Clinical trial results:
A Phase 3, Open-Label, Randomized, Multi-Center Study to Evaluate the Safety and Immunogenicity after One or Two Doses of Novartis Meningococcal ACWY Conjugate Vaccine Administered to Healthy Infants and Toddlers

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

Summary

EudraCT number	2007-004754-82
Trial protocol	DE
Global end of trial date	22 October 2010

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	01 November 2014
Version creation reason	• Correction of full data set Confidence interval shifted among groups.

Trial information

Trial identification

Sponsor protocol code	V59P22

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00667602
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics S.r.l
Sponsor organisation address	Via Fiorentina 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000032-PIP01-07
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	23 May 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 October 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess and compare the immunogenicity of one dose of conjugate meningococcal ACWY vaccine (MenACWY) to one dose of Menjugate® given to healthy toddlers at 12 months of age as measured by the percentage of subjects with serum bactericidal activity using human complement (hSBA) titers ≥1:8 against N. meningitidis serogroup C.

Protection of trial subjects:

Novartis Vaccines or the investigator provided the ethics committee (EC) with all appropriate material, including the Informed Consent Form (ICF), according to local regulations. The EC should also was asked for a written statement regarding the composition of the committee and to comply with GCP (Good Clinical Practices) and with the applicable regulatory requirement(s). The trial was not initiated until appropriate EC approval of the protocol and the ICF was obtained. In addition, all documents were submitted to other authorities in compliance with local jurisdictions. Prior to enrollment, the sponsor and the investigator exchanged written confirmation that their ethical and legal responsibilities had been observed. The EC and, if applicable, other authorities were informed of protocol amendments in accordance with local legal requirements. Appropriate reports on the progress of the study were made to the EC and the sponsor by the investigator in accordance with applicable governmental regulations and in agreement with policy established by the sponsor.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2008
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	Australia: 75
Country: Number of subjects enrolled	Germany: 587
Worldwide total number of subjects	662
EEA total number of subjects	587

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)	662
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:

All participants enrolled were included in the trial

Pre-assignment

Screening details:

Inclusion Criteria:
infants 6 to 8 months old inclusive, who were born after full term pregnancy and previously received three doses of both Prevenar and Infanrix-hexa vaccines at least 30 days before study entry
Exclusion Criteria:
who previously received any meningococcal vaccine

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MenACWY-CRM197 (2dose) +Concomitant Vaccines

Arm description:

Infants received two doses of MenACWY-CRM197 at 6 to 8 and 12 months of age and concomitant dose of PCV7 (Pneumococcal 7-valent Conjugate Vaccine) and DTPa-IPV-HepB-Hib (Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b) at 12 months.

Arm type	Experimental
Investigational medicinal product name	MenACWY-CRM197+PCV7+DTPa-IPV-HepB-Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1.Two 0.5mL doses of MenACWY conjugate vaccine (MenACWYCRM197) was administered by intramuscular injection.
2. One 0.5mL dose of MenACWY conjugate vaccine (MenACWYCRM197) was administered by intramuscular injection.
3. One 0.5mL dose of Pneumococcal 7-valent Conjugate Vaccine (PCV7) was administered by intramuscular injection.
4.One 0.5mL dose of Combined Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b (DTPa-IPVHepB-Hib) vaccine was administered by intramuscular injection.

Arm title	MenACWY-CRM197 (1dose) +Concomitant Vaccines

Arm description:

Infants received one dose of MenACWY-CRM197 at 12 months of age and concomitant dose of PCV7 (Pneumococcal 7-valent Conjugate Vaccine)and DTPa-IPV-HepB-Hib (Diphtheria-Tetanusacellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b) at 12 months of age.

Arm type	Experimental
Investigational medicinal product name	MenACWY-CRM197+PCV7+ DTPa-IPV-HepB-Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1.Two 0.5mL doses of MenACWY conjugate vaccine (MenACWYCRM197) was administered by

intramuscular injection.
2. One 0.5mL dose of MenACWY conjugate vaccine (MenACWYCRM197) was administered by intramuscular injection.
3.One 0.5mL dose of Pneumococcal 7-valent Conjugate Vaccine (PCV7) was administered by intramuscular injection.
4.One 0.5mL dose of Combined Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b (DTPa-IPVHepB-Hib) vaccine was administered by intramuscular injection.

Arm title	MenC (1dose) + Concomitant Vaccines

Arm description:

Infants received one dose of MenC vaccine at 12 months of age and concomitant dose of PCV7 (Pneumococcal 7-valent Conjugate Vaccine) and DTPa-IPV-HepB-Hib (Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b) at 12 months of age.

Arm type	Active comparator
Investigational medicinal product name	MenC + PCV7 + DTPa-IPV-HepB-Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1.One 0.5mL dose of MenC vaccine was administered by intramuscular injection.
2.One 0.5mL dose of Pneumococcal 7-valent Conjugate Vaccine (PCV7) was administered by intramuscular injection.
3.One 0.5mL dose of Combined Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b (DTPa-IPVHepB-Hib) vaccine was administered by intramuscular injection.

Number of subjects in period 1	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines
Started	219	228	215
Completed	211	213	197
Not completed	8	15	18
Consent withdrawn by subject	4	9	10
Administrative reasons	-	-	2
Lost to follow-up	4	5	6
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	MenACWY-CRM197 (2dose) +Concomitant Vaccines
Reporting group description:	
Infants received two doses of MenACWY-CRM197 at 6 to 8 and 12 months of age and concomitant dose of PCV7 (Pneumococcal 7-valent Conjugate Vaccine) and DTPa-IPV-HepB-Hib (Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b) at 12 months.	
Reporting group title	MenACWY-CRM197 (1dose) +Concomitant Vaccines
Reporting group description:	
Infants received one dose of MenACWY-CRM197 at 12 months of age and concomitant dose of PCV7 (Pneumococcal 7-valent Conjugate Vaccine)and DTPa-IPV-HepB-Hib (Diphtheria-Tetanusacellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b) at 12 months of age.	
Reporting group title	MenC (1dose) + Concomitant Vaccines
Reporting group description:	
Infants received one dose of MenC vaccine at 12 months of age and concomitant dose of PCV7 (Pneumococcal 7-valent Conjugate Vaccine) and DTPa-IPV-HepB-Hib (Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b) at 12 months of age.	

Reporting group values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines
Number of subjects	219	228	215
Age categorical			
Units: Subjects			

Age continuous			
As one site has been excluded, the number of subjects included in the analysis are MenACWYCRM197 (2dose) + Concomitant Vaccines N= 196, MenACWY-CRM197 (1dose) + Concomitant Vaccines N= 205 and MenC (1dose) + Concomitant Vaccines N= 193			
Units: days			
arithmetic mean	208.4	209.8	209.3
standard deviation	± 23.7	± 22.2	± 21.9
Gender categorical			
Units: Subjects			
Female	105	106	94
Male	114	122	121

Reporting group values	Total		
Number of subjects	662		
Age categorical			
Units: Subjects			

Age continuous			
As one site has been excluded, the number of subjects included in the analysis are MenACWYCRM197 (2dose) + Concomitant Vaccines N= 196, MenACWY-CRM197 (1dose) + Concomitant Vaccines N= 205 and MenC (1dose) + Concomitant Vaccines N= 193			
Units: days			
arithmetic mean			
standard deviation	-		

Gender categorical Units: Subjects			
Female	305		
Male	357		

End points

End points reporting groups

Reporting group title	MenACWY-CRM197 (2dose) +Concomitant Vaccines

Reporting group description:

Infants received two doses of MenACWY-CRM197 at 6 to 8 and 12 months of age and concomitant dose of PCV7 (Pneumococcal 7-valent Conjugate Vaccine) and DTPa-IPV-HepB-Hib (Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b) at 12 months.

Reporting group title	MenACWY-CRM197 (1dose) +Concomitant Vaccines

Reporting group description:

Infants received one dose of MenACWY-CRM197 at 12 months of age and concomitant dose of PCV7 (Pneumococcal 7-valent Conjugate Vaccine)and DTPa-IPV-HepB-Hib (Diphtheria-Tetanusacellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b) at 12 months of age.

Reporting group title	MenC (1dose) + Concomitant Vaccines

Reporting group description:

Infants received one dose of MenC vaccine at 12 months of age and concomitant dose of PCV7 (Pneumococcal 7-valent Conjugate Vaccine) and DTPa-IPV-HepB-Hib (Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b) at 12 months of age.

Subject analysis set title	Modified Intention-to-treat (MITT) Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

1. Modified Intention-to-treat (MITT) Population, Immune Response One Month after Vaccination at 12 Months of Age
All subjects in the ITT population who:
-actually received a study vaccination, and
-provided at least one evaluable serum sample after vaccination.

Subject analysis set title	Modified Intention-to-treat (MITT) population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

2. Modified Intention-to-treat (MITT) population, Antibody Persistence
All subjects in the ITT population who:
- actually received a study vaccination, and
- provided at least one evaluable serum sample after vaccination, and
- provided an evaluable serum sample at 6-12 months after vaccination at 12 months of age.

Subject analysis set title	Per-protocol (PP) Populations, Immunogenicity
Subject analysis set type	Per protocol

Subject analysis set description:

3. Per-protocol (PP) Population, Immune Response one Month after Vaccination at 12 Months of Age
All subjects in the MITT population who:
- received all the relevant doses of vaccine correctly, and
- provided evaluable serum samples at the relevant time points, and
- had no major protocol deviation as defined prior to database lock.

Subject analysis set title	Per-protocol (PP) Population
Subject analysis set type	Per protocol

Subject analysis set description:

4. Per-protocol (PP) Population, Antibody Persistence
All subjects in the MITT population who:
- received all the relevant doses of vaccine correctly, and
- provided evaluable serum samples at one month after vaccination at 12 months of age and at Visit 6, and
- had no major protocol deviation as defined prior to database lock.

Primary: 1. Percentages of Subjects With Serum Bactericidal Titer ≥ 1:8 Against N.Meningitidis Serogroup C

End point title	1. Percentages of Subjects With Serum Bactericidal Titer ≥ 1:8 Against N.Meningitidis Serogroup C[1]

End point description:

Immunogenicity of one dose of MenACWY-CRM197 vaccine to one dose of MenC vaccine one month post vaccination was measured using serum bactericidal assay with human complement (hSBA) titer ≥ 1:8 against N.meningitidis serogroup C.

End point type	Primary

End point timeframe:

1 month postvaccination

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: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	140		
Units: Percentages of subjects				
number (confidence interval 95%)	83 (77 to 89)	92 (86 to 95)		

Statistical analyses

Statistical analysis title	statistical analysis 1

Statistical analysis description:

The primary criterion for immunogenicity was that the lower limit of the two-sided 95% confidence interval (CI) for the difference between one dose of MenACWY-CRM197 and MenC in the percentage of subjects with hSBA ≥1:8 for serogroup C at 1 month following the 12 months vaccination was greater than -10% .

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (1dose) +Concomitant Vaccines
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	-1

Secondary: 2. Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:4 Against N.Meningitidis Serogroup C

End point title	2. Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:4 Against N.Meningitidis Serogroup C[2]

End point description:

Immunogenicity of one dose of MenACWY-CRM197 vaccine to one dose of MenC vaccine one month post vaccination was assessed as percentage of subjects with serum bactericidal activity using human complement (hSBA) titers ≥ 1:4 against N.meningitidis serogroup C.

End point type	Secondary

End point timeframe:

1 month postvaccination at 12 months of age

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	153		
Units: Percentages of subjects				
number (confidence interval 95%)	90 (85 to 94)	97 (93 to 99)		

Statistical analyses

Statistical analysis title	statistical analysis 1
Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	-2

Notes:

[3] - The primary criterion for immunogenicity was that the lower limit of the two-sided 95% confidence interval (CI) for the difference between one dose of MenACWY-CRM197 and MenC in the percentage of subjects with hSBA ≥ 1:4 for serogroup C at 1 month following the 12 months vaccination was greater than -10%.

Secondary: 3. Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:8 and Titer ≥ 1:4 Against N. Meningitidis Serogroups A, C, W, Y

End point title	3. Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:8 and Titer ≥ 1:4 Against N. Meningitidis Serogroups A, C, W, Y[4]

End point description:

1. Immunogenicity of two doses of MenACWY-CRM197 vaccine to one dose of MenC vaccine one month postvaccination was assessed and compared as percentages of subjects with serum bactericidal titer

with human complement (hSBA) ≥ 1:8, ≥ 1:4 against N.meningitidis Serogroup C.
2. Immunogenicity of two doses of MenACWY-CRM197 vaccine one month postvaccination was assessed as percentages of subjects with serum bactericidal titer with human complement (hSBA) ≥ 1:8, ≥ 1:4 against N.meningitidis Serogroup A, W, Y.

End point type	Secondary

End point timeframe:

1 month postvaccination

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	23		
Units: Percentages of subjects				
number (confidence interval 95%)				
titer ≥ 1:8, prevacc, Men A, (N=159,23)	21 (15 to 29)	0 (0 to 15)		
titer ≥ 1:8, postvacc, Men A (N=166,23)	93 (88 to 97)	0 (0 to 15)		
titer ≥ 1:8, prevacc, Men C (N=161,152)	78 (71 to 84)	6 (3 to 11)		
titer ≥ 1:8, postvacc, Men C (N=167,153)	99 (96 to 100)	92 (86 to 95)		
titer ≥ 1:8, prevacc, Men W, (N=157,23)	68 (60 to 75)	0 (0 to 15)		
titer ≥ 1:8, postvacc, Men W, (N=165,22)	98 (94 to 99)	5 (0 to 23)		
titer ≥ 1:8, prevacc, Men Y, (N=156, 23)	69 (61 to 76)	0 (0 to 15)		
titer ≥ 1:8, postvacc, Men Y, (N=163,22)	96 (91 to 98)	5 (0 to 23)		
titer ≥ 1:4, prevacc, Men A, (N=159,23)	26 (19 to 33)	0 (0 to 15)		
titer ≥ 1:4, postvacc, Men A, (N=166,23)	95 (91 to 98)	0 (0 to 15)		
titer ≥ 1:4, prevacc, Men C, (N=161,152)	88 (81 to 92)	7 (4 to 13)		
titer ≥ 1:4, postvacc, Men C, (N=167,153)	99 (96 to 100)	97 (93 to 99)		
titer ≥ 1:4, prevacc, Men W, (N=157,23)	74 (66 to 81)	0 (0 to 15)		
titer ≥ 1:4, postvacc, Men W, (N=165,22)	98 (94 to 99)	5 (0 to 23)		
titer ≥ 1:4, prevacc, Men Y, (N=156,23)	78 (71 to 84)	0 (0 to 15)		
titer ≥ 1:4, postvacc, Men Y, (N=163,22)	99 (96 to 100)	5 (0 to 23)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparisons to MenC were based on the percentages of subjects with response (hSBA ≥1:8, one month

postvaccination) to serogroup C. MenACWY was determined to be noninferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY and MenC in the percentage of subjects with response towards serogroup C was greater than -10%.

Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	72
Confidence interval	
level	95 %
sides	2-sided
lower limit	64
upper limit	79

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Comparisons to MenC were based on the percentages of subjects with response (hSBA ≥1:8, one month postvaccination) to serogroup C. MenACWY was determined to be noninferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY and MenC in the percentage of subjects with response towards serogroup C was greater than -10%.

Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Median difference (final values)
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	13

Statistical analysis title	statistical Analysis 3

Statistical analysis description:

Comparisons to MenC were based on the percentages of subjects with response (hSBA ≥1:4, prevaccination) to serogroup C. MenACWY was determined to be noninferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY and MenC in the percentage of subjects with response towards serogroup C was greater than -10%.

Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines

Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	80
Confidence interval	
level	95 %
sides	2-sided
lower limit	73
upper limit	86

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparisons to MenC were based on the percentages of subjects with response (hSBA ≥1:4,one month postvaccination) to serogroup C. MenACWY was determined to be noninferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY and MenC in the percentage of subjects with response towards serogroup C was greater than -10%.

Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	5

Secondary: 4. Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:8 and Titer ≥ 1:4 Against N. Meningitidis Serogroups A, W, Y

End point title	4. Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:8 and Titer ≥ 1:4 Against N. Meningitidis Serogroups A, W, Y[5]

End point description:

Immunogenicity for one dose of MenACWY was assessed as percentages of subjects with serum bactericidal titer with human complement (hSBA) ≥ 1:8 and titer ≥ 1:4 by serogroups A, W, Y. Serogroup C is not shown here as it is shown in other outcome measures.

End point type	Secondary

End point timeframe:

12 months and 1 month postvaccination at 12 months of age.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (1dose) +Concomitant Vaccines			
Subject group type	Reporting group			
Number of subjects analysed	175			
Units: Percentages of subjects				
number (confidence interval 95%)				
titer ≥ 1:8, pre-vacc, Men A, (N=171)	1 (0.015 to 3)			
titer ≥ 1:8, post-vacc, Men A, (N=172)	49 (41 to 57)			
titer ≥ 1:8, pre-vacc, Men W, (N=168)	3 (1 to 7)			
titer ≥ 1:8, post-vacc, Men W, (N=170)	61 (53 to 68)			
titer ≥ 1:8, pre-vacc, Men Y, (N=160)	3 (1 to 6)			
titer ≥ 1:8, post-vacc, Men Y, (N=167)	50 (42 to 58)			
titer ≥ 1:4, pre-vacc, Men A, (N=171)	1 (0.015 to 3)			
titer ≥ 1:4, post-vacc, Men A, (N=172)	58 (50 to 65)			
titer ≥ 1:4, pre-vacc, Men W, (N=168)	4 (1 to 8)			
titer ≥ 1:4, post-vacc, Men W, (N=170)	62 (55 to 70)			
titer ≥ 1:4, pre-vacc, Men Y, (N=160)	3 (1 to 6)			
titer ≥ 1:4, post-vacc, Men Y, (N=167)	56 (48 to 63)			

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Human Serum Bactericidal Activity Geometric Mean Titers After One Dose of MenACWY-CRM197 and MenC Against N.Meningitidis Serogroup C

End point title	5. Human Serum Bactericidal Activity Geometric Mean Titers After One Dose of MenACWY-CRM197 and MenC Against N.Meningitidis Serogroup C[6]

End point description:

Immunogenicity of one dose of MenACWY-CRM197 vaccine to one dose of MenC vaccine one month post vaccination was assessed with geometric mean titer (GMT) of serum bactericidal assay with human complement (hSBA) against N. meningitidis serogroup C.

End point type	Secondary

End point timeframe:

1 month postvaccination.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	152		
Units: Titers				
number (confidence interval 95%)				

Prevaccination (month 12) (N=174, 152)	2.11 (1.77 to 2.51)	2.29 (1.9 to 2.75)		
Postvaccination (month 13) (N=175,153)	22 (18 to 28)	31 (24 to 39)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Human Serum Bactericidal Activity Geometric Mean Titers After One Dose of MenACWY-CRM197 and MenC Against N.Meningitidis Serogroup C

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	326
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.12

Notes:

[7] - For comparison of the Geometric Mean Titers at one month prevaccination at 12 months of age, MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the 2-sided 95% CI for the ratio of the MenACWY-CRM197 to MenC Geometric Mean Titers for serogroup C was greater than 0.5.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Human Serum Bactericidal Activity Geometric Mean Titers After One Dose of MenACWY-CRM197 and MenC Against N.Meningitidis Serogroup C

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	326
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.93

Notes:

[8] - For comparison of the Geometric Mean Titers at one month postvaccination at 12 months of age, MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the 2-sided 95% CI for the ratio of the MenACWY-CRM197 to MenC Geometric Mean Titers for serogroup C was greater than 0.5.

Secondary: 6. Human Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroups A, W, Y

End point title	6. Human Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroups A, W, Y[9]

End point description:

Immunogenicity of one dose of MenACWY-CRM197 one month postvaccination was assessed with GMT of serum bactericidal assay with hSBA against Serogroups A, W, Y.

End point type	Secondary

End point timeframe:

1 month postvaccination.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (1dose) +Concomitant Vaccines			
Subject group type	Reporting group			
Number of subjects analysed	172			
Units: Titers				
number (confidence interval 95%)				
prevacc, Men A (N=171)	1.99 (1.72 to 2.3)			
postvacc Men A (N=172)	10 (7.71 to 13)			
prevacc, Men W (N=168)	2.12 (1.71 to 2.62)			
postvacc Men W (N=170)	14 (10 to 19)			
prevacc, Men Y (N=160)	1.92 (1.59 to 2.32)			
postvacc Men Y (N=167)	7.05 (5.43 to 9.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Human Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroups A, C, W, Y

End point title	7. Human Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroups A, C, W, Y[10]

End point description:

1. The immunogenicity of two doses of MenACWY-CRM197, to a single dose of MenC was assessed and compared as measured by human Serum Bactericidal Activity Geometric Mean Titers directed against N. meningitidis serogroup C.
2. The immunogenicity of two doses of MenACWY-CRM197, to a single dose of MenC was assessed as measured by human Serum Bactericidal Activity Geometric Mean Titers directed against N. meningitidis serogroups A, W, Y.

End point type	Secondary

End point timeframe:

1 month postvaccination

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167	153		
Units: Participants				
geometric mean (confidence interval 95%)				
prevacc, Men A (N=159,23)	3.4 (2.92 to 3.97)	2 (1.46 to 2.73)		
postvacc Men A (N=166,23)	75 (56 to 99)	2.22 (1.22 to 4.04)		
prevacc, Men C (N=161,152)	23 (19 to 28)	2.29 (1.9 to 2.75)		
postvacc, Men C (N=167,153)	249 (197 to 314)	31 (24 to 39)		
prevacc, Men W (N=157,23)	14 (11 to 17)	1.71 (1.06 to 2.74)		
postvacc, Men W (N=165,22)	213 (153 to 295)	2 (0.99 to 4.03)		
prevacc, Men Y (N=156,23)	11 (9.44 to 14)	1.76 (1.18 to 2.63)		
postvacc, Men Y (N=163,22)	156 (119 to 205)	1.93 (1.06 to 3.52)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Human Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroups A, C, W, Y	
Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Method	ANOVA
Parameter estimate	Ratio
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.43
upper limit	13

Notes:

[11] - For comparison of the GMTs (one month postvaccination), MenACWY was determined to be noninferior to MenC if the lower limit of the two-sided 95% CI for the ratio of the MenACWY to MenC GMTs for serogroup C was greater than 0.5 .

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Human Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroups A, C, W, Y	
Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Method	ANOVA
Parameter estimate	Ratio
Point estimate	8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.35
upper limit	10

Notes:

[12] - For comparison of the GMTs (one month postvaccination), MenACWY was determined to be noninferior to MenC if the lower limit of the two-sided 95% CI for the ratio of the MenACWY to MenC GMTs for serogroup C was greater than 0.5 .

Secondary: 8. Percentages of Subjects With Seroresponse Rates After One Dose of DTPa-IPV-HepB-Hib (Concomitant Vaccine)

End point title	8. Percentages of Subjects With Seroresponse Rates After One Dose of DTPa-IPV-HepB-Hib (Concomitant Vaccine)

End point description:

The immunogenicity of one dose of MenC to one dose of DTPa-IPV-HepB-Hib concomitant vacccine was assessed.
For Pertussis antigens, Pertussis Toxin (PT), Filamentous Hemagglutinin (FHA) and Pertactin (PRN), the seroresponse in initially seronegative subjects (pre-vaccination antibody concentration < LLQ) is defined as post-vaccination antibody concentration
>= LLQ; in initially seropositive subjects (pre-vaccination antibody concentration >=LLQ) seroresponse is defined as at least two fold increase of the pre-vaccinationantibody concentration.
Diptheria and Tetanus: primary endpoint ELISA (Enzyme-linked immunosorbent assay) >=0.1 (international unit -IU) IU/mL and the secondary endpoint is ELISA>=1.0 IU/mL.
Polio type 1, 2 and 3: bNT (neutralization test) with >=1:8.
HepB (HBV): primary endpoint ELISA >=10mU/mL.
PRP-T: primary endpoint ≥ 0.15 mcg/mL and ≥ 1.00 mcg/mL.

End point type	Secondary

End point timeframe:

1 month postvaccination.

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	168	173	152	
Units: Percentages of subjects]				
arithmetic mean (confidence interval				

95%)				
Anti-Diphtheria Toxin ≥ 0.1 IU/mL N=(168,173,152)	100 (98 to 100)	100 (98 to 100)	100 (98 to 100)	
Anti-Diphtheria Toxin ≥ 1.0 IU/mL N=(168,173,152)	99 (96 to 100)	98 (95 to 100)	98 (94 to 100)	
Anti-Tetanus Toxin ≥ 0.1 IU/mL N= (168,173,152)	100 (98 to 100)	100 (98 to 100)	100 (98 to 100)	
Anti-Tetanus Toxin ≥ 1.0 IU/mL N= (168,173,152)	96 (92 to 98)	96 (92 to 98)	97 (93 to 99)	
FHA ELISA (N=160,169,152)	97 (93 to 99)	91 (86 to 95)	96 (92 to 99)	
PRN ELISA (N=160,169,152)	99 (97 to 100)	98 (94 to 99)	99 (95 to 100)	
PT ELISA (N=159,165,151)	97 (93 to 99)	95 (90 to 97)	97 (92 to 99)	
polio 1 (N=157,161,148)	100 (98 to 100)	100 (98 to 100)	99 (96 to 100)	
polio 2 (N=157,161,148)	100 (98 to 100)	99 (97 to 100)	100 (98 to 100)	
polio 3 (N=146,151,143)	100 (98 to 100)	100 (98 to 100)	100 (97 to 100)	
Hep B (N=157,161,147)	99 (97 to 100)	99 (96 to 100)	99 (96 to 100)	
Anti-PRP (HIB) ≥ 0.15 µg/mL (N=168,173,151)	100 (98 to 100)	100 (98 to 100)	100 (98 to 100)	
Anti-PRP (HIB) ≥ 1.0 µg/mL (N=168,173,151)	100 (98 to 100)	98 (95 to 100)	99 (96 to 100)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Diptheria Toxin ≥0.1 IU/mL, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	2

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Diptheria Toxin ≥0.1 IU/mL, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference

in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	2

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Diptheria Toxin ≥1.0 IU/mL, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	5

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Diptheria Toxin ≥1.0 IU/mL, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines

Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	4

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Tetanus Toxin ≥ 0.1 IU/mL, one month postvaccination) given concomitantly with one dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, for any of the antigens, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	2

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Tetanus Toxin ≥ 0.1 IU/mL, one month postvaccination) given concomitantly with one dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, for any of the antigens, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0

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

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Tetanus Toxin ≥ 1.0 IU/mL, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	3

Notes:

[13] - Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Tetanus Toxin ≥ 0.1 IU/mL, one month postvaccination) given concomitantly with one dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, for any of the antigens, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Statistical analysis title	Statistical Analysis 8

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Tetanus Toxin ≥ 1.0 IU/mL, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	3

Notes:

[14] - Immunogenicity of DTPa-IPV-HepB-Hib, given at 12 months of age concomitantly with one dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, for any of the antigens, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Statistical analysis title	Statistical Analysis 9

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (polio 1, one month postvaccination), given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	percentage differnce
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	4

Statistical analysis title	Statistical Analysis 10

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (polio 1, one month postvaccination), given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	4

Statistical analysis title	Statistical Analysis 11

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (polio 2, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	3

Statistical analysis title	Statistical Analysis 12

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (polio 2, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	2

Statistical analysis title	Statistical Analysis 13

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (polio 3, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines

Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	3

Statistical analysis title	Statistical analysis 14

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (polio 3, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	3

Notes:

[15] - Immunogenicity of DTPa-IPV-HepB-Hib (Anti-Diptheria Toxin ≥0.1 IU/mL, one month postvaccination) given concomitantly with two
dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower
limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off
level specified for that antigen was greater than -10%.

Statistical analysis title	Statistical analysis 15

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti- PRP ≥ 0.15 µg/mL, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines

Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	2

Statistical analysis title	Statistical analysis 16

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti- PRP ≥ 0.15 µg/mL, one month postvaccination) given concomitantly with one dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (1dose) +Concomitant Vaccines
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	2

Statistical analysis title	Statistical analysis 17

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti- PRP ≥ 1.0 µg/mL, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	4

Statistical analysis title	Statistical analysis 18

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Anti- PRP ≥ 1.0 µg/mL, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (1dose) +Concomitant Vaccines
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	2

Statistical analysis title	Statistical analysis 19

Statistical analysis description:

PeImmunogenicity of DTPa-IPV-HepB-Hib (Hep B, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	3

Statistical analysis title	Statistical analysis 20

Statistical analysis description:

Immunogenicity of DTPa-IPV-HepB-Hib (Hep B, one month postvaccination) given concomitantly with two dose of MenACWY was considered non-inferior to DTPa-IPV-HepB-Hib given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (1dose) +Concomitant Vaccines
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3

Secondary: 9. Percentages of Subjects With Seroresponse Rates After One Dose of PCV7 (Concomitant Vaccine)

End point title	9. Percentages of Subjects With Seroresponse Rates After One Dose of PCV7 (Concomitant Vaccine)

End point description:

To compare the immunogenicity of PCV7 (Pneumococcal 7-valent Conjugate)Vaccine when given concomitantly with one dose or two doses of MenACWY-CRM197 or with MenC to infants at 12 months of age. Seroresponse for PCV7 (PnC 4, PnC 6B, PnC 9V, PnC 14, PnC 18C, PnC 19F, PnC 23F) is defined as: a subject with primary endpoint ELISA ≥ 0.35 mcg/mL and secondary endpoint ELISA ≥ 1.0 mcg/mL.

End point type	Secondary

End point timeframe:

1 month postvaccination.

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	168	150	
Units: Percentages of subjects				
arithmetic mean (confidence interval 95%)				
PNC 4 N=(163,168,150)	83 (76 to 88)	82 (75 to 88)	87 (81 to 92)	
PNC 6B N=(163,168,149)	92 (87 to 96)	91 (86 to 95)	97 (93 to 99)	
PNC 9V N=(163,168,150)	90 (85 to 94)	89 (83 to 93)	93 (88 to 97)	

PNC 14 N=(163,167,150)	99 (96 to 100)	99 (97 to 100)	99 (96 to 100)	
PNC 18C N=(163,168,150)	71 (63 to 77)	76 (68 to 82)	86 (79 to 91)	
PNC 19 F N=(163,168,150)	81 (74 to 87)	80 (74 to 86)	90 (84 to 94)	
PNC 23 F N=(163,168,150)	88 (82 to 92)	89 (83 to 93)	94 (89 to 97)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Immunogenicity of PCV7 (PNC4, one month postvaccination) given concomitantly with one dose of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	3

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Immunogenicity of PCV7(PNC 6B, one month postvaccination) given concomitantly with one dose of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	-1

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Immunogenicity of PCV7(PNC 9V, one month postvaccination) given concomitantly with MenACWY-CRM197 or MenC was considered non-inferior, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than -10%.	
Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	2

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Immunogenicity of PCV7 (PNC 14, one month postvaccination) given concomitantly with one dose of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.	
Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	3

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Immunogenicity of PCV7(PNC 18C, one month postvaccination) given concomitantly with one dose of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.	
Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines

Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19
upper limit	-2

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

Immunogenicity of PCV7 (PNC 19F, one month postvaccination), given concomitantly with one dose of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17
upper limit	-2

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:

Immunogenicity of PCV7 (PNC 23F, one month postvaccination) given concomitantly with one dose of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	1

Statistical analysis title	Statistical Analysis 8

Statistical analysis description:

Immunogenicity of PCV7 (PNC4, one month postvaccination) given concomitantly with two doses of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	4

Statistical analysis title	Statistical Analysis 9

Statistical analysis description:

Immunogenicity of PCV7 (PNC6B, one month postvaccination) given concomitantly with two doses of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	0

Notes:

[16] - Immunogenicity of PCV7 (PNC4, one month postvaccination)given concomitantly with one dose of MenACWY was considered noninferior
to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the

percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Statistical analysis title	Statistical Analysis 10
Statistical analysis description:	
Immunogenicity of PCV7 (PNC 9V, one month postvaccination) given concomitantly with two doses of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.	
Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	3

Statistical analysis title	Statistical Analysis 11
Statistical analysis description:	
Immunogenicity of PCV7 (PNC14, one month postvaccination) given concomitantly with two doses of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.	
Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3

Statistical analysis title	Statistical Analysis 12
Statistical analysis description:	
Immunogenicity of PCV7 (PNC18C, one month postvaccination) given concomitantly with two doses of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.	

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24
upper limit	-6

Statistical analysis title	Statistical Analysis 13

Statistical analysis description:

Immunogenicity of PCV7 (PNC19F, one month postvaccination) given concomitantly with two doses of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17
upper limit	-1

Statistical analysis title	Statistical Analysis 14

Statistical analysis description:

Immunogenicity of PCV7 (PNC23F, one month postvaccination) given concomitantly with two doses of MenACWY was considered non-inferior to PCV7 given concomitantly with one dose of MenC, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response was greater than the cut-off level specified for that antigen was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	0

Secondary: 10. Persistence of Immune Response Measured as Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:8 and Titer ≥ 1:4 Against N.Meningitidis Serogroup C

End point title	10. Persistence of Immune Response Measured as Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:8 and Titer ≥ 1:4 Against N.Meningitidis Serogroup C

End point description:

Persistence of immune response to either one or two doses of MenACWY-CRM197 or one dose of MenC as measured by serum bactericidal assay with human complement (hSBA) titers ≥ 1:8, and titers ≥ 1:4 directed against N.meningitidis serogroup C (only for subjects enrolled in Australia).

End point type	Secondary

End point timeframe:

1 month postvaccination and 6-18 months postvaccination

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	14	13	
Units: Percentages of subjects				
geometric mean (confidence interval 95%)				
hSBA ≥ 1:8, postvacc, Men C.N=(17,14,13)	100 (80 to 100)	86 (57 to 98)	92 (64 to 100)	
hSBA ≥ 1:8, perisistence, Men C.N=(17,14,13)	71 (44 to 90)	64 (35 to 87)	54 (25 to 81)	
hSBA ≥ 1:4, postvacc, Men C.N=(17,14,13)	100 (80 to 100)	93 (66 to 100)	100 (75 to 100)	
hSBA ≥ 1:4, persistence, Men C.N=(17,14,13)	76 (50 to 93)	71 (42 to 92)	77 (46 to 95)	

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Persistence of Immune Response Measured as Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:8 ,and Titer ≥ 1:4 Against N.Meningitidis Serogroups A, W, Y

End point title	11. Persistence of Immune Response Measured as Percentages of Subjects With Human Serum Bactericidal Titer ≥ 1:8 ,and Titer ≥ 1:4 Against N.Meningitidis Serogroups A, W, Y

End point description:

Persistence of immune response to either one or two doses of MenACWY-CRM197 or one dose of MenC as measured by serum bactericidal assay with human complement (hSBA) titer ≥ 1:8 and titer ≥ 1:4 directed against N. meningitidis serogroups A, W and Y (only for subjects enrolled in Australia).

End point type	Secondary

End point timeframe:

1 month postvaccination and 6-18 months postvaccination

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	14	13	
Units: Percentages of subjects				
number (confidence interval 95%)				
hsBA ≥ 1:8, postvacc, MenA (N=17,12,2)	88 (64 to 99)	42 (15 to 72)	0 (0 to 84)	
hsBA ≥ 1:8, persistence, MenA (N=16,14,12)	31 (11 to 59)	7 (0 to 34)	0 (0 to 26)	
hSBA ≥ 1:4, postvacc, MenA (N=17,12,2)	100 (80 to 100)	50 (21 to 79)	0 (0 to 84)	
hSBA ≥ 1:4, persistence, MenA (N=16,14,12)	38 (15 to 65)	14 (2 to 43)	0 (0 to 26)	
hSBA ≥ 1:8, postvacc, MenW (N=17,12,2)	100 (80 to 100)	67 (35 to 90)	0 (0 to 84)	
hSBA ≥ 1:8, persistence, MenW (N=16,14,12)	75 (48 to 93)	71 (42 to 92)	0 (0 to 26)	
hSBA ≥ 1:4, postvacc, MenW (N=17,12,2)	100 (80 to 100)	67 (35 to 90)	0 (0 to 84)	
hSBA ≥ 1:4, persistence, MenW (N=16,14,12)	88 (62 to 98)	71 (42 to 92)	0 (0 to 26)	
hSBA ≥ 1:8, postvacc, MenY (N=17,12,2)	100 (80 to 100)	33 (10 to 65)	0 (0 to 84)	
hSBA ≥ 1:8, persistence, MenY (N=14,14,12)	79 (49 to 95)	79 (49 to 95)	0 (0 to 26)	
hSBA ≥ 1:4, postvacc, MenY (N=17,12,2)	100 (80 to 100)	50 (21 to 79)	0 (0 to 84)	
hSBA ≥ 1:4, persistence, MenY (N=14,14,12)	86 (57 to 98)	93 (66 to 100)	0 (0 to 26)	

Statistical analyses

No statistical analyses for this end point

Secondary: 12. Persistence of Human Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroup C

End point title	12. Persistence of Human Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroup C

End point description:

Persistence of immunogenicity of either one or two doses of MenACWY or one dose of MenC as measured by human serum bactericidal activity geometric mean titers directed against N.meningitidis

serogroup C (only for subjects enrolled in Australia).

End point type	Secondary

End point timeframe:

1 month postvaccination and 6-18 months postvaccination

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	14	13	
Units: Titers				
geometric mean (confidence interval 95%)				
Month 13	241 (139 to 419)	36 (19 to 66)	30 (16 to 56)	
6 - 18 months after month 12	15 (7.45 to 29)	12 (5.65 to 25)	8.95 (4.15 to 19)	

Statistical analyses

No statistical analyses for this end point

Secondary: 13. Persistence of Human Serum Bactericidal Activity Geometric Mean Titers against N.Meningitidis Serogroup A, W, Y

End point title	13. Persistence of Human Serum Bactericidal Activity Geometric Mean Titers against N.Meningitidis Serogroup A, W, Y[17]

End point description:

Immunogenicity of two doses of MenACWY to one dose of MenACWY as measured by hSBA GMTs directed against N.meningitidis serogroups A, W, Y (only for subjects enrolled in Australia)

End point type	Secondary

End point timeframe:

6-18 months postvaccination

Notes:

[17] - 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: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	14		
Units: Titers				
geometric mean (confidence interval 95%)				

Month 12, SerA (N=17,12)	47 (26 to 86)	6.69 (3.28 to 14)		
6-18 Months after Mont 12, SerA (N=16,14)	4.41 (2.78 to 7)	2.78 (1.7 to 4.56)		
Mont 12, SerW (N=16,14)	180 (95 to 340)	13 (6.26 to 28)		
6-18 Months after Month 12, SerW (N=16,14)	20 (10 to 39)	20 (9.77 to 42)		
Month 12, SerY (N=16,14)	151 (93 to 246)	5.13 (2.87 to 9.17)		
6-8 Months after Month 12, SerY (N=14,14)	22 (12 to 38)	16 (9.15 to 28)		

Statistical analyses

No statistical analyses for this end point

Secondary: 14. Percentages of Subjects With Rabbit Serum Bactericidal ≥ 1:8, ≥ 1:128 and Four Fold Rise Against N.Meningitidis Serogroup C

End point title	14. Percentages of Subjects With Rabbit Serum Bactericidal ≥ 1:8, ≥ 1:128 and Four Fold Rise Against N.Meningitidis Serogroup C

End point description:

1. Immunogenicity of one dose of MenACWY-CRM197 vaccine to one dose of MenC vaccine one month post vaccination was assessed as percentages of subjects with serum bactericidal titer with rabbit complement (rSBA) ≥ 1:8, ≥ 1:128, and four fold rise in titer against N.meningitidis Serogroup C.
2. Immunogenicity of two doses of MenACWY-CRM197 vaccine to one dose of MenC vaccine one month post vaccination was assessed as percentages of subjects with serum bactericidal titer with rabbit complement (rSBA) ≥ 1:8, ≥ 1:128, and four fold rise in titer against N.meningitidis Serogroup C

End point type	Secondary

End point timeframe:

One month postvaccination

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	157	145	
Units: Percentage Of Subjects				
arithmetic mean (confidence interval 95%)				
rSBA titer ≥ 1:8, prevacc (N=140,140,139)	72 (64 to 79)	4 (1 to 8)	1 (0 to 5)	
rSBA titer ≥ 1:8, postvacc (N=156,157,145)	98 (94 to 100)	92 (86 to 96)	97 (92 to 99)	
rSBA titer ≥ 1:128, prevacc (N=140,140,139)	31 (23 to 39)	1 (0.018 to 4)	0 (0 to 3)	
rSBA titer ≥ 1:128, postvacc (N=156,157,145)	92 (87 to 96)	75 (68 to 82)	88 (82 to 93)	
four fold rise (N=132,140,139)	86 (79 to 92)	91 (86 to 95)	96 (92 to 99)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (rSBA ≥1:8; prevaccination),MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the twosided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	71
Confidence interval	
level	95 %
sides	2-sided
lower limit	63
upper limit	78

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (rSBA ≥1:8, one month postvaccination), MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.C

Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenACWY-CRM197 (1dose) +Concomitant Vaccines
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	6

Notes:

[18] - For the comparisons to MenC based on percentages of subjects with response (rSBA ≥1:8), MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the twosided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (rSBA ≥1:8, prevaccination), MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	7

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (rSBA ≥1:8, one month postvaccination), MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	1

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (rSBA ≥1:128, prevaccination), MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	31
Confidence interval	
level	95 %
sides	2-sided
lower limit	24
upper limit	39

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (rSBA ≥1:128, one month postvaccination),MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the twosided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	11

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (rSBA ≥1:128, prevaccination), MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (1dose) +Concomitant Vaccines
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage difference
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	4

Statistical analysis title	Statistical Analysis 8

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (rSBA ≥1:128, one month postvaccination),MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the twosided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	-13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22
upper limit	-5

Statistical analysis title	Statistical Analysis 9

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (four-fold rise in titers),MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the twosided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Comparison groups	MenC (1dose) + Concomitant Vaccines v MenACWY-CRM197 (2dose) +Concomitant Vaccines
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	-10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17
upper limit	-4

Statistical analysis title	Statistical Analysis 10

Statistical analysis description:

For the comparisons to MenC based on percentages of subjects with response (four-fold rise in titers),MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the twosided 95% CI for the difference between MenACWY-CRM197 and MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	1

Notes:

[19] - For the comparisons to MenC based on percentages of subjects with response (four-fold rise in titers), MenACWY-CRM197 was
determined to be non-inferior to MenC if the lower limit of the two-sided 95% CI for the difference between MenACWY-CRM197 and
MenC in the percentage of subjects with response against serogroup C was greater than -10%.

Secondary: 15. Percentages of Subjects With Rabbit Serum Bactericidal ≥ 1:8, ≥ 1:128, and Four Fold Rise Against N.Meningitidis Serogroup A, W, Y

End point title	15. Percentages of Subjects With Rabbit Serum Bactericidal ≥ 1:8, ≥ 1:128, and Four Fold Rise Against N.Meningitidis Serogroup A, W, Y[20]

End point description:

1. Immunogenicity of one dose of MenACWY-CRM197 vaccine to one dose of MenC vaccine one month post vaccination was assessed as percentages ofsubjects with serum bactericidal titer with rabbit complement (rSBA) ≥ 1:8, ≥ 1:128, and four fold rise in titer against N.meningitidis Serogroup A, W, Y.
2. Immunogenicity of two doses of MenACWY-CRM197 vaccine to one dose of MenC vaccine one month post vaccination was assessed as percentages of subjects with serum bactericidal titer with rabbit complement (rSBA) ≥ 1:8, ≥ 1:128, and four fold rise in titer against N.meningitidis Serogroup A, W, Y.

End point type	Secondary

End point timeframe:

One month postvaccination

Notes:

[20] - 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: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	83		
Units: Percentage of Subjects				
number (confidence interval 95%)				
rSBA titer ≥ 1:128, Men A	100 (95 to 100)	98 (92 to 100)		

rSBA titer ≥ 1:128, Men W	96 (89 to 99)	93 (85 to 97)		
rSBA titer ≥ 1:128, Men Y	89 (80 to 95)	86 (76 to 92)		
rSBA titer ≥ 1:8, Men A	100 (95 to 100)	98 (92 to 100)		
rSBA titer ≥ 1:8, Men W	100 (95 to 100)	95 (88 to 99)		
rSBA titer ≥ 1:8, Men Y	97 (91 to 100)	88 (79 to 94)		
4-fold rise rSBA titer, MenA (N=73,82)	75 (64 to 85)	95 (88 to 99)		
4-fold rise rSBA titer, MenW (N=59,73)	95 (86 to 99)	95 (87 to 99)		
4-fold rise rSBA titer, MenY (N=32,47)	91 (75 to 98)	87 (74 to 95)		

Statistical analyses

No statistical analyses for this end point

Secondary: 16. Rabbit Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroup C

End point title	16. Rabbit Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroup C

End point description:

1. Immunogenicity of one dose of MenACWY-CRM197 to one dose of MenC vaccine at 12 months of age was assessed with geometric mean titer (GMT) of serum bactericidal assay with rabbit complement (rSBA) against Serogroup C.
2. Immunogenicity of two doses of MenACWY-CRM197 to one dose of MenC vaccine at 6 to 8 and 12 months of age was assessed with geometric mean titer (GMT) of serum bactericidal assay with rabbit complement (rSBA) against Serogroup C.

End point type	Secondary

End point timeframe:

One month post vaccination

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	157	145	
Units: Titers				
geometric mean (confidence interval 95%)				
GMT, prevacc (N=140,140,139)	26 (21 to 33)	2.22 (1.76 to 2.8)	2.03 (1.62 to 2.54)	
GMT, postvacc (N=156,157,145)	353 (260 to 479)	131 (98 to 176)	266 (197 to 359)	

Statistical analyses

Statistical analysis title	statistical analysis 1

Statistical analysis description:

For comparison of the Geometric Mean Titers at one month postvaccination at 12 months of age,MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the 2-sided 95% CI for the ratio of the MenACWY-CRM197 to MenC Geometric Mean Titers for serogroup C was greater than 0.5

Comparison groups	MenACWY-CRM197 (2dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.83

Notes:

[21] - For comparison of the Geometric Mean Titers at one month postvaccination at 12 months of age, MenACWY-CRM197 was determined to be non-inferior to MenC if the lower limit of the 2-sided 95% CI for the ratio of the MenACWY-CRM197 to MenC Geometric Mean Titers for serogroup C was greater than 0.5

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

For comparison of the Geometric Mean Titers at one month postvaccination at 12 months of age, MenACWY–CRM197 was determined to be non-inferior to MenC if the lower limit of the 2-sided 95% CI for the ratio of the MenACWY-CRM197 to MenC Geometric Mean Titers for serogroup C was greater than 0.5.

Comparison groups	MenACWY-CRM197 (1dose) +Concomitant Vaccines v MenC (1dose) + Concomitant Vaccines
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.68

Secondary: 17. Rabbit Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroup A, W, Y

End point title	17. Rabbit Serum Bactericidal Activity Geometric Mean Titers Against N.Meningitidis Serogroup A, W, Y[22]

End point description:

1. Immunogenicity of one dose of MenACWY-CRM197 to one dose of MenC vaccine at 12 months of age was assessed with GMT of SBA with rabbit complement (rSBA) against Serogroup A, W, Y.
2. Immunogenicity of two doses of MenACWY-CRM197 to one dose of MenC vaccine at 6 to 8 and 12

months of age was assessed with geometric mean titer (GMT) of serum bactericidal assay with rabbit complement (rSBA) against Serogroup A, W, Y.

End point type	Secondary

End point timeframe:

One month postvaccination

Notes:

[22] - 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: No statistical analysis is associated to this endpoint.

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	83		
Units: Titers				
geometric mean (confidence interval 95%)				
GMT, prevacc, Men A (N=73,82)	281 (134 to 587)	6.83 (3.34 to 14)		
GMT, postvacc, Men A	3136 (2013 to 4886)	3258 (2113 to 5022)		
GMT, prevacc, Men W (N=59,75)	20 (12 to 33)	2.32 (1.46 to 3.69)		
GMT, postvacc, Men W	708 (421 to 1191)	1306 (786 to 2169)		
GMT, prevacc, Men Y (N=32,49)	22 (12 to 40)	2.4 (1.42 to 4.06)		
GMT, postvacc, Men Y (N=76,81)	574 (320 to 1028)	598 (336 to 1066)		

Statistical analyses

No statistical analyses for this end point

Secondary: 18. Number of Subjects Who Reported Solicited Local and Systemic Reactions (Day 1 to Day 7 Postvaccination), After Any Vaccination

End point title	18. Number of Subjects Who Reported Solicited Local and Systemic Reactions (Day 1 to Day 7 Postvaccination), After Any Vaccination

End point description:

Safety was assessed as the number of subjects who reported solicited local reactions from day 1 to day 7 postvaccination for all the three vaccination groups.
safety was assessed as the number of subjects who reported solicited systemic reactions from day 1 to day 7 Following the Month 12 vaccination in all three vaccination groups

End point type	Secondary

End point timeframe:

From day 1 to day 7 postvaccination

End point values	MenACWY-CRM197 (2dose) +Concomitant Vaccines	MenACWY-CRM197 (1dose) +Concomitant Vaccines	MenC (1dose) + Concomitant Vaccines	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	195	192	179	
Units: Number				
Any Local (N=195,192,179)	130	131	135	
Tenderness (MenACWY 197/MenC; N=194,192,178)	57	65	44	
Erythema (MenACWY 197/MenC; N=194,192,178)	94	62	64	
Induration (MenACWY 197/MenC; N=194,192,178)	53	24	43	
Tenderness (DTPa-HepB-Hib; N=189,190,176)	62	83	73	
Erythema (DTPa-HepB-Hib; N=189,190,176)	80	81	96	
Induration (DTPa-HepB-Hib; N=189,190,176)	62	66	81	
Tenderness (PCV7; N=189,190,176)	58	68	60	
Erythema (PCV7; N=189,190,176)	71	68	77	
Induration (PCV7; N=189,190,176)	50	50	59	
Any Systemic reactions (N=195,192,179)	173	149	150	
Change in eating habits (N=194,191,177)	87	66	49	
Sleepiness (N=194,191,179)	156	99	94	
Persisten crying (N=194,191,177)	100	93	76	
Irritability (N=194,191,177)	85	68	73	
Vomiting (N=194,191,179)	29	18	16	
Diarrhoea (N=194,191,179)	46	41	42	
Rash (N=194,191,179)	20	17	7	
Fever ≥ 38.5 C (N=195,192,179)	60	62	50	
Others (N=191,192,179)	58	62	62	
Analgesic-Antipyretic medication (N=195,192,179)	64	62	62	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout study period.

Adverse event reporting additional description:

Post-injection solicited Adverse Events (AEs) were collected from Days 1-7 after any vaccination. Other AEs and Serious AEs collected for group MenACWY-CRM197 (2dose) +Concomitant Vaccine (CV) were collected from days 1 to 180 (Month 6-8) and in MenACWY-CRM197 (1 dose) + CV and MenC (1 dose)+ CV were collected from day 1 to 6 months (Month 12)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	MenACWY-CRM197(2dose) +Concomitant Vaccines

Reporting group description:

Infants received two doses of MenACWY-CRM197 at 6-8 months and 12 months and Concomitant dose of PCV7 and DTPa-IPV-HepB-Hib at 12 months.

Reporting group title	MenC (1dose) +Concomitant Vaccines

Reporting group description:

Infants received one dose of MenC vaccine at 12 months and Concomitant dose of PCV7 and DTPa-IPV-HepB-Hib at 12 months.

Reporting group title	MenACWY-CRM197(1dose) +Concomitant Vaccines

Reporting group description:

Infants received one dose of MenACWY-CRM197 at 12 months and Concomitant dose of PCV7 and DTPa-IPV-HepB-Hib at 12 months

Serious adverse events	MenACWY-CRM197(2dose) +Concomitant Vaccines	MenC (1dose) +Concomitant Vaccines	MenACWY-CRM197(1dose) +Concomitant Vaccines
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 195 (6.67%)	12 / 179 (6.70%)	19 / 192 (9.90%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neuroblastoma			
subjects affected / exposed	0 / 195 (0.00%)	0 / 179 (0.00%)	1 / 192 (0.52%)
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			
Accidental exposure			

subjects affected / exposed	0 / 195 (0.00%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 195 (0.51%)	0 / 179 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	1 / 195 (0.51%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 195 (0.00%)	1 / 179 (0.56%)	0 / 192 (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			
Febrile convulsion			
subjects affected / exposed	0 / 195 (0.00%)	1 / 179 (0.56%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 195 (0.00%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hyperpyrexia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Food Allergy			

subjects affected / exposed	0 / 195 (0.00%)	1 / 179 (0.56%)	0 / 192 (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			
Amphthous stomatitis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 179 (0.00%)	0 / 192 (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			
subjects affected / exposed	0 / 195 (0.00%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception			
subjects affected / exposed	1 / 195 (0.51%)	0 / 179 (0.00%)	0 / 192 (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
Stomatitis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 179 (0.56%)	0 / 192 (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			
subjects affected / exposed	0 / 195 (0.00%)	0 / 179 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 195 (1.03%)	0 / 179 (0.00%)	0 / 192 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 195 (0.00%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis			
subjects affected / exposed	2 / 195 (1.03%)	0 / 179 (0.00%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			
subjects affected / exposed	0 / 195 (0.00%)	1 / 179 (0.56%)	0 / 192 (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
Febrile infection			
subjects affected / exposed	0 / 195 (0.00%)	1 / 179 (0.56%)	0 / 192 (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			
subjects affected / exposed	3 / 195 (1.54%)	4 / 179 (2.23%)	4 / 192 (2.08%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 195 (0.51%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	1 / 195 (0.51%)	0 / 179 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 195 (0.00%)	3 / 179 (1.68%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 195 (0.00%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			

subjects affected / exposed	1 / 195 (0.51%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 179 (0.56%)	0 / 192 (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
Tonsillitis			
subjects affected / exposed	0 / 195 (0.00%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 195 (0.51%)	0 / 179 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 195 (0.00%)	1 / 179 (0.56%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 195 (1.03%)	1 / 179 (0.56%)	0 / 192 (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

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

Non-serious adverse events	MenACWY-CRM197(2dose) +Concomitant Vaccines	MenC (1dose) +Concomitant Vaccines	MenACWY-CRM197(1dose) +Concomitant Vaccines
Total subjects affected by non-serious adverse events			
subjects affected / exposed	192 / 195 (98.46%)	170 / 179 (94.97%)	184 / 192 (95.83%)
Nervous system disorders			
Crying			

subjects affected / exposed	100 / 195 (51.28%)	76 / 179 (42.46%)	93 / 192 (48.44%)
occurrences (all)	148	86	113
Somnolence			
subjects affected / exposed	126 / 195 (64.62%)	94 / 179 (52.51%)	99 / 192 (51.56%)
occurrences (all)	197	106	118
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	110 / 195 (56.41%)	110 / 179 (61.45%)	102 / 192 (53.13%)
occurrences (all)	299	251	223
Injection site induration			
subjects affected / exposed	86 / 195 (44.10%)	104 / 179 (58.10%)	82 / 192 (42.71%)
occurrences (all)	197	197	163
Injection site pain			
subjects affected / exposed	90 / 195 (46.15%)	84 / 179 (46.93%)	97 / 192 (50.52%)
occurrences (all)	195	184	226
Pyrexia			
subjects affected / exposed	127 / 195 (65.13%)	102 / 179 (56.98%)	111 / 192 (57.81%)
occurrences (all)	218	158	167
Eye disorders			
Conjunctivitis			
subjects affected / exposed	36 / 195 (18.46%)	18 / 179 (10.06%)	15 / 192 (7.81%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	54 / 195 (27.69%)	44 / 179 (24.58%)	44 / 192 (22.92%)
occurrences (all)	80	57	60
Enteritis			
subjects affected / exposed	13 / 195 (6.67%)	5 / 179 (2.79%)	4 / 192 (2.08%)
occurrences (all)	15	5	5
Teething			
subjects affected / exposed	21 / 195 (10.77%)	7 / 179 (3.91%)	6 / 192 (3.13%)
occurrences (all)	25	10	8
Vomiting			
subjects affected / exposed	38 / 195 (19.49%)	19 / 179 (10.61%)	24 / 192 (12.50%)
occurrences (all)	47	25	27
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	25 / 195 (12.82%)	10 / 179 (5.59%)	11 / 192 (5.73%)
occurrences (all)	34	16	17
Skin and subcutaneous tissue disorders			
Dermatitis Diaper			
subjects affected / exposed	24 / 195 (12.31%)	9 / 179 (5.03%)	20 / 192 (10.42%)
occurrences (all)	37	13	30
Rash			
subjects affected / exposed	28 / 195 (14.36%)	7 / 179 (3.91%)	24 / 192 (12.50%)
occurrences (all)	36	9	28
Psychiatric disorders			
Irritability			
subjects affected / exposed	85 / 195 (43.59%)	73 / 179 (40.78%)	68 / 192 (35.42%)
occurrences (all)	132	86	88
Eating disorder			
subjects affected / exposed	87 / 195 (44.62%)	49 / 179 (27.37%)	66 / 192 (34.38%)
occurrences (all)	113	54	80
Infections and infestations			
Bronchitis			
subjects affected / exposed	47 / 195 (24.10%)	29 / 179 (16.20%)	29 / 192 (15.10%)
occurrences (all)	70	50	52
Gastroenteritis			
subjects affected / exposed	22 / 195 (11.28%)	12 / 179 (6.70%)	14 / 192 (7.29%)
occurrences (all)	23	21	18
Nasopharyngitis			
subjects affected / exposed	19 / 195 (9.74%)	14 / 179 (7.82%)	14 / 192 (7.29%)
occurrences (all)	25	34	19
Otitis media			
subjects affected / exposed	33 / 195 (16.92%)	21 / 179 (11.73%)	22 / 192 (11.46%)
occurrences (all)	50	32	43
Rhinitis			
subjects affected / exposed	24 / 195 (12.31%)	8 / 179 (4.47%)	7 / 192 (3.65%)
occurrences (all)	27	10	9
Upper respiratory tract infection			
subjects affected / exposed	67 / 195 (34.36%)	29 / 179 (16.20%)	31 / 192 (16.15%)
occurrences (all)	109	49	48
Viral infection			

subjects affected / exposed occurrences (all)	38 / 195 (19.49%) 56	26 / 179 (14.53%) 44	26 / 192 (13.54%) 45

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes: