91;96]	42	32	39	33
Anti-5 ≥ 0.15 µg/mL (PIII[M3]) [N=96;104;93;103]	95	102	93	101
Anti-5 ≥ 0.35 µg/mL (PRE) [N=97;92;91;96]	10	5	9	14
Anti-5 ≥ 0.35 µg/mL (PIII[M3]) [N=96;104;93;103]	84	86	80	92
Anti-6B ≥ 0.15 µg/mL (PRE) [N=97;92;91;96]	55	42	41	50
Anti-6B ≥ 0.15 µg/mL (PIII[M3]) [N=96;104;93;103]	88	95	88	90
Anti-6B ≥ 0.35 µg/mL (PRE) [N=97;92;91;96]	27	19	20	26
Anti-6B ≥ 0.35 µg/mL (PIII[M3]) [N=96;104;93;103]	71	82	75	81
Anti-7F ≥ 0.15 µg/mL (PRE) [N=98;92;92;96]	38	43	44	49
Anti-7F ≥ 0.15 µg/mL (PIII[M3]) [N=96;104;93;103]	96	102	93	103
Anti-7F ≥ 0.35 µg/mL (PRE) [N=98;92;92;96]	13	18	20	16
Anti-7F ≥ 0.35 µg/mL (PIII[M3]) [N=96;104;93;103]	94	99	93	103
Anti-9V ≥ 0.15 µg/mL (PRE) [N=97;93;92;96]	38	44	35	43
Anti-9V ≥ 0.15 µg/mL (PIII[M3]) [N=96;104;93;103]	94	102	90	103
Anti-9V ≥ 0.35 µg/mL (PRE) [N=97;93;92;96]	9	18	12	16
Anti-9V ≥ 0.35 µg/mL (PIII[M3]) [N=96;104;93;103]	92	99	88	99
Anti-14 ≥ 0.15 µg/mL (PRE) [N=97;92;90;95]	72	69	74	80
Anti-14 ≥ 0.15 µg/mL (PIII[M3]) [N=96;103;95;103]	96	103	95	103
Anti-14 ≥ 0.35 µg/mL (PRE) [N=97;92;90;95]	53	57	57	67
Anti-14 ≥ 0.35 µg/mL (PIII[M3]) [N=96;103;95;103]	96	103	95	103
Anti-18C ≥ 0.15 µg/mL (PRE) [N=96;93;91;94]	30	44	45	43
Anti-18C ≥ 0.15 µg/mL (PIII[M3]) [N=96;103;94;103]	96	101	93	103
Anti-18C ≥ 0.35 µg/mL (PRE) [N=96;93;91;94]	14	18	20	10
Anti-18C ≥ 0.35 µg/mL (PIII[M3]) [N=96;103;94;103]	90	100	89	101

Anti-19F \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=96;93;91;96]	41	61	51	53
Anti-19F \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=96;104;95;103]	94	100	94	102
Anti-19F \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=96;93;91;96]	21	30	27	23
Anti-19F \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=96;104;95;103]	92	94	90	99
Anti-23F \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=97;92;90;96]	37	38	29	40
Anti-23F \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=95;104;94;103]	90	99	91	98
Anti-23F \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=97;92;90;96]	16	13	13	18
Anti-23F \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=95;104;94;103]	83	83	77	86

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-pneumococcal antibody

End point title	Concentration of Anti-pneumococcal antibody
End point description: Concentrations were presented as geometric mean concentrations (GMCs).	
End point type	Secondary
End point timeframe: At Month 0 and Month 3, Primary Phase	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	104	95	103
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-1 (PRE) [N=98;92;90;97]	0.09 (0.08 to 0.1)	0.1 (0.09 to 0.12)	0.1 (0.09 to 0.12)	0.1 (0.09 to 0.11)
Anti-1 (PIII[M3]) [N=96;104;93;103]	1.36 (1.15 to 1.62)	1.13 (0.96 to 1.34)	1.26 (1.06 to 1.5)	1.02 (0.88 to 1.18)
Anti-4 (PRE) [N=98;93;92;95]	0.09 (0.08 to 0.09)	0.09 (0.08 to 0.09)	0.09 (0.08 to 0.1)	0.09 (0.08 to 0.09)
Anti-4 (PIII[M3]) [N=96;104;95;103]	1.84 (1.58 to 2.15)	1.56 (1.31 to 1.86)	1.77 (1.5 to 2.1)	1.6 (1.37 to 1.85)
Anti-5 (PRE) [N=97;92;91;96]	0.13 (0.11 to 0.15)	0.12 (0.1 to 0.13)	0.13 (0.11 to 0.15)	0.12 (0.11 to 0.15)
Anti-5 (PIII[M3]) [N=96;104;93;103]	0.82 (0.71 to 0.95)	0.7 (0.61 to 0.81)	0.77 (0.66 to 0.89)	0.74 (0.65 to 0.85)
Anti-6B (PRE) [N=97;92;91;96]	0.18 (0.15 to 0.21)	0.15 (0.13 to 0.19)	0.15 (0.13 to 0.19)	0.18 (0.15 to 0.22)
Anti-6B (PIII[M3]) [N=96;104;93;103]	0.79 (0.62 to 1)	0.9 (0.71 to 1.14)	1.08 (0.84 to 1.38)	0.86 (0.67 to 1.12)

Anti-7F (PRE) [N=98;92;92;96]	0.13 (0.11 to 0.16)	0.17 (0.13 to 0.21)	0.16 (0.13 to 0.2)	0.15 (0.13 to 0.18)
Anti-7F (PIII[M3]) [N=96;104;93;103]	1.91 (1.63 to 2.23)	1.84 (1.56 to 2.18)	2.13 (1.82 to 2.49)	1.87 (1.62 to 2.15)
Anti-9V (PRE) [N=97;93;92;96]	0.13 (0.11 to 0.15)	0.15 (0.13 to 0.18)	0.13 (0.11 to 0.15)	0.14 (0.12 to 0.17)
Anti-9V (PIII[M3]) [N=96;104;93;103]	1.31 (1.1 to 1.56)	1.12 (0.97 to 1.29)	1.22 (1.02 to 1.46)	1.21 (1.07 to 1.38)
Anti-14 (PRE) [N=97;92;90;95]	0.5 (0.37 to 0.67)	0.61 (0.44 to 0.85)	0.59 (0.44 to 0.79)	0.74 (0.56 to 0.99)
Anti-14 (PIII[M3]) [N=96;103;95;103]	7.55 (6.4 to 8.9)	7.4 (6.35 to 8.62)	8.51 (7.09 to 10.22)	6.04 (5.04 to 7.24)
Anti-18C (PRE) [N=96;93;91;94]	0.13 (0.11 to 0.16)	0.16 (0.13 to 0.2)	0.17 (0.14 to 0.21)	0.14 (0.12 to 0.16)
Anti-18C (PIII[M3]) [N=96;103;94;103]	2.14 (1.74 to 2.64)	1.77 (1.47 to 2.13)	2.39 (1.96 to 2.93)	2.8 (2.4 to 3.27)
Anti-19F (PRE) [N=96;93;91;96]	0.15 (0.13 to 0.19)	0.23 (0.19 to 0.28)	0.2 (0.16 to 0.25)	0.19 (0.15 to 0.23)
Anti-19F (PIII[M3]) [N=96;104;95;103]	3.01 (2.37 to 3.82)	2.6 (2.01 to 3.35)	2.89 (2.26 to 3.69)	2.85 (2.29 to 3.54)
Anti-23F (PRE) [N=97;92;90;96]	0.14 (0.11 to 0.16)	0.14 (0.11 to 0.17)	0.13 (0.11 to 0.15)	0.15 (0.12 to 0.17)
Anti-23F(PIII[M3]) [N=95;104;94;103]	0.96 (0.78 to 1.18)	0.85 (0.69 to 1.06)	1.08 (0.86 to 1.36)	0.94 (0.77 to 1.16)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-pneumococcal antibody ≥ 0.15 $\mu\text{g/mL}$ and ≥ 0.35 $\mu\text{g/mL}$

End point title	Number of subjects with Anti-pneumococcal antibody ≥ 0.15 $\mu\text{g/mL}$ and ≥ 0.35 $\mu\text{g/mL}$
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End point description:

Concentrations ≥ 0.15 $\mu\text{g/mL}$ (seropositivity), ≥ 0.35 $\mu\text{g/mL}$ and concentrations in a randomized subset of 25% of subjects, at pre-booster dose and one month post-booster dose

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Booster Phase

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	100	85	95
Units: Subjects				
Anti-1 ≥ 0.15 $\mu\text{g/mL}$ (PRE) [N=95;93;83;96]	18	15	19	18
Anti-1 ≥ 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	92	99	82	95
Anti-1 ≥ 0.35 $\mu\text{g/mL}$ (PRE) [N=95;93;83;96]	3	9	10	8
Anti-1 ≥ 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	88	92	78	84

Anti-4 \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=95;94;85;94]	12	11	14	14
Anti-4 \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;84;95]	92	99	84	95
Anti-4 \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=95;94;85;94]	2	2	2	1
Anti-4 \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;84;95]	91	97	82	91
Anti-5 \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=94;93;84;95]	44	34	39	34
Anti-5 \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	91	99	82	93
Anti-5 \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=94;93;84;95]	10	5	9	15
Anti-5 \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	81	85	71	84
Anti-6B \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=94;93;84;95]	55	43	41	49
Anti-6B \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	84	93	77	82
Anti-6B \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=94;93;84;95]	27	20	20	24
Anti-6B \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	68	79	65	75
Anti-7F \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=95;93;85;95]	39	42	46	51
Anti-7F \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	92	99	82	95
Anti-7F \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=95;93;85;95]	18	18	24	17
Anti-7F \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	90	96	82	95
Anti-9V \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=94;94;85;95]	38	43	33	41
Anti-9V \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	90	99	79	95
Anti-9V \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=94;94;85;95]	8	17	12	16
Anti-9V \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;82;95]	87	96	76	91
Anti-14 \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=94;93;83;94]	70	68	67	78
Anti-14 \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;84;95]	92	100	84	95
Anti-14 \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=94;93;83;94]	52	56	53	64
Anti-14 \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;84;95]	92	100	84	95
Anti-18C \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=93;94;84;93]	28	46	44	40
Anti-18C \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;99;83;95]	92	97	82	95
Anti-18C \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=93;94;84;93]	14	20	19	9
Anti-18C \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;99;83;95]	86	96	80	94
Anti-19F \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=93;94;84;95]	42	61	49	52
Anti-19F \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;84;95]	90	96	83	94
Anti-19F \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=93;94;84;95]	25	30	26	25

Anti-19F \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;84;95]	89	90	81	91
Anti-23F \geq 0.15 $\mu\text{g/mL}$ (PRE) [N=94;93;83;95]	34	38	29	39
Anti-23F \geq 0.15 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;83;95]	87	96	81	90
Anti-23F \geq 0.35 $\mu\text{g/mL}$ (PRE) [N=94;93;83;95]	16	14	12	17
Anti-23F \geq 0.35 $\mu\text{g/mL}$ (PIII[M3]) [N=92;100;83;95]	79	80	67	79

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-pneumococcal antibody

End point title	Concentration of Anti-pneumococcal antibody
End point description: Concentrations are presented as geometric mean concentrations (GMCs).	
End point type	Secondary
End point timeframe: At Month 0 and Month 3, Booster Phase	

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	100	85	95
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-1 (PRE) [N=95;93;83;96]	0.09 (0.08 to 0.1)	0.1 (0.09 to 0.12)	0.11 (0.09 to 0.13)	0.1 (0.09 to 0.11)
Anti-1 (PIII[M3]) [N=92;100;82;95]	1.3 (1.09 to 1.56)	1.17 (0.99 to 1.37)	1.31 (1.08 to 1.58)	1 (0.85 to 1.17)
Anti-4 (PRE) [N=95;94;85;94]	0.09 (0.08 to 0.1)	0.09 (0.08 to 0.09)	0.09 (0.08 to 0.1)	0.09 (0.08 to 0.1)
Anti-4 (PIII[M3]) [N=92;100;84;95]	1.74 (1.5 to 2.03)	1.6 (1.35 to 1.88)	1.81 (1.51 to 2.18)	1.57 (1.35 to 1.83)
Anti-5 (PRE) [N=94;93;84;95]	0.13 (0.12 to 0.15)	0.12 (0.1 to 0.13)	0.14 (0.12 to 0.16)	0.13 (0.11 to 0.15)
Anti-5 (PIII[M3]) [N=92;100;82;95]	0.8 (0.69 to 0.93)	0.71 (0.62 to 0.82)	0.78 (0.66 to 0.92)	0.74 (0.64 to 0.85)
Anti-6B (PRE) [N=94;93;84;95]	0.18 (0.15 to 0.22)	0.16 (0.13 to 0.19)	0.17 (0.13 to 0.21)	0.17 (0.14 to 0.21)
Anti-6B (PIII[M3]) [N=92;100;82;95]	0.78 (0.6 to 1)	0.93 (0.73 to 1.18)	1.04 (0.8 to 1.36)	0.87 (0.66 to 1.14)
Anti-7F (PRE) [N=95;93;85;95]	0.15 (0.12 to 0.18)	0.16 (0.13 to 0.2)	0.18 (0.15 to 0.23)	0.16 (0.13 to 0.19)
Anti-7F (PIII[M3]) [N=92;100;82;95]	1.96 (1.65 to 2.32)	1.88 (1.61 to 2.21)	2.21 (1.88 to 2.61)	1.8 (1.55 to 2.08)
Anti-9V (PRE) [N=94;94;85;95]	0.13 (0.11 to 0.15)	0.14 (0.12 to 0.17)	0.13 (0.11 to 0.16)	0.14 (0.12 to 0.16)

Anti-9V (PIII[M3]) [N=92;100;82;95]	1.29 (1.07 to 1.55)	1.14 (1 to 1.3)	1.21 (0.99 to 1.49)	1.2 (1.05 to 1.38)
Anti-14 (PRE) [N=94;93;83;94]	0.51 (0.37 to 0.69)	0.57 (0.41 to 0.79)	0.6 (0.44 to 0.81)	0.71 (0.53 to 0.96)
Anti-14 (PIII[M3]) [N=92;100;84;95]	7.58 (6.38 to 9.01)	7.49 (6.43 to 8.73)	8.8 (7.31 to 10.58)	5.99 (4.96 to 7.22)
Anti-18C (PRE) [N=93;94;84;93]	0.13 (0.1 to 0.15)	0.17 (0.14 to 0.2)	0.18 (0.14 to 0.22)	0.13 (0.11 to 0.15)
Anti-18C (PIII[M3]) [N=92;99;83;95]	2.06 (1.67 to 2.54)	1.76 (1.45 to 2.12)	2.52 (2.05 to 3.08)	2.92 (2.5 to 3.4)
Anti-19F (PRE) [N=93;94;84;95]	0.17 (0.14 to 0.21)	0.23 (0.18 to 0.28)	0.21 (0.17 to 0.27)	0.19 (0.16 to 0.24)
Anti-19F (PIII[M3]) [N=92;100;84;95]	3.22 (2.53 to 4.1)	2.49 (1.91 to 3.24)	3.08 (2.42 to 3.92)	2.82 (2.23 to 3.56)
Anti-23F (PRE) [N=94;93;83;95]	0.13 (0.11 to 0.16)	0.14 (0.11 to 0.17)	0.13 (0.11 to 0.17)	0.14 (0.12 to 0.17)
Anti-23F (PIII[M3]) [N=92;100;83;95]	0.93 (0.75 to 1.16)	0.87 (0.7 to 1.08)	1.04 (0.82 to 1.33)	0.93 (0.75 to 1.15)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) $\geq 0.1\text{IU/ml}$

End point title	Number of subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) $\geq 0.1\text{IU/ml}$
End point description:	
Concentration $\geq 0.1 \mu\text{g/mL}$ in a randomized subset of 25% of subjects, at pre-primary vaccination dose and one month post-primary vaccination dose	
End point type	Secondary
End point timeframe:	
At Month 0 and Month 3, Primary Phase	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	117	113	123	115
Units: Subjects				
Anti-D (PRE) [N=116;106;117;110]	37	43	56	39
Anti-D (PIII[M3]) [N=117;113;123;115]	117	113	123	115
Anti-TT (PRE) [N=116;107;116;111]	104	91	107	91
Anti-TT (PIII[M3]) [N=117;113;123;114]	117	113	123	114

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-D and Anti-TT antibody

End point title	Concentration of Anti-D and Anti-TT antibody
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End point description:

Concentrations were presented as geometric mean concentrations (GMCs).

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Primary Phase

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	117	113	123	115
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D (PRE) [N=116;106;117;110]	0.092 (0.077 to 0.11)	0.098 (0.082 to 0.117)	0.133 (0.108 to 0.165)	0.093 (0.078 to 0.112)
Anti-D (PIII[M3]) [N=117;113;123;115]	2.171 (1.893 to 2.49)	2.64 (2.274 to 3.065)	3.005 (2.657 to 3.4)	2.488 (2.169 to 2.855)
Anti-TT (PRE) [N=116;107;116;111]	0.484 (0.393 to 0.596)	0.496 (0.388 to 0.636)	0.727 (0.581 to 0.909)	0.5 (0.387 to 0.647)
Anti-TT (PIII[M3]) [N=117;113;123;114]	3.137 (2.79 to 3.527)	3.37 (2.98 to 3.811)	2.847 (2.523 to 3.212)	4.339 (3.833 to 4.912)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-D and Anti-TT ≥ 0.1IU/mL

End point title	Number of subjects with Anti-D and Anti-TT ≥ 0.1IU/mL
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End point description:

Concentration ≥ 0.1 µg/mL in a randomized subset of 25% of subjects, at pre-booster dose and one month post-booster dose

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Booster Phase

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	106	117	113
Units: Subjects				
Anti-D (PRE) [N=110;103;113;112]	35	44	55	36
Anti-D (PIII[M3]) [N=110;106;117;113]	110	106	117	113
Anti-TT (PRE) [N=110;104;112;113]	97	91	103	94

Anti-TT (PIII[M3]) [N=110;106;117;112]	110	106	117	112
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Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-D and Anti-TT antibody

End point title	Concentration of Anti-D and Anti-TT antibody
End point description: Concentrations were presented as geometric mean concentrations (GMCs).	
End point type	Secondary
End point timeframe: At Month 0 and Month 3, Booster Phase	

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	106	117	113
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D (PRE) [N=110;103;113;112]	0.093 (0.077 to 0.112)	0.106 (0.087 to 0.129)	0.136 (0.109 to 0.169)	0.086 (0.073 to 0.102)
Anti-D (PIII[M3]) [N=110;106;117;113]	2.148 (1.864 to 2.475)	2.537 (2.177 to 2.957)	2.987 (2.628 to 3.396)	2.57 (2.245 to 2.942)
Anti-TT (PRE) [N=110;104;112;113]	0.484 (0.387 to 0.605)	0.571 (0.444 to 0.733)	0.749 (0.597 to 0.941)	0.516 (0.401 to 0.664)
Anti-TT (PIII[M3]) [N=110;106;117;112]	3.125 (2.772 to 3.523)	3.285 (2.897 to 3.724)	2.832 (2.501 to 3.206)	4.375 (3.858 to 4.961)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) ≥ 5EL/ml

End point title	Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) ≥ 5EL/ml
End point description: Concentration ≥ 5 EL.U/mL in a randomized subset of 25% of subjects, at pre-primary vaccination dose and one month post-primary vaccination dose	
End point type	Secondary
End point timeframe: At Month 0 and Month 3, Primary Phase	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	117	112	123	115
Units: Subjects				
Anti-PT (PRE) [N=112;103;113;109]	23	32	28	31
Anti-PT (PIII[M3]) [N=117;111;122;115]	117	111	122	115
Anti-FHA (PRE) [N=114;104;115;109]	83	85	93	78
Anti-FHA (PIII[M3]) [N=117;111;123;115]	117	111	123	115
Anti-PRN (PRE) [N=115;104;116;110]	31	39	44	32
Anti-PRN (PIII[M3]) [N=117;112;122;115]	117	112	122	115

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-PT, Anti-FHA and Anti-PRN

End point title	Concentration of Anti-PT, Anti-FHA and Anti-PRN
End point description:	Concentrations were presented as geometric mean concentrations (GMCs).
End point type	Secondary
End point timeframe:	At Month 0 and Month 3, Primary Phase

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	117	112	123	115
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT (PRE) [N=112;103;113;109]	3.4 (3 to 3.8)	3.9 (3.3 to 4.5)	3.6 (3.2 to 4.2)	4.1 (3.5 to 4.9)
Anti-PT (PIII[M3]) [N=117;111;122;115]	52.7 (46.5 to 59.8)	56.3 (49.5 to 64)	56.5 (50.5 to 63.1)	56.4 (50.6 to 63)
Anti-FHA (PRE) [N=114;104;115;109]	9.7 (8 to 11.9)	13.2 (10.7 to 16.4)	11.4 (9.4 to 13.9)	11.9 (9.4 to 15.1)
Anti-FHA (PIII[M3]) [N=117;111;123;115]	124.3 (109 to 141.8)	149.2 (131.2 to 169.6)	139.1 (123.2 to 157.1)	132 (115.1 to 151.3)
Anti-PRN (PRE) [N=115;104;116;110]	4 (3.4 to 4.7)	5 (4 to 6.2)	4.6 (3.9 to 5.4)	4.7 (3.8 to 5.9)
Anti-PRN (PIII[M3]) [N=117;112;122;115]	122 (104.1 to 143.1)	134.9 (119 to 152.9)	118.2 (101.5 to 137.7)	132 (113.6 to 153.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-PT, Anti-FHA and Anti-PRN \geq 5EL.U/mL

End point title	Number of subjects with Anti-PT, Anti-FHA and Anti-PRN \geq 5EL.U/mL
End point description: Concentration \geq 5EL.U/mL in a randomized subset of 25% of subjects, at pre-booster dose and one month post-booster dose	
End point type	Secondary
End point timeframe: At Month 0 and Month 3, Booster Phase	

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	109	105	117	113
Units: Subjects				
Anti-PT (PRE) [N=106;101;110;111]	21	31	30	31
Anti-PT (PIII[M3]) [N=109;104;116;113]	109	104	116	113
Anti-FHA (PRE) [N=108;102;111;111]	76	85	92	78
Anti-FHA (PIII[M3]) [N=109;104;117;113]	109	104	117	113
Anti-PRN (PRE) [N=109;102;112;112]	30	42	44	33
Anti-PRN (PIII[M3]) [N=109;105;116;113]	109	105	116	113

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-PT, Anti-FHA and Anti-PRN

End point title	Concentration of Anti-PT, Anti-FHA and Anti-PRN
End point description: Concentrations were presented as geometric mean concentrations (GMCs).	
End point type	Secondary
End point timeframe: At Month 0 and Month 3, Booster Phase	

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	109	105	117	113
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT (PRE) [N=106;101;110;111]	3.3 (3 to 3.8)	3.8 (3.3 to 4.4)	3.8 (3.3 to 4.4)	4 (3.4 to 4.7)
Anti-PT (PIII[M3]) [N=109;104;116;113]	54.2 (47.7 to 61.6)	54.7 (47.8 to 62.5)	56 (50 to 62.8)	56.3 (50.4 to 62.8)
Anti-FHA (PRE) [N=108;102;111;111]	9.1 (7.4 to 11.2)	14.3 (11.5 to 17.7)	12.4 (10.1 to 15.1)	11.3 (8.9 to 14.3)
Anti-FHA (PIII[M3]) [N=109;104;117;113]	125.6 (109.5 to 144.1)	145.9 (127.7 to 166.8)	140.2 (123.5 to 159.1)	134.4 (117.4 to 154)
Anti-PRN (PRE) [N=109;102;112;112]	4 (3.4 to 4.7)	5.3 (4.2 to 6.6)	4.8 (4 to 5.7)	4.6 (3.7 to 5.8)
Anti-PRN (PIII[M3]) [N=109;105;116;113]	118 (99.9 to 139.3)	127.5 (111.7 to 145.6)	116 (98.8 to 136.2)	135 (116.7 to 156.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti- hepatitis B surface antigen (anti-HBs) ≥ 10mIU/ml and ≥ 100mIU/ml

End point title	Number of subjects with anti- hepatitis B surface antigen (anti-HBs) ≥ 10mIU/ml and ≥ 100mIU/ml
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End point description:

Concentrations ≥ 10mIU/mL and ≥ 100mIU/mL in a randomized subset of 25% of subjects, at pre-primary vaccination dose and one month post-primary vaccination dose

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Primary Phase

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	99	84	98	93
Units: Subjects				
Anti-HBs ≥10 mIU/mL (PRE) [N=99;82;98;93]	33	34	39	28
Anti-HBs ≥10 mIU/mL (PIII[M3]) [N=87;84;94;81]	86	84	94	80
Anti-HBs ≥100 mIU/mL (PRE) [N=99;82;98;93]	17	14	14	8
Anti-HBs ≥100 mIU/mL (PIII[M3]) [N=87;84;94;81]	75	79	89	74

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-HBs antibody

End point title	Concentration of Anti-HBs antibody
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End point description:

Concentrations were presented as geometric mean concentrations (GMCs).

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Primary Phase

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	99	84	98	93
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs (PRE) [N=99;82;98;93]	11.8 (7.6 to 18.4)	13.7 (8.4 to 22.4)	11.2 (7.6 to 16.5)	7.5 (5.4 to 10.5)
Anti-HBs (PIII[M3]) [N=87;84;94;81]	697.1 (518.4 to 937.4)	732.2 (555.1 to 965.8)	848.3 (663.7 to 1084.1)	715.3 (520.8 to 982.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-HBs antibody ≥ 10 mIU/mL and ≥ 100 mIU/mL

End point title	Number of subjects with Anti-HBs antibody ≥ 10 mIU/mL and ≥ 100 mIU/mL
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End point description:

Concentrations ≥ 10 mIU/mL and ≥ 100 mIU/mL in a randomized subset of 25% of subjects, at pre-booster dose and one month post-booster dose

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Booster Phase

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	80	94	95
Units: Subjects				
Anti-HBs ≥10 mIU/mL (PRE) [N=92;79;94;95]	28	34	37	31
Anti-HBs ≥10 mIU/mL (PIII[M3]) [N=80;80;88;83]	79	80	88	82
Anti-HBs ≥100 mIU/mL (PRE) [N=92;79;94;95]	14	12	14	9
Anti-HBs ≥100 mIU/mL (PIII[M3]) [N=80;80;88;83]	71	75	83	76

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-HBs antibody

End point title	Concentration of Anti-HBs antibody
End point description:	
Concentrations were presented as geometric mean concentrations (GMCs).	
End point type	Secondary
End point timeframe:	
At Month 0 and Month 3, Booster Phase	

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	80	94	95
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs (PRE) [N=92;79;94;95]	10.6 (6.7 to 16.7)	12.7 (8.4 to 19.1)	11.5 (7.7 to 17.2)	7.8 (5.7 to 10.8)
Anti-HBs (PIII[M3]) [N=80;80;88;83]	753.5 (558.9 to 1016)	792.6 (593.3 to 1058.9)	883.8 (684.6 to 1140.8)	719.9 (528.1 to 981.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polyribosyl ribitol phosphate (anti-PRP) ≥0.15µg/ml and ≥1.0 µg/ml

End point title	Number of subjects with anti-polyribosyl ribitol phosphate (anti-PRP) ≥0.15µg/ml and ≥1.0 µg/ml
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End point description:

Concentrations $\geq 0.15 \mu\text{g/mL}$ and $\geq 1.0 \mu\text{g/mL}$ in a randomized subset of 25% of subjects, at pre-primary vaccination dose and one month post-primary vaccination dose

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Primary Phase

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119	113	123	114
Units: Subjects				
Anti-PRP $\geq 0.15 \mu\text{g/mL}$ (PRE) [N=113;106;113;109]	46	55	46	47
Anti-PRP $\geq 0.15 \mu\text{g/mL}$ (PIII[M3]) [N=119;113;123;114]	119	113	121	113
Anti-PRP $\geq 0.1 \mu\text{g/mL}$ (PRE) [N=113;106;113;109]	9	19	10	7
Anti-PRP $\geq 0.1 \mu\text{g/mL}$ (PIII[M3]) [N=119;113;123;114]	106	101	94	106

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-PRP antibody

End point title	Concentration of Anti-PRP antibody
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End point description:

Concentrations were presented as geometric mean concentrations (GMCs).

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Primary Phase

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119	113	123	114
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-PRP (PRE) [N=113;106;113;109]	0.158 (0.131 to 0.191)	0.213 (0.168 to 0.27)	0.162 (0.132 to 0.198)	0.162 (0.133 to 0.196)
Anti-PRP (PIII[M3]) [N=119;113;123;114]	4.011 (3.275 to 4.912)	3.573 (2.946 to 4.334)	2.752 (2.144 to 3.534)	4.662 (3.788 to 5.739)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-PRP antibody ≥ 0.15 $\mu\text{g/mL}$ and ≥ 1.0 $\mu\text{g/mL}$

End point title	Number of subjects with Anti-PRP antibody ≥ 0.15 $\mu\text{g/mL}$ and ≥ 1.0 $\mu\text{g/mL}$
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End point description:

Concentrations ≥ 0.15 $\mu\text{g/mL}$ and ≥ 1.0 $\mu\text{g/mL}$ in a randomized subset of 25% of subjects, at pre-booster dose and one month post-booster dose

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Booster Phase

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	106	117	112
Units: Subjects				
Anti-PRP ≥ 0.15 $\mu\text{g/mL}$ (PRE) [N=107;103;109;111]	42	54	48	50
Anti-PRP ≥ 0.15 $\mu\text{g/mL}$ (PIII[M3])[N=111;106;117;112]	111	106	115	111
Anti-PRP ≥ 0.1 $\mu\text{g/mL}$ (PRE) [N=107;103;109;111]	7	16	10	8
Anti-PRP ≥ 0.1 $\mu\text{g/mL}$ (PIII[M3]) [N=111;106;117;112]	98	95	89	105

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-PRP antibody

End point title	Concentration of Anti-PRP antibody
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End point description:

Concentrations were presented as geometric mean concentrations (GMCs).

End point type	Secondary
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End point timeframe:

At Month 0 and Month 3, Booster Phase

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	106	117	112
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP (PRE) [N=107;103;109;111]	0.154 (0.127 to 0.186)	0.207 (0.164 to 0.261)	0.172 (0.139 to 0.213)	0.164 (0.136 to 0.198)
Anti-PRP (PIII[M3]) [N=111;106;117;112]	3.775 (3.059 to 4.658)	3.45 (2.848 to 4.179)	2.795 (2.159 to 3.618)	4.9 (3.973 to 6.043)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-poliovirus type 1, 2 and 3 above cut-off value

End point title	Number of subjects with anti-poliovirus type 1, 2 and 3 above cut-off value
End point description:	
Cut-off ≥1:8 at pre-vaccination, one month after the final priming vaccination, for each of the four serogroups in all subjects	
End point type	Secondary
End point timeframe:	
One month after the final primary vaccination	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	83	90	86
Units: Subjects				
Anti-Polio 1 (PRE) [N=71;58;72;58]	52	46	54	46
Anti-Polio 1 (PIII [M3]) [N=91;83;90;86]	91	83	89	84
Anti-Polio 2 (PRE) [N=64;54;66;62]	39	40	44	41
Anti-Polio 2 (PIII [M3]) [N=81;71;81;72]	81	70	81	70
Anti-Polio 3 (PRE) [N=58;52;60;51]	21	21	11	23
Anti-Polio 3 (PIII [M3]) [N=93;79;87;78]	93	79	87	77

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio type 1, 2 and 3 antibody titers

End point title	Anti-polio type 1, 2 and 3 antibody titers
End point description: Titers are expressed as Geometric Mean Titers (GMTs)	
End point type	Secondary
End point timeframe: One month after the final primary vaccination	

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	83	90	86
Units: Titres				
geometric mean (confidence interval 95%)				
Anti-Polio 1 (PRE) [N=71;58;72;58]	32.7 (22.5 to 47.5)	40.2 (27.3 to 59.3)	28.1 (20.1 to 39.3)	30.7 (21.5 to 43.9)
Anti-Polio 1 (PIII [M3]) [N=91;83;90;86]	279.6 (222.4 to 351.5)	317.9 (227.6 to 444)	424.1 (323.1 to 556.6)	277.7 (200.7 to 384.1)
Anti-Polio 2 (PRE) [N=64;54;66;62]	19.4 (13.2 to 28.7)	28 (18.4 to 42.5)	17.4 (12.7 to 23.8)	22.9 (15.6 to 33.5)
Anti-Polio 2 (PIII [M3]) [N=81;71;81;72]	225.2 (173.2 to 292.6)	244.8 (173.3 to 345.9)	274.5 (202.1 to 372.8)	232.7 (160.8 to 336.6)
Anti-Polio 3 (PRE) [N=58;52;60;51]	11.5 (7.6 to 17.5)	11.7 (7.8 to 17.5)	5.9 (4.7 to 7.5)	14.2 (8.8 to 22.8)
Anti-Polio 3 (PIII [M3]) [N=93;79;87;78]	642.7 (478.7 to 862.8)	675 (486.3 to 936.9)	674 (525.5 to 864.5)	494.3 (347.4 to 703.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polio type 1, 2 and 3 above cut-off value

End point title	Number of subjects with anti-polio type 1, 2 and 3 above cut-off value
End point description: Cut-off $\geq 1:8$ at pre-vaccination, one month after the final priming vaccination, for each of the four serogroups in all subjects	
End point type	Secondary
End point timeframe: At pre booster dose and one month post booster dose	

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	80	89	90
Units: Subjects				
Anti-Polio 1 (PRE) [N=65;55;70;55]	49	43	55	43
Anti-Polio 1 (PIII [M3]) [N=85;80;89;90]	85	80	88	88
Anti-Polio 2 (PRE) [N=56;54;65;60]	35	38	44	40
Anti-Polio 2 (PIII [M3]) [N=75;70;79;77]	75	69	79	75
Anti-Polio 3 (PRE) [N=51;48;57;48]	20	17	11	20
Anti-Polio 3 (PIII [M3]) [N=88;77;84;82]	88	77	84	81

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio type 1, 2 and 3 antibody titers

End point title	Anti-polio type 1, 2 and 3 antibody titers
End point description:	
Titers are expressed as Geometric Mean Titers (GMTs)	
End point type	Secondary
End point timeframe:	
At pre booster dose and one month post booster dose	

End point values	Nimenrix™ 3 Booster Group	Nimenrix™ 2 Booster Group	Menjugate® Booster Group	NeisVac-C™ Booster Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	80	89	90
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1 (PRE) [N=65;55;70;55]	34.7 (23.5 to 51.1)	39 (26 to 58.3)	33 (23.5 to 46.4)	30.3 (20.9 to 43.8)
Anti-Polio 1 (PIII [M3]) [N=85;80;89;90]	275.6 (218 to 348.5)	300.3 (214.1 to 421.3)	418.3 (316.5 to 552.9)	282.1 (205.9 to 386.4)
Anti-Polio 2 (PRE) [N=56;54;65;60]	20.4 (13.4 to 31)	26.4 (17.2 to 40.6)	18.2 (13.1 to 25.1)	24.2 (16.2 to 36.3)
Anti-Polio 2 (PIII [M3]) [N=75;70;79;77]	221.8 (171.9 to 286.3)	258.4 (181.2 to 368.6)	280.9 (204.1 to 386.6)	231 (162.3 to 328.6)
Anti-Polio 3 (PRE) [N=51;48;57;48]	12.4 (7.9 to 19.6)	10.7 (7 to 16.4)	6.3 (4.8 to 8.4)	13.8 (8.3 to 22.9)
Anti-Polio 3 (PIII [M3]) [N=88;77;84;82]	653.5 (488.7 to 873.9)	704.7 (517.5 to 959.5)	666.8 (518.3 to 857.8)	532 (380.5 to 743.9)

Statistical analyses

No statistical analyses for this end point

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

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

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary
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End point timeframe:

From Primary vaccination up to ESFU contact

End point values	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group	NeisVac-C™ Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	528	524	516	527
Units: Subjects				
Any SAE(s)	54	56	45	52

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

- Solicited local and general symptoms: during the 8 day - (Day 0-Day 7) after each vaccination
- Unsolicited adverse events: during the 31 day (Day 0 - Day 30) after each vaccination
- SAEs: throughout the entire study (Day 0-Extended safety follow-up)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Nimenrix™ 3 Group
Reporting group description: -	
Reporting group title	Nimenrix™ 2 Group
Reporting group description: -	
Reporting group title	Menjugate® Group
Reporting group description: -	
Reporting group title	NeisVac-C™ Group
Reporting group description: -	

Serious adverse events	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 528 (10.23%)	56 / 524 (10.69%)	45 / 516 (8.72%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Kawasaki's disease (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Kawasaki's disease (Booster)			
subjects affected / exposed ^[1]	0 / 4 (0.00%)	0 / 511 (0.00%)	0 / 503 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	5 / 524 (0.95%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Inguinal hernia, obstructive (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia (Booster)			
subjects affected / exposed ^[2]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Immune system disorders			
Milk allergy (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Reproductive system and breast disorders			
Balanoposthitis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testicular retraction (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Balanoposthitis (Booster)			
subjects affected / exposed ^[3]	0 / 497 (0.00%)	0 / 511 (0.00%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testicular retraction (Booster)			
subjects affected / exposed ^[4]	1 / 497 (0.20%)	0 / 511 (0.00%)	0 / 503 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity (Primary)			

subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apparent life threatening event (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Asphyxia (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngospasm (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Rhinitis allergic (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Bronchial hyperreactivity (Booster)			
subjects affected / exposed ^[5]	0 / 497 (0.00%)	1 / 511 (0.20%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma (Booster)			

subjects affected / exposed ^[6]	0 / 497 (0.00%)	0 / 511 (0.00%)	0 / 503 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm (Booster)			
subjects affected / exposed ^[7]	0 / 497 (0.00%)	0 / 511 (0.00%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Breath holding (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Investigations			
Alanine aminotransferase increased (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Aspartate aminotransferase increased (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	4 / 516 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion (Primary)			

subjects affected / exposed	1 / 528 (0.19%)	1 / 524 (0.19%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn (Primary)			
subjects affected / exposed	2 / 528 (0.38%)	1 / 524 (0.19%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Near drowning (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Thermal burn (Booster)			
subjects affected / exposed ^[8]	2 / 497 (0.40%)	1 / 511 (0.20%)	0 / 503 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion (Booster)			
subjects affected / exposed ^[9]	0 / 497 (0.00%)	0 / 511 (0.00%)	0 / 503 (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
Contusion (Booster)			

subjects affected / exposed ^[10]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Skull fracture (Booster)			
subjects affected / exposed ^[11]	1 / 497 (0.20%)	0 / 511 (0.00%)	0 / 503 (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
Congenital, familial and genetic disorders			
Laryngomalacia (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Plagiocephaly (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Wolff-Parkinson-White syndrome (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy (Primary)			

subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain injury (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Cerebral haemangioma (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Hypotonia (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion (Booster)			
subjects affected / exposed ^[12]	0 / 497 (0.00%)	0 / 511 (0.00%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain injury (Booster)			
subjects affected / exposed ^[13]	1 / 497 (0.20%)	0 / 511 (0.00%)	0 / 503 (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
Blood and lymphatic system disorders			
Lymphadenitis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis (Booster)			
subjects affected / exposed ^[14]	0 / 497 (0.00%)	0 / 511 (0.00%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Conjunctivitis allergic (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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			
Enteritis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	3 / 524 (0.57%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting (Primary)			
subjects affected / exposed	2 / 528 (0.38%)	1 / 524 (0.19%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphthous stomatitis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	2 / 524 (0.38%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Gastrooesophageal reflux disease (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Inguinal hernia (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aphthous stomatitis (Booster)	subjects affected / exposed ^[15]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Vomiting (Booster)	subjects affected / exposed ^[16]	1 / 497 (0.20%)	0 / 511 (0.00%)	0 / 503 (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
Diarrhoea (Booster)	subjects affected / exposed ^[17]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Enteritis (Booster)	subjects affected / exposed ^[18]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Inguinal hernia, obstructive (Booster)	subjects affected / exposed ^[19]	1 / 497 (0.20%)	0 / 511 (0.00%)	0 / 503 (0.00%)
	occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders				
Dermatitis atopic (Primary)	subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
	occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash (Primary)	subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Urticaria (Primary)	subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Haematuria (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscle spasms (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Sacroiliitis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Torticollis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Arthritis (Booster)			
subjects affected / exposed ^[20]	0 / 497 (0.00%)	0 / 511 (0.00%)	0 / 503 (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
Sacroiliitis (Booster)			
subjects affected / exposed ^[21]	0 / 497 (0.00%)	0 / 511 (0.00%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Torticollis (Booster)			
subjects affected / exposed ^[22]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations Bronchiolitis (Primary) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	12 / 528 (2.27%) 0 / 12 0 / 0	10 / 524 (1.91%) 0 / 10 0 / 0	9 / 516 (1.74%) 0 / 9 0 / 0
Bronchitis (Primary) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	9 / 528 (1.70%) 0 / 9 0 / 0	4 / 524 (0.76%) 0 / 4 0 / 0	1 / 516 (0.19%) 0 / 1 0 / 0
Gastroenteritis (Primary) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	6 / 528 (1.14%) 0 / 6 0 / 0	3 / 524 (0.57%) 0 / 3 0 / 0	5 / 516 (0.97%) 0 / 5 0 / 0
Pneumonia (Primary) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	3 / 528 (0.57%) 0 / 3 0 / 0	3 / 524 (0.57%) 0 / 3 0 / 0	2 / 516 (0.39%) 0 / 2 0 / 0
Upper respiratory tract infection (Primary) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	4 / 528 (0.76%) 0 / 4 0 / 0	2 / 524 (0.38%) 0 / 2 0 / 0	2 / 516 (0.39%) 0 / 2 0 / 0
Gastroenteritis rotavirus (Primary) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 528 (0.38%) 0 / 2 0 / 0	2 / 524 (0.38%) 0 / 2 0 / 0	1 / 516 (0.19%) 0 / 1 0 / 0
Pyelonephritis (Primary) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 528 (0.19%) 0 / 1 0 / 0	1 / 524 (0.19%) 0 / 1 0 / 0	1 / 516 (0.19%) 0 / 1 0 / 0
Respiratory syncytial virus bronchiolitis (Primary) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 528 (0.38%) 0 / 3 0 / 0	3 / 524 (0.57%) 0 / 3 0 / 0	2 / 516 (0.39%) 0 / 2 0 / 0

Bronchopneumonia (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	4 / 516 (0.78%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media (Primary)			
subjects affected / exposed	3 / 528 (0.57%)	0 / 524 (0.00%)	2 / 516 (0.39%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection (Primary)			
subjects affected / exposed	3 / 528 (0.57%)	1 / 524 (0.19%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	1 / 524 (0.19%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial pyelonephritis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Nasopharyngitis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	2 / 524 (0.38%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Influenza (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Laryngitis (Primary)			

subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Oral candidiasis (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection (Primary)			
subjects affected / exposed	2 / 528 (0.38%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Anal abscess (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Atypical pneumonia (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Bacteraemia (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Cellulitis (Primary)			

subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Conjunctivitis bacterial (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Encephalitis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Epstein-Barr virus infection (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Escherichia urinary tract infection (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Exanthema subitum (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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 bacterial (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus (Primary)			

subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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 salmonella (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Genital candidiasis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
H1N1 influenza (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (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
Hand-foot-and-mouth disease (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	1 / 516 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Intervertebral discitis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Oral herpes (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Osteomyelitis (Primary)			

subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Pharyngitis (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Pneumonia respiratory syncytial viral (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Rotavirus infection (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Sepsis (Primary)			

subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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
Tonsillitis (Primary)			
subjects affected / exposed	1 / 528 (0.19%)	0 / 524 (0.00%)	0 / 516 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral rash (Primary)			
subjects affected / exposed	0 / 528 (0.00%)	1 / 524 (0.19%)	0 / 516 (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
Bronchitis (Booster)			
subjects affected / exposed ^[23]	3 / 497 (0.60%)	4 / 511 (0.78%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia (Booster)			
subjects affected / exposed ^[24]	1 / 497 (0.20%)	2 / 511 (0.39%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis (Booster)			
subjects affected / exposed ^[25]	1 / 497 (0.20%)	0 / 511 (0.00%)	3 / 503 (0.60%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia (Booster)			
subjects affected / exposed ^[26]	1 / 497 (0.20%)	0 / 511 (0.00%)	2 / 503 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media (Booster)			
subjects affected / exposed ^[27]	1 / 497 (0.20%)	0 / 511 (0.00%)	2 / 503 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection (Booster)			

subjects affected / exposed ^[28]	1 / 497 (0.20%)	0 / 511 (0.00%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis (Booster)			
subjects affected / exposed ^[29]	1 / 497 (0.20%)	0 / 511 (0.00%)	0 / 503 (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
Nasopharyngitis (Booster)			
subjects affected / exposed ^[30]	0 / 497 (0.00%)	1 / 511 (0.20%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute (Booster)			
subjects affected / exposed ^[31]	1 / 497 (0.20%)	0 / 511 (0.00%)	0 / 503 (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
Anal abscess (Booster)			
subjects affected / exposed ^[32]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Encephalitis (Booster)			
subjects affected / exposed ^[33]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Gastroenteritis salmonella (Booster)			
subjects affected / exposed ^[34]	0 / 497 (0.00%)	0 / 511 (0.00%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Genital candidiasis (Booster)			
subjects affected / exposed ^[35]	0 / 497 (0.00%)	0 / 511 (0.00%)	0 / 503 (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
Hand-foot-and-mouth disease (Booster)			

subjects affected / exposed ^[36]	0 / 497 (0.00%)	0 / 511 (0.00%)	1 / 503 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis (Booster)			
subjects affected / exposed ^[37]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Laryngitis (Booster)			
subjects affected / exposed ^[38]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Lung infection (Booster)			
subjects affected / exposed ^[39]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Oral herpes (Booster)			
subjects affected / exposed ^[40]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (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
Pneumonia bacterial (Booster)			
subjects affected / exposed ^[41]	0 / 497 (0.00%)	1 / 511 (0.20%)	0 / 503 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute (Booster)			
subjects affected / exposed ^[42]	0 / 497 (0.00%)	0 / 511 (0.00%)	0 / 503 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection (Booster)			
subjects affected / exposed ^[43]	1 / 497 (0.20%)	0 / 511 (0.00%)	0 / 503 (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
Metabolism and nutrition disorders			
Decreased appetite (Primary)			

subjects affected / exposed	0 / 528 (0.00%)	0 / 524 (0.00%)	0 / 516 (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	NeisVac-C™ Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	52 / 527 (9.87%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Kawasaki's disease (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Kawasaki's disease (Booster)			
subjects affected / exposed ^[1]	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia (Primary)			
subjects affected / exposed	3 / 527 (0.57%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia, obstructive (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia (Booster)			
subjects affected / exposed ^[2]	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Milk allergy (Primary)			

subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Balanoposthitis (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Testicular retraction (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Balanoposthitis (Booster)			
subjects affected / exposed ^[3]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Testicular retraction (Booster)			
subjects affected / exposed ^[4]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Apparent life threatening event (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asphyxia (Primary)			

subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthma (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchospasm (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laryngospasm (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rhinitis allergic (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchial hyperreactivity (Booster)			
subjects affected / exposed ^[5]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthma (Booster)			
subjects affected / exposed ^[6]	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchospasm (Booster)			
subjects affected / exposed ^[7]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Breath holding (Primary)			

subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood alkaline phosphatase increased (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Concussion (Primary)			
subjects affected / exposed	2 / 527 (0.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Contusion (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thermal burn (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint dislocation (Primary)			

subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Near drowning (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skull fracture (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thermal burn (Booster)			
subjects affected / exposed ^[8]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion (Booster)			
subjects affected / exposed ^[9]	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Contusion (Booster)			
subjects affected / exposed ^[10]	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skull fracture (Booster)			
subjects affected / exposed ^[11]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Laryngomalacia (Primary)			

subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Plagiocephaly (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Wolff-Parkinson-White syndrome (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion (Primary)			
subjects affected / exposed	2 / 527 (0.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Epilepsy (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain injury (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral haemangioma (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Hypotonia (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion (Booster)			
subjects affected / exposed ^[12]	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Brain injury (Booster)			
subjects affected / exposed ^[13]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphadenitis (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphadenitis (Booster)			
subjects affected / exposed ^[14]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Conjunctivitis allergic (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enteritis (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting (Primary)			

subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aphthous stomatitis (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematemesis (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aphthous stomatitis (Booster)				
subjects affected / exposed ^[15]	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting (Booster)				
subjects affected / exposed ^[16]	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea (Booster)				

subjects affected / exposed ^[17]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis (Booster)			
subjects affected / exposed ^[18]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia, obstructive (Booster)			
subjects affected / exposed ^[19]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis atopic (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urticaria (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscle spasms (Primary)			

subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sacroiliitis (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Torticollis (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis (Booster)			
subjects affected / exposed ^[20]	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sacroiliitis (Booster)			
subjects affected / exposed ^[21]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Torticollis (Booster)			
subjects affected / exposed ^[22]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis (Primary)			
subjects affected / exposed	14 / 527 (2.66%)		
occurrences causally related to treatment / all	0 / 14		
deaths causally related to treatment / all	0 / 0		
Bronchitis (Primary)			

subjects affected / exposed	8 / 527 (1.52%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis (Primary)				
subjects affected / exposed	3 / 527 (0.57%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia (Primary)				
subjects affected / exposed	4 / 527 (0.76%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis rotavirus (Primary)				
subjects affected / exposed	2 / 527 (0.38%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis (Primary)				
subjects affected / exposed	4 / 527 (0.76%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchiolitis (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media (Primary)				

subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection (Primary)				
subjects affected / exposed	2 / 527 (0.38%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Conjunctivitis (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial pyelonephritis (Primary)				
subjects affected / exposed	2 / 527 (0.38%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Nasopharyngitis (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media acute (Primary)				
subjects affected / exposed	2 / 527 (0.38%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Influenza (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Laryngitis (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oral candidiasis (Primary)				

subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenovirus infection (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal abscess (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atypical pneumonia (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacteraemia (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis (Primary)			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Conjunctivitis bacterial (Primary)			

subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Croup infectious (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalitis (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epstein-Barr virus infection (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Exanthema subitum (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis bacterial (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis norovirus (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis salmonella (Primary)				

subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Genital candidiasis (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
H1N1 influenza (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hand-foot-and-mouth disease (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes simplex (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral discitis (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oral herpes (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pertussis (Primary)				

subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngitis (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rotavirus infection (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis (Primary)				
subjects affected / exposed	1 / 527 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tonsillitis (Primary)				

subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral rash (Primary)				
subjects affected / exposed	0 / 527 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis (Booster)				
subjects affected / exposed ^[23]	2 / 506 (0.40%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia (Booster)				
subjects affected / exposed ^[24]	2 / 506 (0.40%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis (Booster)				
subjects affected / exposed ^[25]	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia (Booster)				
subjects affected / exposed ^[26]	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media (Booster)				
subjects affected / exposed ^[27]	0 / 506 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection (Booster)				
subjects affected / exposed ^[28]	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis (Booster)				

subjects affected / exposed ^[29]	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nasopharyngitis (Booster)				
subjects affected / exposed ^[30]	0 / 506 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media acute (Booster)				
subjects affected / exposed ^[31]	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess (Booster)				
subjects affected / exposed ^[32]	0 / 506 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalitis (Booster)				
subjects affected / exposed ^[33]	0 / 506 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis salmonella (Booster)				
subjects affected / exposed ^[34]	0 / 506 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Genital candidiasis (Booster)				
subjects affected / exposed ^[35]	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hand-foot-and-mouth disease (Booster)				
subjects affected / exposed ^[36]	0 / 506 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral discitis (Booster)				

subjects affected / exposed ^[37]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laryngitis (Booster)			
subjects affected / exposed ^[38]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung infection (Booster)			
subjects affected / exposed ^[39]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oral herpes (Booster)			
subjects affected / exposed ^[40]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial (Booster)			
subjects affected / exposed ^[41]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute (Booster)			
subjects affected / exposed ^[42]	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection (Booster)			
subjects affected / exposed ^[43]	0 / 506 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite (Primary)			
subjects affected / exposed	1 / 527 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[34] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[35] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[36] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[37] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[38] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[39] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[40] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[41] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[42] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[43] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

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

Non-serious adverse events	Nimenrix™ 3 Group	Nimenrix™ 2 Group	Menjugate® Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	419 / 528 (79.36%)	436 / 524 (83.21%)	439 / 516 (85.08%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed	319 / 528 (60.42%)	332 / 524 (63.36%)	344 / 516 (66.67%)
occurrences (all)	319	332	344
Redness			
subjects affected / exposed	363 / 528 (68.75%)	369 / 524 (70.42%)	391 / 516 (75.78%)
occurrences (all)	363	369	391
Swelling			
subjects affected / exposed	326 / 528 (61.74%)	318 / 524 (60.69%)	343 / 516 (66.47%)
occurrences (all)	326	318	343
Drowsiness			

subjects affected / exposed occurrences (all)	376 / 528 (71.21%) 376	365 / 524 (69.66%) 365	370 / 516 (71.71%) 370
Irritability subjects affected / exposed occurrences (all)	419 / 528 (79.36%) 419	436 / 524 (83.21%) 436	439 / 516 (85.08%) 439
Loss of appetite subjects affected / exposed occurrences (all)	295 / 528 (55.87%) 295	325 / 524 (62.02%) 325	307 / 516 (59.50%) 307
Temperature/(Rectally $\geq 38.0^{\circ}\text{C}$) subjects affected / exposed occurrences (all)	272 / 528 (51.52%) 272	274 / 524 (52.29%) 274	277 / 516 (53.68%) 277
Respiratory, thoracic and mediastinal disorders Rhinitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	32 / 528 (6.06%) 32	27 / 524 (5.15%) 27	33 / 516 (6.40%) 33
Infections and infestations Upper respiratory tract infection (post-primary) alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	82 / 528 (15.53%) 82	86 / 524 (16.41%) 86	80 / 516 (15.50%) 80
Nasopharyngitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	43 / 528 (8.14%) 43	34 / 524 (6.49%) 34	46 / 516 (8.91%) 46
Bronchiolitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	41 / 528 (7.77%) 41	34 / 524 (6.49%) 34	33 / 516 (6.40%) 33
Bronchitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	34 / 528 (6.44%) 34	0 / 524 (0.00%) 0	0 / 516 (0.00%) 0
Upper respiratory tract infection (post-booster)			

alternative assessment type: Non-systematic			
subjects affected / exposed	38 / 528 (7.20%)	54 / 524 (10.31%)	53 / 516 (10.27%)
occurrences (all)	38	54	53

Non-serious adverse events	NeisVac-C™ Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	441 / 527 (83.68%)		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	327 / 527 (62.05%)		
occurrences (all)	327		
Redness			
subjects affected / exposed	371 / 527 (70.40%)		
occurrences (all)	371		
Swelling			
subjects affected / exposed	317 / 527 (60.15%)		
occurrences (all)	317		
Drowsiness			
subjects affected / exposed	377 / 527 (71.54%)		
occurrences (all)	377		
Irritability			
subjects affected / exposed	441 / 527 (83.68%)		
occurrences (all)	441		
Loss of appetite			
subjects affected / exposed	312 / 527 (59.20%)		
occurrences (all)	312		
Temperature/(Rectally $\geq 38.0^{\circ}\text{C}$)			
subjects affected / exposed	275 / 527 (52.18%)		
occurrences (all)	275		
Respiratory, thoracic and mediastinal disorders			
Rhinitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 527 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Upper respiratory tract infection (post-primary) alternative assessment type: Non- systematic subjects affected / exposed occurrences (all)	74 / 527 (14.04%) 74		
Nasopharyngitis alternative assessment type: Non- systematic subjects affected / exposed occurrences (all)	36 / 527 (6.83%) 36		
Bronchiolitis alternative assessment type: Non- systematic subjects affected / exposed occurrences (all)	44 / 527 (8.35%) 44		
Bronchitis alternative assessment type: Non- systematic subjects affected / exposed occurrences (all)	31 / 527 (5.88%) 31		
Upper respiratory tract infection (post-booster) alternative assessment type: Non- systematic subjects affected / exposed occurrences (all)	44 / 527 (8.35%) 44		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 December 2010	<p>An inconsistency between inclusion criteria and Table 5 was noticed and Table 5 has been corrected according to inclusion criteria.</p> <p>The age for administration of the booster dose has been clarified.</p> <p>Procedure for reporting Guillain Barre syndrome (GBS) has been added.</p> <p>New cold chain deviation wording has been incorporated.</p>
25 May 2011	<p>The sample size of the study population is increased by approximately 50%, i.e., 680 additional subjects will be enrolled in the study to reach the target samples size of 1650 evaluable subjects to demonstrate the co-primary objectives of this study.</p> <p>The serum bactericidal assay (SBA) is a functional measure of the ability of antibodies in conjunction with complement to kill bacteria and is considered the assay of choice for measurement of functional anti-meningococcal antibodies in vitro. It is well known that, as there is no standardized SBA testing, the inter-laboratory variability could have an important impact on the measured bactericidal titers. Depending on the laboratory where the SBA testing is to be performed, differences around 1% in the percentage of subjects with seroprotective titers may occur. It has been estimated that 50% sample size increase would be necessary to demonstrate all the sequential co-primary objectives regardless of the laboratory where the testing is performed.</p> <p>The primary endpoint of the current study is to assess the immunogenicity induced by the components of the investigational vaccine in terms of rSBA titres $\geq 1:8$ for each of the four serogroups (A, C, W-135 and Y) in all subjects, one month after the final priming vaccination. In addition, rSBA titres $\geq 1:8$ and $\geq 1:128$ will also be assessed at any blood sampling time point during the study in a subset of subjects in all vaccine groups as secondary endpoints. To support the data obtained by rSBA testing, hSBA testing will also be performed and in addition antibody concentrations against meningococcal polysaccharides (PS) are planned to be assessed by ELISA (anti-PS testing). Now, GSK Biologicals decided not to perform anti-PS testing at any blood sampling time point for the following reasons:</p> <ul style="list-style-type: none">- the World Health Organization (WHO) considers SBA the primary means of assessing immune response to meningococcal conjugate vaccines [WHO, 2006; WHO, 1999].
30 July 2012	<p>A measles outbreak in Spain impacted 2 centers participating in the study and the local authorities recommended vaccinating subjects from 9 months old onwards. The protocol is amended to allow administration of Measles, Mumps, Rubella (MMR) or Measles, Mumps, Rubella and Varicella (MMRV) vaccine throughout the study in line with local governmental recommendations. It is preferable that the vaccine not be given within 30 days prior or after a dose of study vaccine (with the day of vaccination considered Day 0).</p> <p>The introduction was updated with the current licensing status of MenACWY-TT and competitor vaccines.</p> <p>Several sections were updated to clarify that the Immune Mediated Disease (IMD) report should only be used in case of Guillain-Barre syndrome (GBS).</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported