Clinical trial results:
Immune Lot Consistency, Immunogenicity, and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Adolescents and Adults Aged 10 to 55 Years

Summary

EudraCT number	2018-001468-48
Trial protocol	Outside EU/EEA
Global end of trial date	28 February 2017

Results information

Result version number	v1 (current)
This version publication date	29 December 2018
First version publication date	29 December 2018

Trial information

Trial identification

Sponsor protocol code	MET43

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02842853
WHO universal trial number (UTN)	U1111-1161-3060

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	1 Discovery Drive, Swiftwater, United States, 18370
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001930-PIP01-16
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To demonstrate the immune lot consistency of the antibody responses to meningococcal serogroups A, C, Y, and W following the administration of a single dose of Meningococcal Polysaccharide (Serogroups A, C, Y and W) Tetanus Toxoid (MenACYW) conjugate vaccine with respect to serum bactericidal assay using human complement (hSBA) geometric mean titers (GMTs).
2) To demonstrate the non-inferiority of the antibody responses to meningococcal serogroups A, C, Y, and W following the administration of a single dose of MenACYW conjugate vaccine (pooled Lots 1 to 3) compared to those observed following the administration of a single dose of Menactra®.

Protection of trial subjects:

Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 July 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 3344
Worldwide total number of subjects	3344
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	992
Adolescents (12-17 years)	536

Adults (18-64 years)	1816
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled in 90 centers in the United States (US) from 15 July 2016 to 16 August 2016.

Pre-assignment

Screening details:

A total of 3344 subjects who met all inclusion and none of the exclusion criteria were enrolled and randomized in the study.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: MenACYW Conjugate Vaccine Lot 1

Arm description:

Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 1a) and adults aged 18 to 55 years (Group 1b) received a single dose of MenACYW conjugate vaccine from lot 1.

Arm type	Experimental
Investigational medicinal product name	MenACYW conjugate vaccine: Meningococcal Polysaccharide (Serogroups A, C, Y, and W) Tetanus Toxoid Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL of MenACYW conjugate vaccine was administered as single dose, into the deltoid muscle of the arm.

Arm title	Group 2: MenACYW Conjugate Vaccine Lot 2

Arm description:

Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 2a) and adults aged 18 to 55 years (Group 2b) received a single dose of MenACYW conjugate vaccine from lot 2.

Arm type	Experimental
Investigational medicinal product name	MenACYW conjugate vaccine: Meningococcal Polysaccharide (Serogroups A, C, Y, and W) Tetanus Toxoid Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL of MenACYW conjugate vaccine was administered as single dose, into the deltoid muscle of the arm.

Arm title	Group 3: MenACYW Conjugate Vaccine Lot 3

Arm description:

Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 3a) and adults aged 18 to 55 years (Group 3b) received a single dose of MenACYW conjugate vaccine from lot 3.

Arm type	Experimental

Investigational medicinal product name	MenACYW conjugate vaccine: Meningococcal Polysaccharide (Serogroups A, C, Y, and W) Tetanus Toxoid Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL of MenACYW conjugate vaccine was administered as single dose, into the deltoid muscle of the arm.

Arm title	Group 4: Menactra®

Arm description:

Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 4a) and adults aged 18 to 55 years (Group 4b) received a single dose of Menactra®.

Arm type	Active comparator
Investigational medicinal product name	Menactra®: Meningococcal (Groups A, C, Y, and W-135) Polysaccharide Diptheria Toxoid Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL of Menactra® was administered as single dose, into the deltoid muscle of the arm.

Number of subjects in period 1	Group 1: MenACYW Conjugate Vaccine Lot 1	Group 2: MenACYW Conjugate Vaccine Lot 2	Group 3: MenACYW Conjugate Vaccine Lot 3
Started	902	895	906
Vaccinated	895	886	900
Safety Analysis Set	895	883	898
Completed	879	861	885
Not completed	23	34	21
Consent withdrawn by subject	11	13	9
Lost to follow-up	9	13	10
Subject met exclusion criteria	-	1	-
Non-compliance with the protocol	3	7	2

Number of subjects in period 1	Group 4: Menactra®
Started	641
Vaccinated	636
Safety Analysis Set	635
Completed	617
Not completed	24
Consent withdrawn by subject	8
Lost to follow-up	11
Subject met exclusion criteria	-
Non-compliance with the protocol	5

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: MenACYW Conjugate Vaccine Lot 1
Reporting group description:	
Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 1a) and adults aged 18 to 55 years (Group 1b) received a single dose of MenACYW conjugate vaccine from lot 1.	
Reporting group title	Group 2: MenACYW Conjugate Vaccine Lot 2
Reporting group description:	
Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 2a) and adults aged 18 to 55 years (Group 2b) received a single dose of MenACYW conjugate vaccine from lot 2.	
Reporting group title	Group 3: MenACYW Conjugate Vaccine Lot 3
Reporting group description:	
Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 3a) and adults aged 18 to 55 years (Group 3b) received a single dose of MenACYW conjugate vaccine from lot 3.	
Reporting group title	Group 4: Menactra®
Reporting group description:	
Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 4a) and adults aged 18 to 55 years (Group 4b) received a single dose of Menactra®.	

Reporting group values	Group 1: MenACYW Conjugate Vaccine Lot 1	Group 2: MenACYW Conjugate Vaccine Lot 2	Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects	902	895	906
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	257	270	255
Adolescents (12-17 years)	145	130	142
Adults (18-64 years)	500	495	509
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	27.4	27.1	27.3
standard deviation	± 15.6	± 15.7	± 15.5
Gender categorical			
Units: Subjects			
Female	535	531	496
Male	367	364	410

Reporting group values	Group 4: Menactra®	Total	
Number of subjects	641	3344	
Age categorical			
Units: Subjects			
In utero	0	0	

Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	210	992	
Adolescents (12-17 years)	119	536	
Adults (18-64 years)	312	1816	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	25.6		
standard deviation	± 15.4	-	
Gender categorical			
Units: Subjects			
Female	357	1919	
Male	284	1425	

End points

End points reporting groups

Reporting group title	Group 1: MenACYW Conjugate Vaccine Lot 1
Reporting group description:	
Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 1a) and adults aged 18 to 55 years (Group 1b) received a single dose of MenACYW conjugate vaccine from lot 1.	
Reporting group title	Group 2: MenACYW Conjugate Vaccine Lot 2
Reporting group description:	
Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 2a) and adults aged 18 to 55 years (Group 2b) received a single dose of MenACYW conjugate vaccine from lot 2.	
Reporting group title	Group 3: MenACYW Conjugate Vaccine Lot 3
Reporting group description:	
Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 3a) and adults aged 18 to 55 years (Group 3b) received a single dose of MenACYW conjugate vaccine from lot 3.	
Reporting group title	Group 4: Menactra®
Reporting group description:	
Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 4a) and adults aged 18 to 55 years (Group 4b) received a single dose of Menactra®.	
Subject analysis set title	MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Subject analysis set type	Per protocol
Subject analysis set description:	
Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years and adults aged 18 to 55 years received a single dose of MenACYW conjugate vaccine from any of the lots 1, 2 or 3.	

Primary: Geometric Mean Titers (GMTs) of Meningococcal Serogroups A, C, Y, And W Antibodies Following Vaccination With 3 Lots of MenACYW Conjugate

End point title	Geometric Mean Titers (GMTs) of Meningococcal Serogroups A, C, Y, And W Antibodies Following Vaccination With 3 Lots of MenACYW Conjugate[1]
End point description:	
Antibody titers against Meningococcal Serogroups A, C, Y, and W were measured by hSBA. Analysis was performed on Per-Protocol Analysis Set (PPAS) defined for accessing the ACYW immune response data for all subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result. The subjects who presented protocol deviations were excluded from per-protocol analysis set. Here, "n" signifies number of subjects with available data for each category, for each arm respectively.	
End point type	Primary
End point timeframe:	
Day 30 (post-vaccination)	

Notes:

[1] - 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: This endpoint was evaluated for reported arms only.

End point values	Group 1: MenACYW Conjugate Vaccine Lot 1	Group 2: MenACYW Conjugate Vaccine Lot 2	Group 3: MenACYW Conjugate Vaccine Lot 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	843	820	845	
Units: Titer				
geometric mean (confidence interval 95%)				
Serogroup A (n= 843, 819, 843)	84.9 (75.8 to 95.1)	96.5 (86.4 to 108)	97.9 (87.7 to 109)	

Serogroup C (n= 841, 820, 845)	326 (286 to 372)	305 (267 to 349)	352 (307 to 405)	
Serogroup Y (n= 843, 820, 844)	213 (191 to 238)	210 (188 to 234)	218 (194 to 246)	
Serogroup W (n= 843, 820, 844)	84.5 (75.1 to 95.1)	81.6 (72.7 to 91.5)	87.2 (77.2 to 98.5)	

Statistical analyses

Statistical analysis title	Serogroup A: Lot 1 vs Lot 2
Statistical analysis description:	
Actual number of subjects analyzed = 1662.	
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 2: MenACYW Conjugate Vaccine Lot 2
Number of subjects included in analysis	1663
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Parameter estimate	GMT Ratio
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.751
upper limit	1.03

Notes:

[2] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% confidence interval (CI) for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup A: Lot 2 vs Lot 3
Statistical analysis description:	
Actual number of subjects analyzed = 1662.	
Comparison groups	Group 2: MenACYW Conjugate Vaccine Lot 2 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1665
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Parameter estimate	GMT Ratio
Point estimate	0.985
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.843
upper limit	1.15

Notes:

[3] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup A: Lot 1 vs Lot 3
Statistical analysis description:	
Actual number of subjects analyzed = 1686.	
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 3: MenACYW Conjugate Vaccine Lot 3

Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	equivalence[4]
Parameter estimate	GMT Ratio
Point estimate	0.867
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.02

Notes:

[4] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup C: Lot 1 vs Lot 2

Statistical analysis description:

Actual number of subjects analyzed = 1661.

Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 2: MenACYW Conjugate Vaccine Lot 2
Number of subjects included in analysis	1663
Analysis specification	Pre-specified
Analysis type	equivalence[5]
Parameter estimate	GMT Ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.888
upper limit	1.29

Notes:

[5] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup C: Lot 2 vs Lot 3
Comparison groups	Group 2: MenACYW Conjugate Vaccine Lot 2 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1665
Analysis specification	Pre-specified
Analysis type	equivalence[6]
Parameter estimate	GMT Ratio
Point estimate	0.866
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.714
upper limit	1.05

Notes:

[6] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup C: Lot 1 vs Lot 3

Statistical analysis description:

Actual number of subjects analyzed = 1686.

Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	equivalence[7]
Parameter estimate	GMT Ratio
Point estimate	0.927
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.766
upper limit	1.12

Notes:

[7] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup Y: Lot 1 vs Lot 2
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 2: MenACYW Conjugate Vaccine Lot 2
Number of subjects included in analysis	1663
Analysis specification	Pre-specified
Analysis type	equivalence[8]
Parameter estimate	GMT Ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.869
upper limit	1.19

Notes:

[8] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup Y: Lot 2 vs Lot 3

Statistical analysis description:

Actual number of subjects analyzed = 1664.

Comparison groups	Group 2: MenACYW Conjugate Vaccine Lot 2 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1665
Analysis specification	Pre-specified
Analysis type	equivalence[9]
Parameter estimate	GMT Ratio
Point estimate	0.961
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.816
upper limit	1.13

Notes:

[9] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup Y: Lot 1 vs Lot 3

Statistical analysis description:

Actual number of subjects analyzed = 1687.

Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	equivalence[10]
Parameter estimate	GMT Ratio
Point estimate	0.975
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.829
upper limit	1.15

Notes:

[10] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup W: Lot 1 vs Lot 2
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 2: MenACYW Conjugate Vaccine Lot 2
Number of subjects included in analysis	1663
Analysis specification	Pre-specified
Analysis type	equivalence[11]
Parameter estimate	GMT Ratio
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.878
upper limit	1.22

Notes:

[11] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup W: Lot 2 vs Lot 3

Statistical analysis description:

Actual number of subjects analyzed = 1664.

Comparison groups	Group 2: MenACYW Conjugate Vaccine Lot 2 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1665
Analysis specification	Pre-specified
Analysis type	equivalence[12]
Parameter estimate	GMT Ratio
Point estimate	0.936
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.791
upper limit	1.11

Notes:

[12] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Statistical analysis title	Serogroup W: Lot 1 vs Lot 3

Statistical analysis description:

Actual number of subjects analyzed = 1687.

Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	equivalence[13]
Parameter estimate	GMT Ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.818
upper limit	1.15

Notes:

[13] - Lot consistency was demonstrated across the 3 lots, if, for each pair of lots and each antigen, the 2-sided 95% CI for the ratio of the GMTs lies between 1/2 and 2.

Primary: Percentage of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y And W Following Vaccination With Either MenACYW Conjugate Vaccine or Menactra® Vaccine

End point title	Percentage of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y And W Following Vaccination With Either MenACYW Conjugate Vaccine or Menactra® Vaccine[14]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. The hSBA vaccine seroresponse for serogroups A, C, Y, and W was defined as post-vaccination hSBA titers >= 1:16 for subjects with pre-vaccination hSBA titers < 1:8 or at least a 4-fold increase in hSBA titers from pre- to post-vaccination for subjects with pre-vaccination hSBA titers >= 1:8. Analysis was performed on PPAS. Here, "n" signifies number of subjects with available data for each category, for each arm respectively.

End point type	Primary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[14] - 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: This endpoint was evaluated for reported arms only.

End point values	Group 4: Menactra®	MenACYW conjugate vaccine (Group 1, 2, 3 pooled)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	593	2508		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Serogroup A (n= 593, 2503)	54.6 (50.5 to 58.7)	73.8 (72.0 to 75.5)		
Serogroup C (n= 593, 2503)	47.9 (43.8 to 52.0)	88.8 (87.5 to 90.0)		
Serogroup Y (n= 593, 2505)	73.4 (69.6 to 76.9)	91.4 (90.3 to 92.5)		
Serogroup W (n= 593, 2505)	61.2 (57.2 to 65.2)	80.3 (78.7 to 81.8)		

Statistical analyses

Statistical analysis title	Serogroup A
Statistical analysis description:	
Actual number of subjects analyzed = 3096.	
Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	3101
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Parameter estimate	Percentage Difference
Point estimate	19.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.8
upper limit	23.5

Notes:

[15] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Statistical analysis title	Serogroup C
Statistical analysis description:	
Actual number of subjects analyzed = 3096.	
Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	3101
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Parameter estimate	Percentage Difference
Point estimate	40.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.7
upper limit	45

Notes:

[16] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Statistical analysis title	Serogroup Y
Statistical analysis description:	
Actual number of subjects analyzed = 3098.	
Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)

Number of subjects included in analysis	3101
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
Parameter estimate	Percentage Difference
Point estimate	18.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.5
upper limit	21.9

Notes:

[17] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Statistical analysis title	Serogroup W

Statistical analysis description:

Actual number of subjects analyzed = 3098.

Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	3101
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	Percentage Difference
Point estimate	19.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.9
upper limit	23.3

Notes:

[18] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Secondary: Percentage of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y And W Following Vaccination With Either MenACYW Conjugate Vaccine or Menactra® Vaccine in Adults

End point title	Percentage of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y And W Following Vaccination With Either MenACYW Conjugate Vaccine or Menactra® Vaccine in Adults[19]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. The hSBA vaccine seroresponse for serogroups A, C, Y, and W was defined as post-vaccination hSBA titers >= 1:16 for subjects with pre-vaccination hSBA titers < 1:8 or at least a 4-fold increase in hSBA titers from pre- to post-vaccination for subjects with pre-vaccination hSBA titers >= 1:8. Analysis was performed on PPAS. Only adults aged 18-55 years who received a single dose of Menactra® (Group 4b) or MenACYW conjugate vaccine (Group 1b-3b) from any of the lots 1, 2 or 3, were included in this endpoint analysis. Here, "n" signifies number of subjects with available data for each category, for each arm respectively.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[19] - 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: This endpoint was evaluated for reported arms only.

End point values	Group 4: Menactra®	MenACYW conjugate vaccine (Group 1, 2, 3 pooled)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	293	1410		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Serogroup A (n= 293, 1406)	53.9 (48.0 to 59.7)	73.5 (71.2 to 75.8)		
Serogroup C (n= 293, 1406)	42.3 (36.6 to 48.2)	83.4 (81.4 to 85.3)		
Serogroup Y (n= 293, 1408)	60.8 (54.9 to 66.4)	88.1 (86.3 to 89.8)		
Serogroup W (n= 293, 1408)	50.2 (44.3 to 56.0)	77.0 (74.7 to 79.2)		

Statistical analyses

Statistical analysis title	Serogroup A
Statistical analysis description:	
Actual number of subjects analyzed = 1699.	
Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	1703
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Parameter estimate	Percentage Difference
Point estimate	19.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.5
upper limit	25.8

Notes:

[20] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Statistical analysis title	Serogroup C
Statistical analysis description:	
Actual number of subjects analyzed = 1699.	
Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)

Number of subjects included in analysis	1703
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Parameter estimate	Percentage Difference
Point estimate	41.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	35
upper limit	46.9

Notes:

[21] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Statistical analysis title	Serogroup Y

Statistical analysis description:

Actual number of subjects analyzed = 1701.

Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	1703
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
Parameter estimate	Percentage Difference
Point estimate	27.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.7
upper limit	33.3

Notes:

[22] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Statistical analysis title	Serogroup W

Statistical analysis description:

Actual number of subjects analyzed = 1701.

Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	1703
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
Parameter estimate	Percentage Difference
Point estimate	26.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.7
upper limit	32.9

Notes:

[23] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Secondary: Percentage of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y And W Following Vaccination With Either MenACYW Conjugate Vaccine or Menactra® Vaccine in Adolescents

End point title	Percentage of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y And W Following Vaccination With Either MenACYW Conjugate Vaccine or Menactra® Vaccine in Adolescents[24]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. The hSBA vaccine seroresponse for serogroups A, C, Y, and W was defined as post-vaccination hSBA titers >= 1:16 for subjects with pre-vaccination hSBA titers < 1:8 or at least a 4-fold increase in hSBA titers from pre- to post-vaccination for subjects with pre-vaccination hSBA titers >= 1:8. Analysis was performed on PPAS. Only adolescents aged 10-17 years who received a single dose of Menactra® (Group 4a) or MenACYW conjugate vaccine (Group 1a-3a) from any of the lots 1, 2 or 3, were included in this endpoint analysis. Here, "n" signifies number of subjects with available data for each category, for each arm respectively.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[24] - 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: This endpoint was evaluated for reported arms only.

End point values	Group 4: Menactra®	MenACYW conjugate vaccine (Group 1, 2, 3 pooled)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	300	1098		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Serogroup A (n= 300, 1097)	55.3 (49.5 to 61.0)	74.0 (71.3 to 76.6)		
Serogroup C (n= 300, 1097)	53.3 (47.5 to 59.1)	95.6 (94.2 to 96.8)		
Serogroup Y (n= 300, 1097)	85.7 (81.2 to 89.4)	95.6 (94.2 to 96.8)		
Serogroup W (n= 300, 1097)	72.0 (66.6 to 77.0)	84.5 (82.2 to 86.6)		

Statistical analyses

Statistical analysis title	Serogroup A

Statistical analysis description:

Actual number of subjects analyzed = 1397.

Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	1398
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
Parameter estimate	Percentage Difference
Point estimate	18.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	12.5
upper limit	24.9

Notes:

[25] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Statistical analysis title	Serogroup C

Statistical analysis description:

Actual number of subjects analyzed = 1397.

Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	1398
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
Parameter estimate	Percentage Difference
Point estimate	42.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.6
upper limit	48

Notes:

[26] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Statistical analysis title	Serogroup Y

Statistical analysis description:

Actual number of subjects analyzed = 1397.

Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	1398
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
Parameter estimate	Percentage Difference
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.18
upper limit	14.5

Notes:

[27] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Statistical analysis title	Serogroup W

Statistical analysis description:

Actual number of subjects analyzed = 1397.

Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)

Number of subjects included in analysis	1398
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
Parameter estimate	Percentage Difference
Point estimate	12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.22
upper limit	18.2

Notes:

[28] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference is > -10% for all serogroups.

Secondary: Percentage of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y And W Following Vaccination With 3 Lots of MenACYW Conjugate

End point title	Percentage of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y And W Following Vaccination With 3 Lots of MenACYW Conjugate[29]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. The hSBA vaccine seroresponse for serogroups A, C, Y, and W was defined as post-vaccination hSBA titers >= 1:16 for subjects with pre-vaccination hSBA titers < 1:8 or at least a 4-fold increase in hSBA titers from pre- to post-vaccination for subjects with pre-vaccination hSBA titers >= 1:8. Analysis was performed on PPAS. Here, "n" signifies number of subjects with available data for each category, for each arm respectively.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[29] - 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: This endpoint was evaluated for reported arms only.

End point values	Group 1: MenACYW Conjugate Vaccine Lot 1	Group 2: MenACYW Conjugate Vaccine Lot 2	Group 3: MenACYW Conjugate Vaccine Lot 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	843	820	845	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Serogroup A (n= 842, 818, 843)	71.1 (67.9 to 74.2)	76.5 (73.5 to 79.4)	73.7 (70.6 to 76.6)	
Serogroup C (n= 840, 819, 844)	90.5 (88.3 to 92.4)	89.1 (86.8 to 91.2)	86.7 (84.3 to 88.9)	
Serogroup Y (n= 842, 819, 844)	92.4 (90.4 to 94.1)	91.9 (89.9 to 93.7)	89.9 (87.7 to 91.9)	
Serogroup W (n= 842, 819, 844)	81.5 (78.7 to 84.0)	80.7 (77.8 to 83.4)	78.7 (75.8 to 81.4)	

Statistical analyses

Statistical analysis title	Serogroup A: Lot 1 vs Lot 2
Statistical analysis description:	
Actual number of subjects analyzed = 1660.	
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 2: MenACYW Conjugate Vaccine Lot 2
Number of subjects included in analysis	1663
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.59
upper limit	-1.16

Statistical analysis title	Serogroup A: Lot 2 vs Lot 3
Statistical analysis description:	
Actual number of subjects analyzed = 1661.	
Comparison groups	Group 2: MenACYW Conjugate Vaccine Lot 2 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1665
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	7.01

Statistical analysis title	Serogroup A: Lot 1 vs Lot 3
Statistical analysis description:	
Actual number of subjects analyzed = 1685.	
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.78
upper limit	1.74

Statistical analysis title	Serogroup C: Lot 1 vs Lot 2
Statistical analysis description:	
Actual number of subjects analyzed = 1659.	
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 2: MenACYW Conjugate Vaccine Lot 2
Number of subjects included in analysis	1663
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.58
upper limit	4.28

Statistical analysis title	Serogroup C: Lot 2 vs Lot 3
Statistical analysis description:	
Actual number of subjects analyzed = 1663.	
Comparison groups	Group 2: MenACYW Conjugate Vaccine Lot 2 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1665
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	5.54

Statistical analysis title	Serogroup C: Lot 1 vs Lot 3
Statistical analysis description:	
Actual number of subjects analyzed = 1684.	
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	3.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.708
upper limit	6.79

Statistical analysis title	Serogroup Y: Lot 1 vs Lot 2
Statistical analysis description:	
Actual number of subjects analyzed = 1661.	
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 2: MenACYW Conjugate Vaccine Lot 2
Number of subjects included in analysis	1663
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	3.07

Statistical analysis title	Serogroup Y: Lot 2 vs Lot 3
Statistical analysis description:	
Actual number of subjects analyzed = 1663.	
Comparison groups	Group 2: MenACYW Conjugate Vaccine Lot 2 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1665
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.763
upper limit	4.79

Statistical analysis title	Serogroup Y: Lot 1 vs Lot 3
Statistical analysis description:	
Actual number of subjects analyzed = 1686.	
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 3: MenACYW Conjugate Vaccine Lot 3

Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.248
upper limit	5.2

Statistical analysis title	Serogroup W: Lot 1 vs Lot 2
Statistical analysis description:	
Actual number of subjects analyzed = 1661.	
Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 2: MenACYW Conjugate Vaccine Lot 2
Number of subjects included in analysis	1663
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	4.54

Statistical analysis title	Serogroup W: Lot 2 vs Lot 3
Statistical analysis description:	
Actual number of subjects analyzed = 1663.	
Comparison groups	Group 2: MenACYW Conjugate Vaccine Lot 2 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1665
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.84
upper limit	5.89

Statistical analysis title	Serogroup W: Lot 1 vs Lot 3

Statistical analysis description:

Actual number of subjects analyzed = 1686.

Comparison groups	Group 1: MenACYW Conjugate Vaccine Lot 1 v Group 3: MenACYW Conjugate Vaccine Lot 3
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	6.61

Secondary: Geometric Mean Titers (GMTs) of Meningococcal Serogroups A, C, Y, and W Antibodies Following Vaccination With MenACYW Conjugate and Menactra®

End point title	Geometric Mean Titers (GMTs) of Meningococcal Serogroups A, C, Y, and W Antibodies Following Vaccination With MenACYW Conjugate and Menactra®[30]

End point description:

Antibody titers against Meningococcal Serogroups A, C, Y, and W were measured by hSBA. Analysis was performed on PPAS. Here, "n" signifies number of subjects with available data for each category, for each arm respectively.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[30] - 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: This endpoint was evaluated for reported arms only.

End point values	Group 4: Menactra®	MenACYW conjugate vaccine (Group 1, 2, 3 pooled)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	593	2508		
Units: Titer				
geometric mean (confidence interval 95%)				
Serogroup A (n= 593, 2505)	48.1 (41.8 to 55.2)	92.9 (87.1 to 99.1)		
Serogroup C (n= 593, 2506)	40.7 (33.8 to 49.0)	328 (303 to 354)		
Serogroup Y (n= 593, 2507)	66.4 (56.4 to 78.0)	214 (200 to 228)		
Serogroup W (n= 593, 2507)	44.5 (38.3 to 51.7)	84.4 (78.8 to 90.4)		

Statistical analyses

Statistical analysis title	Serogroup A
Statistical analysis description:	
Actual number of subjects analyzed = 3098.	
Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	3101
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.67
upper limit	2.24

Statistical analysis title	Serogroup C
Statistical analysis description:	
Actual number of subjects analyzed = 3099.	
Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	3101
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	8.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.58
upper limit	9.84

Statistical analysis title	Serogroup Y
Statistical analysis description:	
Actual number of subjects analyzed = 3100.	
Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	3101
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	3.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.71
upper limit	3.84

Statistical analysis title	Serogroup W
Statistical analysis description: Actual number of subjects analyzed = 3100.	
Comparison groups	Group 4: Menactra® v MenACYW conjugate vaccine (Group 1, 2, 3 pooled)
Number of subjects included in analysis	3101
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.61
upper limit	2.24

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) data were collected from Day 0 up to Day 30 post-vaccination. Solicited Reaction (SR) data were collected from Day 0 up to Day 7 post-vaccination.

Adverse event reporting additional description:

A SR was an AE that was prelisted (i.e.,solicited) in the electronic case report form (eCRF) and considered to be related to vaccination (adverse drug reaction). An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the eCRF (i.e.,solicited) in terms of symptom and/or onset post-vaccination. Safety Analysis Set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Group 1 MenACYW Lot 1

Reporting group description:

Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 1a) and adults aged 18 to 55 years (Group 1b) received a single dose of MenACYW conjugate vaccine from lot 1.

Reporting group title	Group 2 MenACYW Lot 2

Reporting group description:

Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 2a) and adults aged 18 to 55 years (Group 2b) received a single dose of MenACYW conjugate vaccine from lot 2.

Reporting group title	Group 3 MenACYW Lot 3

Reporting group description:

Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 3a) and adults aged 18 to 55 years (Group 3b) received a single dose of MenACYW conjugate vaccine from lot 3.

Reporting group title	Group 4 Menactra

Reporting group description:

Healthy, meningococcal-vaccine naive adolescents aged 10 to 17 years (Group 4a) and adults aged 18 to 55 years (Group 4b) received a single dose of Menactra®.

Serious adverse events	Group 1 MenACYW Lot 1	Group 2 MenACYW Lot 2	Group 3 MenACYW Lot 3
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 895 (1.01%)	13 / 883 (1.47%)	6 / 898 (0.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine Leiomyoma			
subjects affected / exposed	1 / 895 (0.11%)	0 / 883 (0.00%)	0 / 898 (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
Pregnancy, puerperium and perinatal conditions			

Abortion Spontaneous			
subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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
Abortion Spontaneous Incomplete			
subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	1 / 895 (0.11%)	1 / 883 (0.11%)	0 / 898 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 895 (0.11%)	0 / 883 (0.00%)	0 / 898 (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
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	1 / 895 (0.11%)	0 / 883 (0.00%)	0 / 898 (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
Throat Tightness			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	0 / 898 (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
Psychiatric disorders			
Conversion Disorder			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	1 / 898 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			

subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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
Disruptive Mood Dysregulation Disorder			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	0 / 898 (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
Somatic Symptom Disorder			
subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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
Suicidal Ideation			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	1 / 898 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Craniocerebral Injury			
subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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
Foot Fracture			
subjects affected / exposed	1 / 895 (0.11%)	0 / 883 (0.00%)	0 / 898 (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			
Coronary Artery Disease			
subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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
Nervous system disorders			
Alcoholic Seizure			

subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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
Migraine			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	1 / 898 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple Sclerosis			
subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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
Paraesthesia			
subjects affected / exposed	1 / 895 (0.11%)	0 / 883 (0.00%)	0 / 898 (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
Presyncope			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	1 / 898 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status Epilepticus			
subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal Ulcer Perforation			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	1 / 898 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Acute			
subjects affected / exposed	1 / 895 (0.11%)	0 / 883 (0.00%)	0 / 898 (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
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	1 / 898 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Henoch-Schonlein Purpura			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	0 / 898 (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			
Nephrolithiasis			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	0 / 898 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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			
Abdominal Abscess			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	1 / 898 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 895 (0.11%)	2 / 883 (0.23%)	0 / 898 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis Perforated			
subjects affected / exposed	0 / 895 (0.00%)	1 / 883 (0.11%)	0 / 898 (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 Norovirus			

subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	0 / 898 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Pseudomonal			
subjects affected / exposed	1 / 895 (0.11%)	0 / 883 (0.00%)	0 / 898 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 895 (0.11%)	0 / 883 (0.00%)	0 / 898 (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			
Diabetes Mellitus Inadequate Control			
subjects affected / exposed	0 / 895 (0.00%)	0 / 883 (0.00%)	0 / 898 (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
Type 2 Diabetes Mellitus			
subjects affected / exposed	1 / 895 (0.11%)	0 / 883 (0.00%)	0 / 898 (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

Serious adverse events	Group 4 Menactra		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 635 (0.79%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine Leiomyoma			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			

subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abortion Spontaneous Incomplete			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Throat Tightness			
subjects affected / exposed	1 / 635 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Conversion Disorder			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			

subjects affected / exposed	0 / 635 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disruptive Mood Dysregulation Disorder				
subjects affected / exposed	1 / 635 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Somatic Symptom Disorder				
subjects affected / exposed	0 / 635 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal Ideation				
subjects affected / exposed	0 / 635 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Craniocerebral Injury				
subjects affected / exposed	0 / 635 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot Fracture				
subjects affected / exposed	0 / 635 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Coronary Artery Disease				
subjects affected / exposed	0 / 635 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Alcoholic Seizure				

subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple Sclerosis			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Status Epilepticus			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal Ulcer Perforation			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis Acute			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Henoch-Schonlein Purpura			
subjects affected / exposed	1 / 635 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 635 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis Perforated			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis Norovirus			

subjects affected / exposed	1 / 635 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia Pseudomonal			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes Mellitus Inadequate Control			
subjects affected / exposed	1 / 635 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 635 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1 MenACYW Lot 1	Group 2 MenACYW Lot 2	Group 3 MenACYW Lot 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	477 / 895 (53.30%)	485 / 883 (54.93%)	489 / 898 (54.45%)
Nervous system disorders			
Headache			
subjects affected / exposed	247 / 895 (27.60%)	248 / 883 (28.09%)	253 / 898 (28.17%)
occurrences (all)	253	254	265
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	45 / 895 (5.03%)	39 / 883 (4.42%)	43 / 898 (4.79%)
occurrences (all)	45	39	43

Injection Site Pain			
subjects affected / exposed	344 / 895 (38.44%)	339 / 883 (38.39%)	333 / 898 (37.08%)
occurrences (all)	344	339	334
Malaise			
subjects affected / exposed	184 / 895 (20.56%)	186 / 883 (21.06%)	189 / 898 (21.05%)
occurrences (all)	184	187	189
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	278 / 895 (31.06%)	271 / 883 (30.69%)	294 / 898 (32.74%)
occurrences (all)	280	272	295

Non-serious adverse events	Group 4 Menactra		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	353 / 635 (55.59%)		
Nervous system disorders			
Headache			
subjects affected / exposed	175 / 635 (27.56%)		
occurrences (all)	178		
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	25 / 635 (3.94%)		
occurrences (all)	25		
Injection Site Pain			
subjects affected / exposed	235 / 635 (37.01%)		
occurrences (all)	235		
Malaise			
subjects affected / exposed	132 / 635 (20.79%)		
occurrences (all)	132		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	192 / 635 (30.24%)		
occurrences (all)	193		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 June 2016	- Updated Clinical Trial Manager information. - Identified the Coordinating Investigator. - Clarified the blood sample collection procedure when antibiotics have been used near the time of collection. - Included information about MET50 since it is a relevant study to age groups in this study. - Indicated that subject termination would only be recorded in the Case Report Form (CRF). - Clarified the definition of Category 3 medications and included the period of collection. - The definition of hSBA vaccine seroresponse was updated at the request of the Center for Biologics Evaluation and Research (CBER). - Indicated the location of the hSBA and rSBA testing. - Indicated the priority of hSBA testing in the event of insufficient sample volume.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported