Clinical trial results:
A Randomized Study to Describe the Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine Administered Concomitantly with Routine Pediatric Vaccines in Healthy Infants and Toddlers

Summary

EudraCT number	2019-004459-35
Trial protocol	Outside EU/EEA
Global end of trial date	16 March 2023

Results information

Result version number	v1
This version publication date	29 September 2023
First version publication date	29 September 2023

Trial information

Trial identification

Sponsor protocol code	MET41

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03673462
WHO universal trial number (UTN)	U1111-1183-6261

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	Discovery Drive, Swiftwater, Pennsylvania, United States, 18370-0187
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001930-PIP01-16
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety profile of Meningococcal Polysaccharide (Serogroups A, C, Y, and W) Tetanus Toxoid (MenACYW) Conjugate vaccine and Meningococcal (Groups A, C, Y and W 135) Oligosaccharide Diphtheria CRM197 Conjugate Vaccine (MENVEO®) when administered concomitantly with routine pediatric vaccines in healthy infants and toddlers.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 2751
Country: Number of subjects enrolled	Puerto Rico: 46
Worldwide total number of subjects	2797
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	2797
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 was conducted at 75 sites in Puerto Rico and the United States from 17 September 2018 to 16 March 2023.

Pre-assignment

Screening details:

A total of 2797 subjects were enrolled and randomised in the study.

Period 1

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

Blinding implementation details:

The meningococcal vaccines (Group 1: MenACYW Conjugate Vaccine and Group 2: MENVEO®) used in the study have different appearances and preparation methods. Hence, the study followed a modified double blind design i.e., with the exception of the personnel administering the vaccine, everyone involved in the study (subjects, care provider, investigator, safety outcomes assessor, Sponsor) was blinded to avoid any bias.

Arms

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

Arm description:

Healthy infants aged greater than equal to (>=) 42 to less than equal to (<=) 89 days (at the time of enrollment) received MenACYW Conjugate Vaccine at the age of Months 2, 4, 6, and 12 along with Pentacel® (DTaP-IPV/Hib) at 2, 4, and 6 months of age; PREVNAR 13® (pneumococcal 13-valent conjugate vaccine; PCV13) at 2, 4, 6, and 12 months of age; RotaTeq® (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; and M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 months of age.

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

Dosage and administration details:

Subjects received MenACYW Conjugate vaccine at 2, 4, 6, and 12 months of age.

Investigational medicinal product name	Rotavirus Vaccine
Investigational medicinal product code	
Other name	RotaTeq®
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects received RotaTeq® vaccine at 2, 4, and 6 months of age.

Investigational medicinal product name	Hepatitis B Vaccine
Investigational medicinal product code	
Other name	ENGERIX-B®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:	
Subjects received ENGERIX-B® vaccine at 2 and 6 months of age.	
Investigational medicinal product name	Pneumococcal 13-valent Conjugate Vaccine
Investigational medicinal product code	
Other name	PREVNAR 13®, PCV13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received PREVNAR 13® vaccine at 2, 4, 6, and 12 months of age.	
Investigational medicinal product name	Measles, Mumps, and Rubella Virus Vaccine
Investigational medicinal product code	
Other name	M-M-R® II
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received M-M-R® II vaccine at 12 months of age.	
Investigational medicinal product name	Varicella Virus Vaccine
Investigational medicinal product code	
Other name	VARIVAX®
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received VARIVAX® vaccine at 12 months of age.	
Investigational medicinal product name	Diphtheria and Tetanus Toxoids and Acellular Pertussis Poliovirus and Haemophilus b Conjugate Vaccine
Investigational medicinal product code	
Other name	Pentacel®
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received Pentacel® vaccine at 2, 4, and 6 months of age.	
Arm title	Group 2: MENVEO® Vaccine

Arm description:

Healthy infants aged >= 42 to <= 89 days (at the time of enrollment) received MENVEO® Conjugate Vaccine at the age of Months 2, 4, 6, and 12 along with Pentacel® (DTaP-IPV/Hib) at 2, 4, and 6 months of age; PREVNAR 13® (PCV13) at 2, 4, 6, and 12 months of age; RotaTeq® (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; and M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 months of age.

Arm type	Active comparator
Investigational medicinal product name	Meningococcal (Groups A, C, Y and W 135) Oligosaccharide Diphtheria CRM197 Conjugate Vaccine
Investigational medicinal product code	
Other name	MENVEO®
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received MENVEO® vaccine at 2, 4, 6, and 12 months of age.	
Investigational medicinal product name	Diphtheria and Tetanus Toxoids and Acellular Pertussis Poliovirus and Haemophilus b Conjugate Vaccine
Investigational medicinal product code	
Other name	Pentacel®
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details: Subjects received Pentacel® vaccine at 2, 4 and 6 months of age.	
Investigational medicinal product name	Pneumococcal 13-valent Conjugate Vaccine
Investigational medicinal product code	
Other name	PREVNAR 13®, PCV13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: Subjects received PREVNAR 13® vaccine at 2, 4, 6, and 12 months of age.	
Investigational medicinal product name	Varicella Virus Vaccine
Investigational medicinal product code	
Other name	VARIVAX®
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use
Dosage and administration details: Subjects received VARIVAX® at 12 months of age.	
Investigational medicinal product name	Hepatitis B Vaccine
Investigational medicinal product code	
Other name	ENGERIX-B®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: Subjects received ENGERIX-B® vaccine at 2 and 6 months of age.	
Investigational medicinal product name	Measles, Mumps, and Rubella Virus Vaccine
Investigational medicinal product code	
Other name	M-M-R® II
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: Subjects received M-M-R® vaccine II at 12 months of age.	
Investigational medicinal product name	Rotavirus Vaccine
Investigational medicinal product code	
Other name	RotaTeq®
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details: Subjects received RotaTeq® vaccine at 2, 4, and 6 months of age.	

Number of subjects in period 1	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine
Started	2099	698
Safety Analysis Set (SafAS)	2080	697
Vaccinated at 2 Months	2080	695
Vaccinated at 4 Months	2005	663
Vaccinated at 6 Months	1951	648
Vaccinated at 12 Months	1838	623

Completed	1799	611
Not completed	300	87
Adverse events	11	1
Withdrawal by Parent/Guardian	162	56
Lost to follow-up	102	19
Protocol deviation	25	11

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: MenACYW Conjugate Vaccine
Reporting group description:	
Healthy infants aged greater than equal to (>=) 42 to less than equal to (<=) 89 days (at the time of enrollment) received MenACYW Conjugate Vaccine at the age of Months 2, 4, 6, and 12 along with Pentacel® (DTaP-IPV/Hib) at 2, 4, and 6 months of age; PREVNAR 13® (pneumococcal 13-valent conjugate vaccine; PCV13) at 2, 4, 6, and 12 months of age; RotaTeq® (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; and M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 months of age.	
Reporting group title	Group 2: MENVEO® Vaccine
Reporting group description:	
Healthy infants aged >= 42 to <= 89 days (at the time of enrollment) received MENVEO® Conjugate Vaccine at the age of Months 2, 4, 6, and 12 along with Pentacel® (DTaP-IPV/Hib) at 2, 4, and 6 months of age; PREVNAR 13® (PCV13) at 2, 4, 6, and 12 months of age; RotaTeq® (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; and M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 months of age.	

Reporting group values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine	Total
Number of subjects	2099	698	2797
Age categorical Units: Subjects			
Age continuous Units: days			
arithmetic mean	64.7	64.9	
standard deviation	± 6.63	± 6.77	-
Gender categorical Units: Subjects			
Female	998	336	1334
Male	1101	362	1463
Race Units: Subjects			
American Indian or Alaska Native	8	0	8
Asian	28	12	40
Black or African American	210	67	277
Native Hawaiian or Other Pacific Islander	10	5	15
White	1719	580	2299
Mixed Origin	102	31	133
Not Reported	10	3	13
Unknown	12	0	12

End points

End points reporting groups

Reporting group title	Group 1: MenACYW Conjugate Vaccine

Reporting group description:

Healthy infants aged greater than equal to (>=) 42 to less than equal to (<=) 89 days (at the time of enrollment) received MenACYW Conjugate Vaccine at the age of Months 2, 4, 6, and 12 along with Pentacel® (DTaP-IPV/Hib) at 2, 4, and 6 months of age; PREVNAR 13® (pneumococcal 13-valent conjugate vaccine; PCV13) at 2, 4, 6, and 12 months of age; RotaTeq® (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; and M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 months of age.

Reporting group title	Group 2: MENVEO® Vaccine

Reporting group description:

Healthy infants aged >= 42 to <= 89 days (at the time of enrollment) received MENVEO® Conjugate Vaccine at the age of Months 2, 4, 6, and 12 along with Pentacel® (DTaP-IPV/Hib) at 2, 4, and 6 months of age; PREVNAR 13® (PCV13) at 2, 4, 6, and 12 months of age; RotaTeq® (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; and M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 months of age.

Primary: Number of Subjects With Immediate Unsolicited Systemic Adverse Events (AEs)

End point title	Number of Subjects With Immediate Unsolicited Systemic Adverse Events (AEs)[1]

End point description:

An AE was any untoward medical occurrence in a clinical investigation subject administered a medicinal product and which did not have any casual relationship with the treatment. An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the case report book (CRB) in terms of diagnosis and/or onset window post-vaccination. Immediate adverse events are unsolicited systemic adverse events occurring in the 30 minutes after injection. Reported AEs for each arm were presented as pre-specified in protocol. Analysis was performed on Safety Analysis Set (SafAS) that included all subjects who have received at least one dose of the study vaccines and have any safety data available.

End point type	Primary

End point timeframe:

Within 30 minutes post-any vaccination

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2080	697		
Units: subjects	7	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Solicited Injection Site Reactions

End point title	Number of Subjects With Solicited Injection Site Reactions[2]

End point description:

A solicited reaction (SR) was an "expected" adverse reaction (AR) (sign or symptom) observed and reported under the conditions (nature and onset) pre-listed in the protocol and CRB and considered as related to the product administered. Solicited injection site reactions included Injection site tenderness, Injection site erythema, and Injection site swelling and were planned to be collected and reported for each vaccine separately; and not planned to be collected for Rotavirus vaccine as the vaccine was administered orally, and no injection site reactions were expected to occur. Reported AEs for each arm were presented as pre-specified in protocol. Analysis was performed on SafAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Within 7 days post any vaccination

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2021	676		
Units: subjects				
MenACYW or MENVEO: Tenderness (n = 2021, 676)	1501	499		
MenACYW or MENVEO: Erythema (n = 2021, 676)	826	257		
MenACYW or MENVEO: Swelling (n = 2019, 676)	557	170		
PENTACEL: Tenderness (n = 2017, 676)	1388	456		
PENTACEL: Erythema (n = 2017, 676)	770	255		
PENTACEL: Swelling (n = 2017, 676)	562	178		
PREVNAR 13: Tenderness (n = 2018, 676)	1464	496		
PREVNAR 13: Erythema (n = 2017,676)	889	298		
PREVNAR 13: Swelling (n = 2017, 676)	656	206		
ENGERIX-B: Tenderness (n= 2013, 674)	1199	395		
ENGERIX-B: Erythema (n = 2013, 675)	539	192		
ENGERIX-B: Swelling (n = 2013, 675)	347	115		
M-M-R II: Tenderness (n = 1756, 588)	786	268		
M-M-R II: Erythema (n = 1755, 588)	409	130		
M-M-R II: Swelling (n = 1754, 588)	221	71		
VARIVAX: Tenderness (n = 1758, 588)	724	252		
VARIVAX: Erythema (n = 1757, 588)	364	129		
VARIVAX: Swelling (n = 1757,588)	208	70		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Solicited Systemic Reactions

End point title	Number of Subjects With Solicited Systemic Reactions[3]

End point description:

A SR was an "expected" AR (sign or symptom) observed and reported under the conditions (nature and onset) pre-listed in the protocol and CRB and considered as related to the product administered. Solicited systemic reactions included fever, vomiting, crying abnormal, drowsiness, appetite loss, and irritability. Reported AEs for each arm were presented as pre-specified in protocol. Analysis was performed on SafAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Within 7 days post-any vaccination

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2019	676		
Units: subjects				
Fever (n = 2002, 671)	724	219		
Vomiting (n = 2018, 676)	542	163		
Crying abnormal (n = 2019, 676)	1437	478		
Drowsiness (n = 2017, 676)	1430	475		
Appetite lost (n = 2018, 676)	1014	350		
Irritability (n = 2018, 676)	1604	536		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Unsolicited Adverse Events

End point title	Number of Subjects With Unsolicited Adverse Events[4]

End point description:

An AE was any untoward medical occurrence in a clinical investigation subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment. An unsolicited AE was an observed AE that does not fulfill the conditions prelisted in the CRB in terms of diagnosis and/or onset window post-vaccination. Unsolicited AEs includes both serious adverse events (SAEs) and non-serious unsolicited AEs. Reported AEs for each arm were presented as pre-specified in protocol. Analysis was performed on SafAS.

End point type	Primary

End point timeframe:

Within 30 days post any vaccination

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2080	697		
Units: subjects	1344	432		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Serious Adverse Events (SAEs) and Adverse Event of Special Interest (AESIs)

End point title	Number of Subjects With Serious Adverse Events (SAEs) and Adverse Event of Special Interest (AESIs)[5]

End point description:

A SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. An AESI (serious or non-serious) was defined as one of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor was appropriate. Reported AEs for each arm were presented as pre-specified in protocol. Analysis was performed on SafAS.

End point type	Primary

End point timeframe:

From day of first vaccination (i.e., at the age of 2 months) up to 6 months after last vaccination (i.e., up to the age of 18 months)

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2080	697		
Units: subjects				
SAE	108	21		
AESI	19	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Medically-attended Adverse Event (MAAEs)

End point title	Number of Subjects With Medically-attended Adverse Event (MAAEs)[6]

End point description:

An MAAE was defined as a new onset of a condition that prompts the subject or subject's parent/guardian to seek unplanned medical advice at a health care provider's office or Emergency Department. Reported AEs for each arm were presented as pre-specified in protocol. Analysis was performed on SafAS.

End point type	Primary

End point timeframe:

From day of first vaccination (i.e., at the age of 2 months) up to 6 months after last vaccination (i.e., up to the age of 18 months)

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2080	697		
Units: subjects	1581	526		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited AE: within 30 days post-any vaccination. SR: within 7 days post-any vaccination. SAE: from day of first vaccination (i.e., at the age of 2 months) up to 6 months post last vaccination (i.e., up to the age of 18 months)

Adverse event reporting additional description:

SR: "expected" AR observed & reported under conditions pre-listed in protocol. Unsolicited AE: AE that does not fulfill conditions prelisted in CRB. SafAS. Reported AEs for each arm presented as pre-specified. In AE section, SR fever, crying abnormal, drowsiness & appetite lost are reported under Pyrexia, crying, somnolence & decreased appetite.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Group 1: MenACYW Conjugate Vaccine

Reporting group description:

Healthy infants aged >= 42 to <= 89 days (at the time of enrollment) received MenACYW Conjugate Vaccine at the age of Months 2, 4, 6, and 12 along with Pentacel® (DTaP-IPV/Hib) at 2, 4, and 6 months of age; PREVNAR 13® (pneumococcal 13-valent conjugate vaccine; PCV13) at 2, 4, 6, and 12 months of age; RotaTeq® (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; and M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 months of age.

Reporting group title	Group 2: MENVEO®

Reporting group description:

Healthy infants aged >= 42 to <= 89 days (at the time of enrollment) received MENVEO® Conjugate Vaccine at the age of Months 2, 4, 6, and 12 along with Pentacel® (DTaP-IPV//Hib) at 2, 4, and 6 months of age; PREVNAR 13® (PCV13) at 2, 4, 6, and 12 months of age; RotaTeq® (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; and M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 months of age.

Serious adverse events	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO®	
Total subjects affected by serious adverse events			
subjects affected / exposed	108 / 2080 (5.19%)	21 / 697 (3.01%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenocortical Carcinoma			
subjects affected / exposed	0 / 2080 (0.00%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Developmental Delay			

subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 2080 (0.10%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden Infant Death Syndrome			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Anaphylactic Reaction			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Respiratory Failure			
subjects affected / exposed	1 / 2080 (0.05%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Distress			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bronchial Hyperreactivity			
subjects affected / exposed	1 / 2080 (0.05%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Stereotypy			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental Status Changes			
subjects affected / exposed	2 / 2080 (0.10%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental Exposure To Product			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural Haematoma			
subjects affected / exposed	2 / 2080 (0.10%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			

subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Fractures			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal Burn			
subjects affected / exposed	2 / 2080 (0.10%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural Haemorrhage			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull Fracture			
subjects affected / exposed	2 / 2080 (0.10%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head Injury			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Congenital, familial and genetic disorders			
Laryngomalacia			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital Absence Of Bile Ducts			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alagille Syndrome			

subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniosynostosis			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Unresponsive To Stimuli			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Seizure Like Phenomena			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	3 / 2080 (0.14%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss Of Consciousness			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotonia			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage Intracranial			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fontanelle Bulging			

subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	2 / 2080 (0.10%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Convulsion			
subjects affected / exposed	15 / 2080 (0.72%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 16	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	1 / 2080 (0.05%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Incarcerated Inguinal Hernia			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising Oesophagitis			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sandifer's Syndrome			

subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	3 / 2080 (0.14%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Eosinophilic			
subjects affected / exposed	0 / 2080 (0.00%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowel Movement Irregularity			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acinetobacter Infection			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Adenoviral Upper Respiratory Infection			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	9 / 2080 (0.43%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis Orbital			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup Infectious			
subjects affected / exposed	0 / 2080 (0.00%)	2 / 697 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr Virus Infection			
subjects affected / exposed	0 / 2080 (0.00%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 2080 (0.05%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Viral			
subjects affected / exposed	4 / 2080 (0.19%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-Foot-And-Mouth Disease			

subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus Bronchiolitis			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae Virus Infection			
subjects affected / exposed	0 / 2080 (0.00%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal Abscess			
subjects affected / exposed	0 / 2080 (0.00%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal Abscess			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 2080 (0.05%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	1 / 2080 (0.05%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	7 / 2080 (0.34%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Syncytial Virus Infection			
subjects affected / exposed	11 / 2080 (0.53%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 11	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus Infection			
subjects affected / exposed	2 / 2080 (0.10%)	2 / 697 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic Shock			
subjects affected / exposed	0 / 2080 (0.00%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal Scalded Skin Syndrome			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 2080 (0.05%)	1 / 697 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			

subjects affected / exposed	3 / 2080 (0.14%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Infection			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	5 / 2080 (0.24%)	3 / 697 (0.43%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure To Thrive			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic Acidosis			
subjects affected / exposed	1 / 2080 (0.05%)	0 / 697 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO®	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1850 / 2080 (88.94%)	629 / 697 (90.24%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	1430 / 2080 (68.75%)	475 / 697 (68.15%)	
occurrences (all)	3459	1127	
General disorders and administration site conditions			
Crying			
subjects affected / exposed	1437 / 2080 (69.09%)	478 / 697 (68.58%)	
occurrences (all)	3323	1123	
Injection Site Bruising			
subjects affected / exposed	293 / 2080 (14.09%)	96 / 697 (13.77%)	
occurrences (all)	596	187	
Injection Site Pain			
subjects affected / exposed	1619 / 2080 (77.84%)	538 / 697 (77.19%)	
occurrences (all)	13051	4339	
Injection Site Swelling			
subjects affected / exposed	870 / 2080 (41.83%)	281 / 697 (40.32%)	
occurrences (all)	3789	1195	
Pyrexia			
subjects affected / exposed	724 / 2080 (34.81%)	219 / 697 (31.42%)	
occurrences (all)	1072	306	
Injection Site Erythema			
subjects affected / exposed	1129 / 2080 (54.28%)	379 / 697 (54.38%)	
occurrences (all)	6149	2023	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	542 / 2080 (26.06%)	163 / 697 (23.39%)	
occurrences (all)	758	236	
Psychiatric disorders			
Irritability			
subjects affected / exposed	1604 / 2080 (77.12%)	536 / 697 (76.90%)	
occurrences (all)	4299	1466	

Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1014 / 2080 (48.75%)	350 / 697 (50.22%)	
occurrences (all)	1850	609	

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

None reported