Clinical trial results:
A phase III open-label randomised study to evaluate the immunogenicity and safety of the concomitant administration of a new Hexavalent DTaP-IPV-HB-Hib combined vaccine (Hexavalent vaccine) given at 2, 3, and 4 months of age with a meningococcal serogroup C conjugate (MenC) vaccine given at 2 and 4 months of age.

Short title:
Concomitant administration of a new hexavalent vaccine (Hexavalent vaccine) with a meningococcal serogroup C conjugate vaccine in healthy infants during primary series immunisation followed by booster vaccination

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2012-005547-24
Trial protocol	FI
Global end of trial date	11 February 2015

Results information

Result version number	v2 (current)
This version publication date	28 April 2016
First version publication date	18 March 2015
Version creation reason	• New data added to full data set The analysis stage is now final and the Form can be completed with the last study period.

Trial information

Trial identification

Sponsor protocol code	HXM01C

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01839175
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur MSD S.N.C.
Sponsor organisation address	162 avenue Jean Jaurès - CS 50712, Lyon Cedex 07, France, 69367
Public contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C., ClinicalTrialsDisclosure@spmsd.com
Scientific contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C., ClinicalTrialsDisclosure@spmsd.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 February 2015
Global end of trial reached?	Yes
Global end of trial date	11 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

PRIMARY SERIES (Period 2):
- To demonstrate that the concomitant administration of the Hexavalent vaccine given at 2, 3 and 4 months of age with a meningococcal serogroup C conjugate (MenC) vaccine given at 2 and 4 months of age is non inferior to the administration of the Hexavalent vaccine without a MenC vaccine concomitantly in term of seroprotection rate for hepatitis B 1 month after the 3rd dose of the Hexavalent vaccine.
- To demonstrate that the concomitant administration of a MenC vaccine given at 2 and 4 months of age with the Hexavalent vaccine given at 2, 3 and 4 months of age induces an acceptable response for MenC in term of seroprotection rate (SPR) 1 month after the 2nd dose of MenC.

BOOSTER (Period 3):
To describe the immunogenicity of a booster dose of the Hexavalent vaccine and of a meningococcal group ACWY conjugate vaccine either co-administered at 12 months of age or given separately.

Protection of trial subjects:

Subjects in the study received 3 injections during primary series (period 2) and 1 injection during the booster part (period 3) of a single dose of the study vaccine DTaP-IPV-HB-Hib supplied in a pre-filled 0.5 mL syringe that was administered by qualified study personnel.
Subjects with allergy to any of the vaccine components were not vaccinated.
After each vaccination, subjects were also kept under observation for 30 minutes to ensure their safety.
Appropriate equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not Applicable

Evidence for comparator:

The control group complies with the recommended vaccination schedules for all vaccines (i.e. Study vaccine and routine vaccines) as per their respective Summaries of Product Characteristics (SmPCs).

Actual start date of recruitment	29 April 2013
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	Finland: 350
Worldwide total number of subjects	350
EEA total number of subjects	350

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)	350
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:

Study subjects were enrolled from 29 April 2013 to 09 August 2013 in 11 clinical centers in Finland.

Pre-assignment

Screening details:

Period 1 (Randomisation): 354 subjects screened.
Period 2 (Primary Series): 350 subjects randomised (1:1); 350 subjects vaccinated (at least 1 dose) and 346 subjects received the 3 doses of the primary series; 345 subjects completed the period.
Period 3 (Booster): 346 subjects randomised (1:1:1); 312 vaccinated; 311 completed the period.

Period 1

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

Blinding implementation details:

This was an open-label study as the number of vaccines administered in each group was different at several visits. Blinding would have required a placebo injection which was not deemed necessary since the primary end points were based on immunological criteria. Serology tests for the Hexavalent vaccine antigens were performed by laboratory staff blinded to subject group.

Arms

Are arms mutually exclusive?	Yes
Arm title	Hexavalent vaccine co-administered with MenC vaccine

Arm description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with 1 dose each at 2, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.
Blood samples were collected (i) at 2 months of age before any vaccination, (ii) at 3 months of age before any other vaccination (=post-dose 1 of MenC vaccine), and (iii) at 5 months of age (=post-dose 3 of Hexavalent vaccine=post-dose 2 of MenC vaccine).

Arm type	Experimental
Investigational medicinal product name	Hexyon® (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima® / Hexaxim®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular (IM) route, 1 dose at 2, 3, and 4 months of age.

Investigational medicinal product name	NeisVac-C®
Investigational medicinal product code	MenC vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route, 1 dose at 2, and 4 months of age.

Arm title	Hexavalent vaccine without MenC vaccine

Arm description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.
Blood samples were collected (i) at 2 months of age before any vaccination, and (ii) at 5 months of

age (=post-dose 3 of Hexavalent vaccine).

Arm type	Active comparator
Investigational medicinal product name	Hexyon® (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima® / Hexaxim®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route, 1 dose at 2, 3, and 4 months of age.

Number of subjects in period 1	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine
Started	175	175
Completed	175	175

Period 2

Period 2 title	Primary Series
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study as the number of vaccines administered in each group was different at several visits. Blinding would have required a placebo injection which was not deemed necessary since the primary end points were based on immunological criteria. Serology tests for the Hexavalent vaccine antigens were performed by laboratory staff blinded to subject group.

Arms

Are arms mutually exclusive?	Yes
Arm title	Hexavalent vaccine co-administered with MenC vaccine

Arm description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with 1 dose each at 2, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.
Blood samples were collected (i) at 2 months of age before any vaccination, (ii) at 3 months of age before any other vaccination (=post-dose 1 of MenC vaccine), and (iii) at 5 months of age (=post-dose 3 of Hexavalent vaccine=post-dose 2 of MenC vaccine).

Arm type	Experimental
Investigational medicinal product name	Hexyon® (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima® / Hexaxim®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route, 1 dose at 2, 3, and 4 months of age.

Investigational medicinal product name	NeisVac-C®
Investigational medicinal product code	MenC vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route, 1 dose at 2, and 4 months of age.

Arm title	Hexavalent vaccine without MenC vaccine

Arm description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.
Blood samples were collected (i) at 2 months of age before any vaccination, and (ii) at 5 months of age (=post-dose 3 of Hexavalent vaccine).

Arm type	Active comparator
Investigational medicinal product name	Hexyon® (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima® / Hexaxim®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route, 1 dose at 2, 3, and 4 months of age.

Number of subjects in period 2	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine
Started	175	175
Completed	173	172
Not completed	2	4
Adverse event, non-fatal	1	2
Transferred to other arm/group	1	-
Lost to follow-up	-	2
Joined	0	1
Transferred in from other group/arm	-	1

Period 3

Period 3 title	Booster
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study as the number of vaccines administered in each group was different at the 12 months vaccination visit (and subsequently at the 13 months vaccination visit). Blinding would have required a placebo injection which was not deemed necessary since the primary end points were based

on immunological criteria. Serology tests for the Hexavalent vaccine antigens and for MenACWY vaccine antigens were performed by laboratory staff blinded to subject group.

Arms

Are arms mutually exclusive?	Yes
Arm title	Hexavalent vaccine co-administered with MenACWY vaccine

Arm description:

Subjects from the Primary Series period received 1 booster dose of Hexavalent vaccine co-administered with 1 dose of MenACWY vaccine at approximately 12 months of age.
Subjects received also routine vaccination: 1 dose of Prevenar 13 ± 1 optional dose of M-M-RvaxPRO at approximately 13 months of age.
Blood samples were collected (i) before Hexavalent vaccine booster dose (=pre-booster), and (ii) 1 month after Hexavalent vaccine booster dose (=post-booster), before any other vaccination.

Arm type	Experimental
Investigational medicinal product name	Hexyon® (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima® / Hexaxim®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (contralateral thigh from MenACWY injection-site), 1 dose at approximately 12 months of age.

Investigational medicinal product name	Nimenrix®
Investigational medicinal product code	MenACWY vaccine
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (contralateral thigh from Hexavalent vaccine injection-site), 1 dose at approximately 12 months of age.

Arm title	Hexavalent vaccine only

Arm description:

Subjects from the Primary Series period received 1 booster dose of Hexavalent vaccine at approximately 12 months of age.
Subjects received also routine vaccination: 1 dose of MenC vaccine + 1 dose of Prevenar 13 ± 1 optional dose of M-M-RvaxPRO at approximately 13 months of age.
Blood samples were collected (i) before Hexavalent vaccine booster dose (=pre-booster), and (ii) 1 month after Hexavalent vaccine booster dose (=post-booster), before any other vaccination.

Arm type	Active comparator
Investigational medicinal product name	Hexyon® (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima® / Hexaxim®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route, 1 dose at approximately 12 months of age.

Arm title	MenACWY vaccine only

Arm description:

Subjects from the Primary Series period received 1 dose of MenACWY vaccine at approximately 12 months of age.
Subjects received also 1 booster dose of Hexavalent vaccine + 1 dose of Prevenar 13 ± 1 optional dose of M-M-RvaxPRO at approximately 13 months of age.
Blood samples were collected (i) before MenACWY vaccine dose, and (ii) 1 month after MenACWY vaccine dose, before any other vaccination.

Arm type	Active comparator

Investigational medicinal product name	Nimenrix®
Investigational medicinal product code	MenACWY vaccine
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route, 1 dose at approximately 12 months of age.

Investigational medicinal product name	Hexyon® (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima® / Hexaxim®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route, 1 dose at approximately 13 months of age.

Number of subjects in period 3[1]	Hexavalent vaccine co-administered with MenACWY vaccine	Hexavalent vaccine only	MenACWY vaccine only
Started	104	105	103
Completed	104	104	103
Not completed	0	1	0
Lost to follow-up	-	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 34 subjects of the Primary Series period (period 2) were not randomised in the Booster period (period 3): 32 "screen failure", and 2 "non-compliance with the protocol".

Baseline characteristics

Reporting groups	
Reporting group title	Hexavalent vaccine co-administered with MenC vaccine
Reporting group description:	
# Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with 1 dose each at 2, and 4 months of age. # Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age. # Blood samples were collected (i) at 2 months of age before any vaccination, (ii) at 3 months of age before any other vaccination (=post-dose 1 of MenC vaccine), and (iii) at 5 months of age (=post-dose 3 of Hexavalent vaccine=post-dose 2 of MenC vaccine).	
Reporting group title	Hexavalent vaccine without MenC vaccine
Reporting group description:	
# Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age. # Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age. # Blood samples were collected (i) at 2 months of age before any vaccination, and (ii) at 5 months of age (=post-dose 3 of Hexavalent vaccine).	

Reporting group values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine	Total
Number of subjects	175	175	350
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	175	175	350
Age continuous Units: days			
arithmetic mean	62.8	63.2	
standard deviation	± 7	± 7	-
Gender categorical Units: Subjects			
Female	83	82	165
Male	92	93	185

End points

End points reporting groups

Reporting group title	Hexavalent vaccine co-administered with MenC vaccine

Reporting group description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with 1 dose each at 2, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.
Blood samples were collected (i) at 2 months of age before any vaccination, (ii) at 3 months of age before any other vaccination (=post-dose 1 of MenC vaccine), and (iii) at 5 months of age (=post-dose 3 of Hexavalent vaccine=post-dose 2 of MenC vaccine).

Reporting group title	Hexavalent vaccine without MenC vaccine

Reporting group description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.
Blood samples were collected (i) at 2 months of age before any vaccination, and (ii) at 5 months of age (=post-dose 3 of Hexavalent vaccine).

Reporting group title	Hexavalent vaccine co-administered with MenC vaccine

Reporting group description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with 1 dose each at 2, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.
Blood samples were collected (i) at 2 months of age before any vaccination, (ii) at 3 months of age before any other vaccination (=post-dose 1 of MenC vaccine), and (iii) at 5 months of age (=post-dose 3 of Hexavalent vaccine=post-dose 2 of MenC vaccine).

Reporting group title	Hexavalent vaccine without MenC vaccine

Reporting group description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.
Blood samples were collected (i) at 2 months of age before any vaccination, and (ii) at 5 months of age (=post-dose 3 of Hexavalent vaccine).

Reporting group title	Hexavalent vaccine co-administered with MenACWY vaccine

Reporting group description:

Subjects from the Primary Series period received 1 booster dose of Hexavalent vaccine co-administered with 1 dose of MenACWY vaccine at approximately 12 months of age.
Subjects received also routine vaccination: 1 dose of Prevenar 13 ± 1 optional dose of M-M-RvaxPRO at approximately 13 months of age.
Blood samples were collected (i) before Hexavalent vaccine booster dose (=pre-booster), and (ii) 1 month after Hexavalent vaccine booster dose (=post-booster), before any other vaccination.

Reporting group title	Hexavalent vaccine only

Reporting group description:

Subjects from the Primary Series period received 1 booster dose of Hexavalent vaccine at approximately 12 months of age.
Subjects received also routine vaccination: 1 dose of MenC vaccine + 1 dose of Prevenar 13 ± 1 optional dose of M-M-RvaxPRO at approximately 13 months of age.
Blood samples were collected (i) before Hexavalent vaccine booster dose (=pre-booster), and (ii) 1 month after Hexavalent vaccine booster dose (=post-booster), before any other vaccination.

Reporting group title	MenACWY vaccine only

Reporting group description:

Subjects from the Primary Series period received 1 dose of MenACWY vaccine at approximately 12 months of age.
Subjects received also 1 booster dose of Hexavalent vaccine + 1 dose of Prevenar 13 ± 1 optional dose of M-M-RvaxPRO at approximately 13 months of age.
Blood samples were collected (i) before MenACWY vaccine dose, and (ii) 1 month after MenACWY vaccine dose, before any other vaccination.

Primary: Primary Series # Seroprotection against Hepatitis B 1 month after vaccination with either Hexavalent vaccine co-administered with MenC vaccine or Hexavalent vaccine without MenC vaccine

End point title	Primary Series # Seroprotection against Hepatitis B 1 month after vaccination with either Hexavalent vaccine co-administered with MenC vaccine or Hexavalent vaccine without MenC vaccine

End point description:

Percentage of subjects with an anti-Hepatitis B surface antigen (Hep B) concentration ≥10 mIU/mL (measured by hepatitis B enhanced Chemiluminescence assay, ECi).
Analysis was done on the Per Protocol Set, i.e., all subjects without any protocol deviation that could interfere with the vaccines immunogenicity.

End point type	Primary

End point timeframe:

1 month post-dose 3 of Hexavalent vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	155		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-Hep B ≥10 mIU/mL	97.5 (93.7 to 99.3)	96.1 (91.8 to 98.6)		

Statistical analyses

Statistical analysis title	Non-inferiority of the immune response

Statistical analysis description:

To demonstrate the non-inferiority of the immune response of the concomitant administration of the Hexavalent vaccine co-administered with MenC vaccine as compared to the Hexavalent vaccine without Men C vaccine 1 month after the 3rd dose.

Comparison groups	Hexavalent vaccine co-administered with MenC vaccine v Hexavalent vaccine without MenC vaccine
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	Wilson score Method without cc
Parameter estimate	Difference in percentages of subjects
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.92
upper limit	5.95

Notes:

[1] - The immune response of Hexavalent vaccine co-administered with MenC vaccine was considered as non-inferior to Hexavalent vaccine without MenC vaccine if the lower bound of the 2-sided 95.0% Confidence Intervals (CI) of the difference in the percentages of subjects with anti-Hep B ≥10 mIU/mL measured 1 month after the 3rd dose was greater than -10%. CI was based on the Wilson score method without continuity correction (cc).

Primary: Primary Series # Seroprotection for MenC 1 month after vaccination with 2 doses of MenC vaccine

End point title	Primary Series # Seroprotection for MenC 1 month after vaccination with 2 doses of MenC vaccine[2]

End point description:

Percentages of subjects with an anti-MenC titer ≥8 (1/dilution (dil)) (measured by Serum Bactericidal Antibody assay with rabbit complement, rSBA) 1 month after 2 doses of MenC vaccine.
The immune response to MenC vaccine was considered as acceptable if the lower bound of the 2-sided 95.0% CI of the percentage of subjects with anti-MenC ≥8 (1/dil) 1 month after the 2nd dose was greater than 90%.
Analysis was done on the Per Protocol Set.

End point type	Primary

End point timeframe:

1 month post-dose 2 of MenC vaccine.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no comparison between groups in this end point.
As specified above, the immune response to MenC vaccine was considered as acceptable if the lower bound of the 2-sided 95.0% CI of the percentage of subjects with anti-MenC ≥8 (1/dil) 1 month after the 2nd dose was greater than 90%. Acceptability criteria was met for MenC.

End point values	Hexavalent vaccine co-administered with MenC vaccine			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-MenC ≥8 (1/dil)	100 (97.7 to 100)			

Statistical analyses

No statistical analyses for this end point

Primary: Booster # Response rates to all Hexavalent vaccine antigens 1 month after Hexavalent vaccine booster dose, co-administered or not with MenACWY

End point title	Booster # Response rates to all Hexavalent vaccine antigens 1 month after Hexavalent vaccine booster dose, co-administered or not with MenACWY[3]

End point description:

Percentages of subjects with anti-D concentration ≥0.10 IU/mL & ≥1.0 IU/mL for Diphtheria (measured by MIT), anti-T concentration ≥0.10 IU/mL & ≥1.0 IU/mL for Tetanus (measured by ELISA), anti-IPV titer ≥8 (1/dil) for Poliovirus types 1, 2, & 3 (measured by MIT), anti-Hep B concentration ≥10 mIU/mL & ≥100 mIU/mL (measured by Hep B ECi), anti-PRP concentration ≥0.15 ug/mL & ≥1.0 ug/mL for Hib (measured by Farr type radioimmunoassay, RIA), anti-PT vaccine response (VR), anti-FHA VR, & 4-fold increase from pre-vaccination to post-booster (PT & FHA) for Pertussis (measured by ELISA).
Pertussis VR was defined as:

- If pre-vaccination (pre-dose 1) antibody concentration <4xLLOQ, post-booster antibody concentration ≥4xLLOQ,
- If pre-vaccination (pre-dose 1) antibody concentration ≥4xLLOQ, post-booster antibody concentration >pre-vaccination antibody concentration.
Analysis was done on the Per Protocol Set.

End point type	Primary

End point timeframe:

1 month post-booster dose of Hexavalent vaccine, co-administered or not with MenACWY.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Objectives of the Booster period (period 3) were only descriptive. Thus no formal statistical hypothesis was tested in this period.

End point values	Hexavalent vaccine co-administered with MenACWY vaccine	Hexavalent vaccine only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	91		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-D ≥0.10 IU/mL (N=87, 91)	100 (95.8 to 100)	100 (96 to 100)		
Anti-D ≥1.0 IU/mL (N=87, 91)	89.7 (81.3 to 95.2)	96.7 (90.7 to 99.3)		
Anti-T ≥0.10 IU/mL (N=87, 91)	100 (95.8 to 100)	100 (96 to 100)		
Anti-T ≥1.0 IU/mL (N=87, 91)	96.6 (90.3 to 99.3)	96.7 (90.7 to 99.3)		
Anti-IPV1 ≥8 (1/dil) (N=87, 91)	98.9 (93.8 to 100)	98.9 (94 to 100)		
Anti-IPV2 ≥8 (1/dil) (N=87, 91)	100 (95.8 to 100)	100 (96 to 100)		
Anti-IPV3 ≥8 (1/dil) (N=87, 90)	100 (95.8 to 100)	100 (96 to 100)		
Anti-Hep B ≥10 mIU/mL (N=87, 91)	98.9 (93.8 to 100)	98.9 (94 to 100)		
Anti-Hep B ≥100 mIU/mL (N=85, 87)	97.7 (91.9 to 99.7)	95.6 (89.1 to 98.8)		
Anti-PRP ≥ 0.15 ug/mL (N=87, 91)	100 (95.8 to 100)	100 (96 to 100)		
Anti-PRP ≥ 1.0 ug/mL (N=87, 91)	97.7 (91.9 to 99.7)	100 (96 to 100)		
Anti-PT VR (N=85, 86)	98.8 (93.6 to 100)	98.8 (93.7 to 100)		
Anti-PT 4-fold (N=85, 86)	83.5 (73.9 to 90.7)	88.4 (79.7 to 94.3)		
Anti-FHA VR (N=85, 89)	100 (95.8 to 100)	100 (95.9 to 100)		
Anti-FHA 4-fold (N=85, 89)	96.5 (90 to 99.3)	92.1 (84.5 to 96.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Booster # Geometric Mean Titers (GMTs) or Concentrations (GMCs) of antibodies to all Hexavalent vaccine antigens 1 month after Hexavalent vaccine booster dose, co-administered or not with MenACWY

End point title	Booster # Geometric Mean Titers (GMTs) or Concentrations (GMCs) of antibodies to all Hexavalent vaccine antigens 1 month after Hexavalent vaccine booster dose, co-administered or not with MenACWY[4]

End point description:

Antibody titers or concentrations were measured for Diphtheria (D) by MIT (IU/mL), for Tetanus (T) by ELISA (IU/mL), for Poliovirus (IPV) types 1, 2, and 3 by MIT (1/dil), for Hepatitis B (Hep B) by ECi (mIU/mL), for Haemophilus influenzae type b (PRP) by Farr type RIA (ug/mL), and for Pertussis antigens (PT & FHA) by ELISA (EU/mL).
Analysis was done on the Per Protocol Set.

End point type	Primary

End point timeframe:

1 month post-booster dose of Hexavalent vaccine, co-administered or not with MenACWY.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Objectives of the Booster period (period 3) were only descriptive. Thus no formal statistical hypothesis was tested in this period.

End point values	Hexavalent vaccine co-administered with MenACWY vaccine	Hexavalent vaccine only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	91		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-D GMC (N=87, 91)	3.07 (2.49 to 3.79)	3.24 (2.69 to 3.91)		
Anti-T GMC (N=87, 91)	6.89 (5.78 to 8.21)	6.25 (5.3 to 7.37)		
Anti-IPV1 GMT (N=87, 91)	2174.05 (1606.18 to 2942.7)	2040.21 (1522.96 to 2733.14)		
Anti-IPV2 GMT (N=87, 91)	1678.14 (1203.6 to 2339.77)	1738.58 (1242.59 to 2432.56)		
Anti-IPV3 GMT (N=87, 90)	3086.91 (2278.1 to 4182.89)	4127.67 (3175.4 to 5365.53)		
Anti-Hep B GMC (N=87, 91)	2230.68 (1597.48 to 3114.87)	2233.15 (1597.3 to 3122.13)		
Anti-PRP GMC (N=87, 91)	22.7 (17.2 to 29.96)	27.82 (21.89 to 35.35)		
Anti-PT GMC (N=87, 91)	111.78 (97.9 to 127.63)	114.72 (102.68 to 128.16)		
Anti-FHA GMC (N=87, 91)	174.98 (153.98 to 198.86)	184.57 (162.43 to 209.72)		

Statistical analyses

No statistical analyses for this end point

Primary: Booster # Response rates to all MenACWY vaccine antigens 1 month after MenACWY vaccine, co-administered or not with Hexavalent vaccine booster dose

End point title	Booster # Response rates to all MenACWY vaccine antigens 1 month after MenACWY vaccine, co-administered or not with Hexavalent vaccine booster dose[5]

End point description:

Percentages of subjects with anti-MenA, anti-MenW-135, and anti-MenY titers ≥8 (1/dil), and anti-MenC titers ≥8 (1/dil) & ≥128 (1/dil) measured by rSBA 1 month after MenACWY, co-administered or not with Hexavalent vaccine booster dose.
Anti-MenC response rates were determined in all subjects, and subjects previously vaccinated or not with MenC vaccine during Primary (Iry) Series ("All subjects", "MenC IrySeries", and "No MenC IrySeries" respectively in the table below).
Analysis was done on the Per Protocol Set.

End point type	Primary

End point timeframe:

1 month after MenACWY vaccine, co-administered or not with Hexavalent vaccine booster dose.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Objectives of the Booster period (period 3) were only descriptive. Thus no formal statistical hypothesis was tested in this period.

End point values	Hexavalent vaccine co-administered with MenACWY vaccine	MenACWY vaccine only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	94		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-MenA ≥8 (1/dil) (N=87,94)	100 (95.8 to 100)	100 (96.2 to 100)		
Anti-MenC ≥8 (1/dil)-All subjects (N=87,94)	98.9 (93.8 to 100)	95.7 (89.5 to 98.8)		
Anti-MenC ≥8 (1/dil)-MenC IrySeries (N=43,47)	100 (91.8 to 100)	97.9 (88.7 to 99.9)		
Anti-MenC ≥8 (1/dil)- No MenC IrySeries (N=44,47)	97.7 (88 to 99.9)	93.6 (82.5 to 98.7)		
Anti-MenC ≥128 (1/dil)-All subjects (N=87,94)	97.7 (91.9 to 99.7)	90.4 (82.6 to 95.5)		
Anti-MenC ≥128 (1/dil)-MenC IrySeries (N=43,47)	100 (91.8 to 100)	97.9 (88.7 to 99.9)		
Anti-MenC ≥128 (1/dil)-No MenC IrySeries (N=44,47)	95.5 (84.5 to 99.4)	83 (69.2 to 92.4)		
Anti-MenW-135 ≥8 (1/dil) (N=87,94)	100 (95.8 to 100)	98.9 (94.2 to 100)		
Anti-MenY ≥8 (1/dil) (N=87,94)	100 (95.8 to 100)	100 (96.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: Booster # Geometric Mean Titers (GMTs) of antibodies to all MenACWY vaccine antigens 1 month after MenACWY vaccine, co-administered or not with Hexavalent vaccine

End point title	Booster # Geometric Mean Titers (GMTs) of antibodies to all MenACWY vaccine antigens 1 month after MenACWY vaccine, co-administered or not with Hexavalent vaccine[6]

End point description:

Antibody titers were measured for MenA, MenC, MenW-135, and MenY (1/dil) by rSBA 1 month after MenACWY, co-administered or not with Hexavalent vaccine booster dose.
Anti-MenC GMTs were determined in all subjects, and subjects previously vaccinated or not with MenC vaccine during Primary (Iry) Series ("All subjects", "MenC IrySeries", and "No MenC IrySeries" respectively in the table below).
Analysis was done on the Per Protocol Set.

End point type	Primary

End point timeframe:

1 month after MenACWY vaccine, co-administered or not with Hexavalent vaccine booster dose.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Objectives of the Booster period (period 3) were only descriptive. Thus no formal statistical hypothesis was tested in this period.

End point values	Hexavalent vaccine co-administered with MenACWY vaccine	MenACWY vaccine only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	94		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-MenA GMT (N=87, 94)	4096 (3335.98 to 5029.17)	5302.07 (4249.49 to 6615.38)		
Anti-MenC GMT-All subjects (N=87, 94)	693.03 (524.15 to 916.33)	620.2 (425.53 to 903.94)		
Anti-MenC GMT-MenC IrySeries (N=43, 47)	1262.73 (901.11 to 1769.46)	1617.53 (1083.22 to 2415.39)		
Anti-MenC GMT-No MenC IrySeries (N=44, 47)	385.59 (264.11 to 562.93)	237.8 (141.85 to 398.66)		
Anti-MenW-135 GMT (N=87, 94)	2148.28 (1650.66 to 2795.91)	2555.07 (1930.58 to 3381.58)		
Anti-MenY GMT (N=87, 94)	1952.4 (1538.58 to 2477.53)	2003.19 (1592.49 to 2519.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Primary Series # Response rates for all Hexavalent vaccine antigens 1 month after 3 doses of Hexavalent vaccine co-administered with MenC vaccine or 3

doses of Hexavalent vaccine without MenC vaccine	
End point title	Primary Series # Response rates for all Hexavalent vaccine antigens 1 month after 3 doses of Hexavalent vaccine co-administered with MenC vaccine or 3 doses of Hexavalent vaccine without MenC vaccine

End point description:

Percentages of subjects with an anti-Hep B concentration ≥10 mIU/mL (measured by Hep B ECi), anti-PRP concentration ≥0.15ug/mL for Hib (measured by Farr type RIA), anti-D concentration ≥0.01 IU/mL and ≥0.1 IU/mL for Diphtheria (measured by MIT), anti-T concentration ≥0.01 IU/mL and ≥0.1 IU/mL for Tetanus (measured by ELISA), anti-IPV titer ≥8 (1/dil) for Poliovirus types 1, 2, and 3 (measured by MIT), anti-PT vaccine response (VR, EU/mL), anti-FHA VR (EU/mL), & 4-fold increase (PT & FHA) for Pertussis (measured by ELISA).
Pertussis VR was defined as:
- If pre-vaccination (pre-dose 1) antibody concentration <4xLLOQ, post-vaccination antibody concentration ≥4xLLOQ,
- If pre-vaccination (pre-dose 1) antibody concentration ≥4xLLOQ, post-vaccination antibody concentration ≥pre-immunisation levels.
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

1 month post-dose 3 of Hexavalent vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	160		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-Hep B ≥10 mIU/mL (N=160, 155)	97.5 (93.7 to 99.3)	96.1 (91.8 to 98.6)		
Anti-PRP ≥0.15 ug/mL (N=160, 158)	98.1 (94.6 to 99.6)	94.3 (89.5 to 97.4)		
Anti-D ≥0.01 IU/mL (N=160, 158)	100 (97.7 to 100)	99.4 (96.5 to 100)		
Anti-D ≥0.1 IU/mL (N=160, 158)	35 (27.6 to 42.9)	41.1 (33.4 to 49.2)		
Anti-T ≥0.01 IU/mL (N=159, 156)	100 (97.7 to 100)	100 (97.7 to 100)		
Anti-T ≥0.1 IU/mL (N=159, 156)	100 (97.7 to 100)	99.4 (96.5 to 100)		
Anti-IPV1 ≥8 (1/dil) (N=159, 152)	100 (97.7 to 100)	98.7 (95.3 to 99.8)		
Anti-IPV2 ≥8 (1/dil) (N=159, 152)	100 (97.7 to 100)	100 (97.6 to 100)		
Anti-IPV3 ≥8 (1/dil) (N=159, 152)	100 (97.7 to 100)	99.3 (96.4 to 100)		
Anti-PT VR (N=154, 154)	98.7 (95.4 to 99.8)	100 (97.6 to 100)		
Anti-PT 4-fold (N=154, 154)	88.3 (82.2 to 92.9)	88.3 (82.2 to 92.9)		
Anti-FHA VR (N=154, 153)	99.4 (96.4 to 100)	100 (97.6 to 100)		
Anti-FHA 4-fold (N=154, 153)	89.6 (83.7 to 93.9)	91.5 (85.9 to 95.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Primary Series # Response rates for MenC 1 month after vaccination with 1 dose or 2 doses of MenC vaccine

End point title	Primary Series # Response rates for MenC 1 month after vaccination with 1 dose or 2 doses of MenC vaccine

End point description:

Percentages of subjects with anti-MenC titers ≥8 (1/dil) or ≥128 (1/dil) (measured by rSBA) 1 month after 1 dose or 1 month after 2 doses of MenC vaccine.
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

1 month post-dose 1 or post-dose 2 of MenC vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-MenC ≥8 (1/dil) post-dose 1 (N=157)	99.4 (96.5 to 100)			
Anti-MenC ≥128 (1/dil) post-dose 1 (N=157)	98.1 (94.5 to 99.6)			
Anti-MenC ≥8 (1/dil) post-dose 2 (N=162)	100 (97.7 to 100)			
Anti-MenC ≥128 (1/dil) post-dose 2 (N=162)	96.3 (92.1 to 98.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Primary Series # Geometric Mean Titers or Concentrations of Antibodies 1 month after 3 doses of Hexavalent vaccine co-administered with MenC vaccine or 3 doses of Hexavalent vaccine without MenC vaccine

End point title	Primary Series # Geometric Mean Titers or Concentrations of Antibodies 1 month after 3 doses of Hexavalent vaccine co-administered with MenC vaccine or 3 doses of Hexavalent

	vaccine without MenC vaccine

End point description:

Antibody titers or concentrations were measured for Hepatitis B (Hep B) by Hep B ECi (mIU/mL), for Haemophilus influenzae type b (PRP) by Farr type RIA (ug/mL), for Diphtheria (D) by MIT (IU/mL), for Tetanus (T) by ELISA (IU/mL), for Poliovirus (IPV) types 1, 2, and 3 by MIT (1/dil), and for Pertussis antigens (PT & FHA) by ELISA (EU/mL)).
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

1 month post-dose 3 of Hexavalent vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	160		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Hep B (N=160, 155)	242.75 (195.05 to 302.11)	267.58 (212.65 to 336.7)		
Anti-PRP (N=160, 158)	3.49 (2.88 to 4.24)	1.89 (1.49 to 2.38)		
Anti-D (N=160, 158)	0.08 (0.07 to 0.1)	0.09 (0.08 to 0.1)		
Anti-T (N=159, 156)	1.17 (1.07 to 1.29)	0.78 (0.7 to 0.87)		
Anti-IPV1 (N=159, 152)	92.49 (75.06 to 113.97)	126.84 (101.46 to 158.56)		
Anti-IPV2 (N=159, 152)	90.9 (73.23 to 112.83)	104.72 (82.66 to 132.67)		
Anti-IPV3 (N=159, 152)	173.3 (138.2 to 217.31)	250.78 (197.56 to 318.34)		
Anti-PT (N=160, 159)	129.74 (118.93 to 141.52)	139.91 (126.98 to 154.15)		
Anti-FHA (N=158, 156)	123.54 (112.47 to 135.69)	147.77 (134.82 to 161.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Primary Series # Geometric Mean Titers of Antibodies 1 month after 1 dose or 2 doses of MenC vaccine co-administered with Hexavalent vaccine

End point title	Primary Series # Geometric Mean Titers of Antibodies 1 month after 1 dose or 2 doses of MenC vaccine co-administered with Hexavalent vaccine

End point description:

Antibody titers were measured by rSBA (1/dil) 1 month after 1 dose or 2 doses of MenC vaccine.
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

1 month post-dose 1 or post-dose 2 of MenC vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-MenC post-dose 1 (N=157)	885.17 (737.06 to 1063.04)			
Anti-MenC post-dose 2 (N=162)	579.64 (505.36 to 664.84)			

Statistical analyses

No statistical analyses for this end point

Secondary: Primary Series # Percentage of subjects reporting solicited injection-site or systemic reactions after Hexavalent vaccine co-administered with MenC vaccine or Hexavalent vaccine without MenC

End point title	Primary Series # Percentage of subjects reporting solicited injection-site or systemic reactions after Hexavalent vaccine co-administered with MenC vaccine or Hexavalent vaccine without MenC

End point description:

Solicited injection-site reactions (ISRs: Erythema, Pain, and Swelling) and solicited systemic reactions (Crying, Decreased appetite, Irritability, Pyrexia, Somnolence, and Vomiting) within 7 days after any Hexavalent vaccine injection with or without MenC vaccine.
Solicited reactions were always considered as related to vaccines.
The percentage of subjects presenting at least once the considered events after any vaccination is reported hereafter.
Analysis was done on the Safety Analysis Set, i.e. all subjects who received at least 1 dose of the study vaccine(s) and who had safety follow-up data.

End point type	Secondary

End point timeframe:

Day 0 up to 7 days following any dose.

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	176		
Units: Percentage of subjects				
number (confidence interval 95%)				
Solicited reaction any dose	100 (97.9 to 100)	100 (97.9 to 100)		
Solicited ISR	89.1 (83.5 to 93.3)	73.9 (66.7 to 80.2)		
Solicited ISR after Hexavalent vaccine	84.5 (78.2 to 89.5)	73.9 (66.7 to 80.2)		
Erythema after Hexavalent vaccine	54.6 (46.9 to 62.1)	55.1 (47.4 to 62.6)		
Pain after Hexavalent vaccine	69 (61.5 to 75.7)	61.9 (54.3 to 69.1)		
Swelling after Hexavalent vaccine	34.5 (27.5 to 42.1)	34.7 (27.7 to 42.2)		
Solicited ISR after MenC vaccine	71.3 (63.9 to 77.9)	0 (0 to 0)		
Erythema after MenC vaccine	44.8 (37.3 to 52.5)	0 (0 to 0)		
Pain after MenC vaccine	60.9 (53.2 to 68.2)	0 (0 to 0)		
Swelling after MenC vaccine	25.9 (19.5 to 33)	0 (0 to 0)		
Solicited systemic reaction	100 (97.9 to 100)	100 (97.9 to 100)		
Crying	85.1 (78.9 to 90)	71 (63.7 to 77.6)		
Decreased appetite	56.3 (48.6 to 63.8)	54.5 (46.9 to 62.1)		
Irritability	95.4 (91.1 to 98)	94.3 (89.8 to 97.2)		
Pyrexia	72.4 (65.1 to 78.9)	72.2 (64.9 to 78.6)		
Somnolence	82.8 (76.3 to 88.1)	85.8 (79.7 to 90.6)		
Vomiting	36.2 (29.1 to 43.8)	26.7 (20.3 to 33.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Booster - Antibody persistence # Response rates to all Hexavalent vaccine antigens at 12 months of age, before Hexavalent vaccine booster dose

End point title	Booster - Antibody persistence # Response rates to all Hexavalent vaccine antigens at 12 months of age, before Hexavalent vaccine booster dose

End point description:

Percentages of subjects with anti-D concentration ≥0.01 IU/mL & ≥0.10 IU/mL for Diphtheria (measured by MIT), anti-T concentration ≥0.01 IU/mL & ≥0.10 IU/mL for Tetanus by ELISA, anti-IPV titer ≥8 (1/dil) for Poliovirus types 1, 2, & 3 by MIT, anti-Hep B concentration ≥10 mIU/mL & ≥100 mIU/mL by Hep B ECi, anti-PRP concentration ≥0.15 ug/mL & ≥1.0 ug/mL for Hib by Farr type RIA,

anti-PT & anti-FHA concentration ≥LLOQ and ≥2xLLOQ for Pertussis by ELISA (LLOQ=2 EU/mL). Analysis was done on the Persistence Analysis Set, i.e., all randomised subjects in the Booster Period with available serology data on Day 0 of the Booster period, and according to Iry series groups.

End point type	Secondary

End point timeframe:

On entry within Booster period, prior to vaccination with Hexavalent vaccine booster dose and/or MenACWY vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	151		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-D ≥0.01 IU/mL (N=151, 150)	98 (94.3 to 99.6)	99.3 (96.3 to 100)		
Anti-D ≥0.10 IU/mL (N=151, 150)	41.1 (33.1 to 49.3)	47.3 (39.1 to 55.6)		
Anti-T ≥0.01 IU/mL (N=151, 150)	100 (97.6 to 100)	100 (97.6 to 100)		
Anti-T ≥0.10 IU/mL (N=151, 150)	100 (97.6 to 100)	92 (86.4 to 95.8)		
Anti-IPV1 ≥8 (1/dil) (N=151, 150)	80.8 (73.6 to 86.7)	84.7 (77.9 to 90)		
Anti-IPV2 ≥8 (1/dil) (N=151, 150)	64.9 (56.7 to 72.5)	76 (68.4 to 82.6)		
Anti-IPV3 ≥8 (1/dil) (N=150, 148)	82 (74.9 to 87.8)	88.5 (82.2 to 93.2)		
Anti-Hep B ≥10 mIU/mL (N=152, 151)	90.1 (84.2 to 94.4)	91.4 (85.7 to 95.3)		
Anti-Hep B ≥100 mIU/mL (N=152, 151)	47.4 (39.2 to 55.6)	51 (42.7 to 59.2)		
Anti-PRP ≥0.15 ug/mL (N=151, 150)	86.8 (80.3 to 91.7)	77.3 (69.8 to 83.8)		
Anti-PRP ≥1.0 ug/mL (N=151, 150)	46.4 (38.2 to 54.6)	47.3 (39.1 to 55.6)		
Anti-PT ≥LLOQ (N=151, 148)	100 (97.6 to 100)	99.3 (96.3 to 100)		
Anti-PT ≥2xLLOQ (N=151, 148)	99.3 (96.4 to 100)	99.3 (96.3 to 100)		
Anti-FHA ≥LLOQ (N=151, 149)	100 (97.6 to 100)	100 (97.6 to 100)		
Anti-FHA ≥2xLLOQ (N=151, 149)	100 (97.6 to 100)	100 (97.6 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Booster - Antibody persistence # Geometric Mean Titers (GMTs) or

Concentrations (GMCs) of antibodies to all Hexavalent vaccine antigens at 12 months of age, before Hexavalent vaccine booster dose

End point title	Booster - Antibody persistence # Geometric Mean Titers (GMTs) or Concentrations (GMCs) of antibodies to all Hexavalent vaccine antigens at 12 months of age, before Hexavalent vaccine booster dose

End point description:

Antibody titers or concentrations were measured for Diphtheria (D) by MIT (IU/mL), for Tetanus (T) by ELISA (IU/mL), for Poliovirus (IPV) types 1, 2, and 3 by MIT (1/dil), for Hepatitis B (Hep B) by ECi (mIU/mL), for Haemophilus influenzae type b (PRP) by Farr type RIA (ug/mL), and for Pertussis antigens (PT & FHA) by ELISA (EU/mL).
Analysis was done on the Persistence Analysis Set.

End point type	Secondary

End point timeframe:

On Day 0 of the Booster period, before Hexavalent vaccine booster dose (pre-booster).

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	151		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-D GMC (N=151, 150)	0.08 (0.06 to 0.09)	0.1 (0.08 to 0.12)		
Anti-T GMC (N=151, 150)	0.61 (0.55 to 0.68)	0.34 (0.29 to 0.39)		
Anti-IPV1 GMT (N=151, 150)	26.7 (20.8 to 34.27)	39.4 (30.4 to 51.07)		
Anti-IPV2 GMT (N=151, 150)	17.67 (13.31 to 23.44)	26.48 (19.83 to 35.35)		
Anti-IPV3 GMT (N=150, 148)	42.44 (32 to 56.27)	73.16 (55.37 to 96.67)		
Anti-Hep B GMC (N=152, 151)	76.58 (59.77 to 98.12)	95.78 (74.89 to 122.5)		
Anti-PRP GMC (N=151, 150)	0.81 (0.64 to 1.04)	0.62 (0.47 to 0.82)		
Anti-PT GMC (N=151, 148)	14.36 (12.77 to 16.16)	16.43 (14.59 to 18.5)		
Anti-FHA GMC (N=151, 149)	30.24 (26.82 to 34.09)	36.46 (32.66 to 40.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Booster # Percentage of subjects reporting solicited injection-site or systemic reactions after vaccination after Hexavalent or MenACWY vaccines, administered concomitantly or separately

End point title	Booster # Percentage of subjects reporting solicited injection-

	site or systemic reactions after vaccination after Hexavalent or MenACWY vaccines, administered concomitantly or separately

End point description:

Solicited Injection Site Reactions (ISRs: Erythema, Pain, Swelling, and extensive swelling of vaccinated limb (extensive swelling of vaccinated limb for Hexavalent vaccine only)) and solicited systemic reactions (Crying, Decreased appetite, Irritability, Pyrexia, Somnolence, and Vomiting) within 7 days after Hexavalent or MenACWY vaccines, administered concomitantly or separately.
Solicited reactions were always considered as related to vaccines.
The percentage of subjects presenting at least once the considered events after any vaccination is reported hereafter.
Analysis was done on the Safety Analysis Set.

End point type	Secondary

End point timeframe:

Day 0 up to 7 days following Hexavalent or MenACWY vaccines, administered concomitantly or separately.

End point values	Hexavalent vaccine co-administered with MenACWY vaccine	Hexavalent vaccine only	MenACWY vaccine only	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	103	105	103	
Units: Percentage of subjects				
number (confidence interval 95%)				
Solicited reaction any dose	93.2 (86.5 to 97.2)	91.4 (84.4 to 96)	77.7 (68.4 to 85.3)	
Solicited ISR	68.9 (59.1 to 77.7)	60 (50 to 69.4)	32 (23.2 to 42)	
Solicited ISR after Hexavalent vaccine	66 (56 to 75.1)	60 (50 to 69.4)	0 (0 to 0)	
Erythema after Hexavalent vaccine	35.9 (26.7 to 46)	26.7 (18.5 to 36.2)	0 (0 to 0)	
Pain after Hexavalent vaccine	57.3 (47.2 to 67)	50.5 (40.5 to 60.4)	0 (0 to 0)	
Swelling after Hexavalent vaccine	25.2 (17.2 to 34.8)	21 (13.6 to 30)	0 (0 to 0)	
Solicited ISR after MenACWY vaccine	47.6 (37.6 to 57.6)	0 (0 to 0)	32 (23.2 to 42)	
Erythema after MenACWY vaccine	16.5 (9.9 to 25.1)	0 (0 to 0)	15.5 (9.1 to 24)	
Pain after MenACWY vaccine	46.6 (36.7 to 56.7)	0 (0 to 0)	17.5 (10.7 to 26.2)	
Swelling after MenACWY vaccine	8.7 (4.1 to 15.9)	0 (0 to 0)	5.8 (2.2 to 12.2)	
Solicited systemic reaction	88.3 (80.5 to 93.8)	85.7 (77.5 to 91.8)	72.8 (63.2 to 81.1)	
Crying	50.5 (40.5 to 60.5)	48.6 (38.7 to 58.5)	30.1 (21.5 to 39.9)	
Decreased appetite	48.5 (38.6 to 58.6)	34.3 (25.3 to 44.2)	30.1 (21.5 to 39.9)	
Irritability	76.7 (67.3 to 84.5)	71.4 (61.8 to 79.8)	48.5 (38.6 to 58.6)	
Pyrexia	30.1 (21.5 to 39.9)	35.2 (26.2 to 45.2)	10.7 (5.5 to 18.3)	
Somnolence	52.4 (42.4 to 62.4)	42.9 (33.2 to 52.9)	32 (23.2 to 42)	
Vomiting	19.4 (12.3 to 28.4)	9.5 (4.7 to 16.8)	11.7 (6.2 to 19.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From D0 to D30 after each vaccination: unsolicited adverse events (AEs).
From the 1st vaccination to the last visit of each period: serious AEs (SAEs) & deaths.
From the end of Primary Series to Booster: related SAEs, deaths & AEs of special interest.

Adverse event reporting additional description:

Analysis of AEs was done on the Safety Set, i.e., all subjects who received at least 1 dose of the study vaccines and who had safety follow-up data.
Unsolicited non-serious systemic AEs (vaccine-related or not) with incidence ≥5% in at least 1 group are presented hereafter.
1 SAE (Pyrexia during Primary Series) was assessed as vaccine-related.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Primary Series # Hexavalent vaccine co-administered with MenC

Reporting group description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with 1 dose each at 2, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.

Reporting group title	Primary Series # Hexavalent vaccine without MenC

Reporting group description:

Subjects received 3 doses of Hexavalent vaccine with 1 dose each at 2, 3, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.

Reporting group title	Booster # MenACWY vaccine only

Reporting group description:

Subjects from the Primary Series period received 1 dose of MenACWY vaccine at approximately 12 months of age.

Reporting group title	Booster # Hexavalent vaccine co-administered with MenACWY

Reporting group description:

Subjects from the Primary Series period received 1 booster dose of Hexavalent vaccine co-administered with 1 dose of MenACWY vaccine at approximately 12 months of age.
Subjects received also routine vaccination: 1 dose of Prevenar 13 ± 1 optional dose of M-MRvaxPRO at approximately 13 months of age.

Reporting group title	Booster # Hexavalent vaccine only

Reporting group description:

Subjects from the Primary Series period received 1 booster dose of Hexavalent vaccine at approximately 12 months of age.
Subjects received also routine vaccination: 1 dose of MenC vaccine + 1 dose of Prevenar 13 ± 1 optional dose of M-M-RvaxPRO at approximately 13 months of age.

Reporting group title	Booster # MenACWY followed by Hexavalent vaccine 1 month later

Reporting group description:

Subjects from the Primary Series period received 1 dose of MenACWY vaccine at approximately 12 months of age.
Subjects received also 1 booster dose of Hexavalent vaccine + 1 dose of Prevenar 13 ± 1 optional dose of M-M-RvaxPRO at approximately 13 months of age.

Serious adverse events	Primary Series # Hexavalent vaccine co-administered with MenC	Primary Series # Hexavalent vaccine without MenC	Booster # MenACWY vaccine only
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 174 (2.87%)	2 / 176 (1.14%)	1 / 103 (0.97%)
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)			
Skin neoplasm bleeding			
subjects affected / exposed	0 / 174 (0.00%)	1 / 176 (0.57%)	0 / 103 (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	Additional description: Severe transient (1 day) SAE occurring concomitantly with Pneumonia respiratory syncytial viral infection 24 days after MenACWY dose in "Booster # MenACWY vaccine only" group; assessed as AE of SpeciaI Interest and not vaccine-related.		
subjects affected / exposed	0 / 174 (0.00%)	0 / 176 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyporesponsive to stimuli	Additional description: Transient (1 day) SAE occurring 170 days after the 3rd dose of the Primary Series schedule and prior to the booster dose in 1 subject of the "Booster # MenACWY vaccine only" group. The AE was assessed as not vaccine-related.		
subjects affected / exposed	0 / 174 (0.00%)	0 / 176 (0.00%)	1 / 103 (0.97%)
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			
Pyrexia			
subjects affected / exposed	1 / 174 (0.57%)	0 / 176 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 176 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 174 (0.00%)	1 / 176 (0.57%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 174 (0.57%)	0 / 176 (0.00%)	0 / 103 (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
Urinary tract infection			
subjects affected / exposed	1 / 174 (0.57%)	0 / 176 (0.00%)	0 / 103 (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
Sepsis			
subjects affected / exposed	0 / 174 (0.00%)	0 / 176 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 174 (0.00%)	0 / 176 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis	Additional description: Severe SAE occurring 115 days after the 3rd dose of the Primary Series schedule and prior to the booster dose in "Primary Series # Hexavalent vaccine co-administered with MenC" group, lasting 42 days; assessed as not vaccine-related.		
subjects affected / exposed	1 / 174 (0.57%)	0 / 176 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Booster # Hexavalent vaccine co-administered with MenACWY	Booster # Hexavalent vaccine only	Booster # MenACWY followed by Hexavalent vaccine 1 month later
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 103 (0.97%)	1 / 105 (0.95%)	0 / 103 (0.00%)
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)			
Skin neoplasm bleeding			

subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion	Additional description: Severe transient (1 day) SAE occurring concomitantly with Pneumonia respiratory syncytial viral infection 24 days after MenACWY dose in "Booster # MenACWY vaccine only" group; assessed as AE of SpeciaI Interest and not vaccine-related.		
subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyporesponsive to stimuli	Additional description: Transient (1 day) SAE occurring 170 days after the 3rd dose of the Primary Series schedule and prior to the booster dose in 1 subject of the "Booster # MenACWY vaccine only" group. The AE was assessed as not vaccine-related.		
subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 103 (0.00%)	1 / 105 (0.95%)	0 / 103 (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
Urinary tract infection			

subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 103 (0.97%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis	Additional description: Severe SAE occurring 115 days after the 3rd dose of the Primary Series schedule and prior to the booster dose in "Primary Series # Hexavalent vaccine co-administered with MenC" group, lasting 42 days; assessed as not vaccine-related.		
subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Primary Series # Hexavalent vaccine co-administered with MenC	Primary Series # Hexavalent vaccine without MenC	Booster # MenACWY vaccine only
Total subjects affected by non-serious adverse events			
subjects affected / exposed	105 / 174 (60.34%)	109 / 176 (61.93%)	60 / 103 (58.25%)
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	9 / 174 (5.17%)	7 / 176 (3.98%)	0 / 103 (0.00%)
occurrences (all)	11	7	0
Injection site induration			
subjects affected / exposed	14 / 174 (8.05%)	9 / 176 (5.11%)	1 / 103 (0.97%)
occurrences (all)	25	10	1
Pyrexia			
subjects affected / exposed	5 / 174 (2.87%)	10 / 176 (5.68%)	5 / 103 (4.85%)
occurrences (all)	6	11	5
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	14 / 174 (8.05%)	12 / 176 (6.82%)	6 / 103 (5.83%)
occurrences (all)	17	15	6
Flatulence			
subjects affected / exposed	7 / 174 (4.02%)	9 / 176 (5.11%)	0 / 103 (0.00%)
occurrences (all)	7	12	0
Teething			
subjects affected / exposed	9 / 174 (5.17%)	5 / 176 (2.84%)	10 / 103 (9.71%)
occurrences (all)	12	5	10
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 174 (5.17%)	9 / 176 (5.11%)	1 / 103 (0.97%)
occurrences (all)	12	9	1
Infections and infestations			
Rhinitis			
subjects affected / exposed	24 / 174 (13.79%)	26 / 176 (14.77%)	7 / 103 (6.80%)
occurrences (all)	34	32	7
Upper respiratory tract infection			
subjects affected / exposed	25 / 174 (14.37%)	27 / 176 (15.34%)	15 / 103 (14.56%)
occurrences (all)	29	27	15
Otitis media			
subjects affected / exposed	4 / 174 (2.30%)	5 / 176 (2.84%)	12 / 103 (11.65%)
occurrences (all)	4	5	13

Non-serious adverse events	Booster # Hexavalent vaccine co-administered with MenACWY	Booster # Hexavalent vaccine only	Booster # MenACWY followed by Hexavalent vaccine 1 month later
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 103 (53.40%)	51 / 105 (48.57%)	45 / 103 (43.69%)
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	6 / 103 (5.83%)	2 / 105 (1.90%)	1 / 103 (0.97%)
occurrences (all)	7	2	1
Injection site induration			
subjects affected / exposed	3 / 103 (2.91%)	2 / 105 (1.90%)	1 / 103 (0.97%)
occurrences (all)	3	2	1
Pyrexia			

subjects affected / exposed	5 / 103 (4.85%)	6 / 105 (5.71%)	24 / 103 (23.30%)
occurrences (all)	5	6	26
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 103 (1.94%)	3 / 105 (2.86%)	1 / 103 (0.97%)
occurrences (all)	2	3	1
Flatulence			
subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Teething			
subjects affected / exposed	5 / 103 (4.85%)	5 / 105 (4.76%)	1 / 103 (0.97%)
occurrences (all)	5	8	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 103 (0.00%)	0 / 105 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Infections and infestations			
Rhinitis			
subjects affected / exposed	5 / 103 (4.85%)	5 / 105 (4.76%)	3 / 103 (2.91%)
occurrences (all)	5	5	3
Upper respiratory tract infection			
subjects affected / exposed	16 / 103 (15.53%)	14 / 105 (13.33%)	3 / 103 (2.91%)
occurrences (all)	18	14	3
Otitis media			
subjects affected / exposed	8 / 103 (7.77%)	8 / 105 (7.62%)	7 / 103 (6.80%)
occurrences (all)	8	8	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 November 2013	Amendment 1 to Protocol (leading to Version 2.0) was produced to provide details regarding the booster vaccination at 12 to 13 months of age with Hexavalent vaccine, 13-valent pneumococcal polysaccharide conjugate vaccine and meningococcal C containing vaccine.

Notes:

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 reported

Notes: