Clinical trial results:
A Phase 3, Open-Label, Randomized, Parallel-Group, Multi-Center Study to Evaluate the Safety and Immunogenicity of Novartis Meningococcal ACWY Conjugate Vaccine When Administered with Routine Infant Vaccinations to Healthy Infants.

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

Summary

EudraCT number	2014-004605-33
Trial protocol	Outside EU/EEA
Global end of trial date	13 November 2009

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	31 January 2015
Version creation reason	• Correction of full data set re-QC study needed because of EudraCT system glitch and updates to results are required.

Trial information

Trial identification

Sponsor protocol code	V59P14

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00474526
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics, Inc
Sponsor organisation address	350 Massachusetts Ave, Cambridge, United States, 02139
Public contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000032-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 August 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 November 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity against Neisseria meningitidis serogroups A, C, W and Y; after four doses of MenACWY-CRM at 2, 4, and 6 and 12 months of age.

Protection of trial subjects:

This trial was performed with the ethical principles that have their origin in the Declaration of Helsinki, that are consistent with Good Clinical Practice (GCP) according to International Conference on Harmonisation (ICH) guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 March 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1530
Country: Number of subjects enrolled	Colombia: 1507
Country: Number of subjects enrolled	United States: 1508
Worldwide total number of subjects	4545
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)	4545
Children (2-11 years)	0
Adolescents (12-17 years)	0

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

Subject disposition

Recruitment

Recruitment details:

All enrolled subjects were included in the study

Pre-assignment

Screening details:

Approximately 4500 infants 2 months of age (55 – 89 days inclusive) were planned to be enrolled and randomized open-label to treatment in a 2:1 ratio, (MenACWY +
routine infant vaccines: routine infant vaccines only), stratified by study site, and geographic region (also in a 2:1 ratio, Latin America: US).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	US1A (MenACWY-CRM + Infant Vaccines)

Arm description:

US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccine. These infants received a fourth dose of MenACWY concomitantly with pneumococcal, HAV, and MMR-V vaccines at 12 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	US1B (MenACWY-CRM + Infant Vaccines)

Arm description:

US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines. These infants received pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a fourth dose of MenACWY at 13 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	US2 (Infant Vaccines Only)

Arm description:

US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	US3 (MenACWY-CRM + Infant Vaccines)

Arm description:

US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccine. These infants received fourth dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	US4A (Infant Vaccines Only)

Arm description:

US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	US4B (Infant Vaccines Only)

Arm description:

US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These subjects received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 13 and a second dose of MenACWY at 15 months of age.

Arm type	Experimental

Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	US4C (Infant Vaccines Only)

Arm description:

US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These subjects received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and one dose of MenACWY at 18 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA1A (MenACWY-CRM + Infant Vaccines)

Arm description:

Latin American LA infants received MenACWY at 2 and 6 months of age; and as part of routine infant vaccination schedule, received, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These subjects received a third dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA1B (MenACWY-CRM + Infant Vaccines)

Arm description:

LA infants received MenACWY at 2 and 6 months of age and as part of routine infant vaccination schedule, received, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These subjects received pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and a third dose of MenACWY at 13 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection

Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA2 (Infant Vaccines Only)

Arm description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA3A (MenACWY-CRM + Infant Vaccines)

Arm description:

LA infants received MenACWY at 2, 4 and 6 months of age; and as part of routine infant vaccination schedule received, DTaP-IPV-HBV, Hib, pneumococcal conjugate vaccine, and rotavirus vaccine. Around 12 months of age, these infants were recommended to receive pneumococcal conjugate vaccine, HAV, and MMR-V. At 16 months of age, these subjects received the fourth dose of MenACWY along with concomitant DTaP and Hib.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA3B (MenACWY-CRM + Infant Vaccines)

Arm description:

LA infants received MenACWY at 2, 4 and 6 months of age; and as part of routine infant vaccination schedule received, DTaP-IPV-HBV, Hib, pneumococcal conjugate vaccine, and rotavirus vaccine. Around 12 months of age, received pneumococcal conjugate vaccine, HAV, and MMR-V. At 16 months of age, these subjects received DTaP and Hib. At 17 months of age, these subjects received the fourth dose of MenACWY.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.

Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA4 (Infant Vaccines Only)

Arm description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, pneumococcal conjugate vaccine, and rotavirus vaccine at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and a second dose of MenACWY along with DTaP and Hib vaccines at 15 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA5 (MenACWY-CRM + Infant Vaccines)

Arm description:

LA infants received MenACWY at 2, 4 and 6 months of age,; and as part of routine infant vaccination schedule received, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines. At 12 months of age, these subjects received the fourth dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA6A (Infant Vaccines Only)

Arm description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 12 and a second dose of MenACWY at 15 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA6B (Infant Vaccines Only)

Arm description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 13 and a second dose of MenACWY at 15 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Arm title	LA6C (Infant Vaccines Only)

Arm description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 18 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 and Routine Vaccines
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml of MenACWY IM injection in the anterolateral area of the right thigh.
Routine vaccines were administered to subjects according to manufacturer instructions.

Number of subjects in period 1	US1A (MenACWY-CRM + Infant Vaccines)	US1B (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)
Started	154	166	159
Completed	121	120	110
Not completed	33	46	49
Adverse event, non-fatal	2	-	2
Death	-	-	-
Inappropriate enrollment	-	1	-
Unable to classify	1	-	-
Withdrawal by Subject	9	24	21
Lost to follow-up	8	6	13
Administrative reason	11	9	9
Protocol deviation	2	6	4

Number of subjects in period 1	US3 (MenACWY-CRM + Infant Vaccines)	US4A (Infant Vaccines Only)	US4B (Infant Vaccines Only)
Started	680	76	70
Completed	561	8	54
Not completed	119	68	16
Adverse event, non-fatal	4	2	1
Death	-	-	-
Inappropriate enrollment	1	2	-
Unable to classify	1	3	2
Withdrawal by Subject	52	38	6
Lost to follow-up	29	11	5
Administrative reason	20	9	1
Protocol deviation	12	3	1

Number of subjects in period 1	US4C (Infant Vaccines Only)	LA1A (MenACWY-CRM + Infant Vaccines)	LA1B (MenACWY-CRM + Infant Vaccines)
Started	203	151	150
Completed	178	145	144
Not completed	25	6	6
Adverse event, non-fatal	1	-	-
Death	-	-	-
Inappropriate enrollment	-	-	-
Unable to classify	-	1	-
Withdrawal by Subject	12	4	4
Lost to follow-up	8	1	-
Administrative reason	1	-	2
Protocol deviation	3	-	-

Number of subjects in period 1	LA2 (Infant Vaccines Only)	LA3A (MenACWY-CRM + Infant Vaccines)	LA3B (MenACWY-CRM + Infant Vaccines)
Started	148	151	150
Completed	121	141	139
Not completed	27	10	11
Adverse event, non-fatal	-	-	-
Death	-	-	-
Inappropriate enrollment	-	-	-
Unable to classify	3	-	-
Withdrawal by Subject	13	5	4
Lost to follow-up	6	2	4
Administrative reason	1	1	1
Protocol deviation	4	2	2

Number of subjects in period 1	LA4 (Infant Vaccines Only)	LA5 (MenACWY-CRM + Infant Vaccines)	LA6A (Infant Vaccines Only)
Started	150	1426	358
Completed	135	1270	281
Not completed	15	156	77
Adverse event, non-fatal	-	-	1
Death	-	3	-
Inappropriate enrollment	-	2	2
Unable to classify	-	20	12
Withdrawal by Subject	4	37	22
Lost to follow-up	6	74	29
Administrative reason	1	1	2
Protocol deviation	4	19	9

Number of subjects in period 1	LA6B (Infant Vaccines Only)	LA6C (Infant Vaccines Only)
Started	170	183
Completed	152	174
Not completed	18	9
Adverse event, non-fatal	1	-
Death	-	-
Inappropriate enrollment	-	-
Unable to classify	6	1
Withdrawal by Subject	1	1
Lost to follow-up	4	5
Administrative reason	-	-
Protocol deviation	6	2

Reporting groups	
Reporting group title	US1A (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccine. These infants received a fourth dose of MenACWY concomitantly with pneumococcal, HAV, and MMR-V vaccines at 12 months of age.	
Reporting group title	US1B (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines. These infants received pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a fourth dose of MenACWY at 13 months of age.	
Reporting group title	US2 (Infant Vaccines Only)
Reporting group description:	
US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age.	
Reporting group title	US3 (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccine. These infants received fourth dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months of age.	
Reporting group title	US4A (Infant Vaccines Only)
Reporting group description:	
US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age.	
Reporting group title	US4B (Infant Vaccines Only)
Reporting group description:	
US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These subjects received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 13 and a second dose of MenACWY at 15 months of age.	
Reporting group title	US4C (Infant Vaccines Only)
Reporting group description:	
US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These subjects received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and one dose of MenACWY at 18 months of age.	
Reporting group title	LA1A (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
Latin American LA infants received MenACWY at 2 and 6 months of age; and as part of routine infant vaccination schedule, received, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These subjects received a third dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months of age.	
Reporting group title	LA1B (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
LA infants received MenACWY at 2 and 6 months of age and as part of routine infant vaccination schedule, received, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These subjects received pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and a third dose of MenACWY at 13 months of age.	
Reporting group title	LA2 (Infant Vaccines Only)
Reporting group description:	
LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received one dose of	

MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age.

Reporting group title	LA3A (MenACWY-CRM + Infant Vaccines)

Reporting group description:

LA infants received MenACWY at 2, 4 and 6 months of age; and as part of routine infant vaccination schedule received, DTaP-IPV-HBV, Hib, pneumococcal conjugate vaccine, and rotavirus vaccine. Around 12 months of age, these infants were recommended to receive pneumococcal conjugate vaccine, HAV, and MMR-V. At 16 months of age, these subjects received the fourth dose of MenACWY along with concomitant DTaP and Hib.

Reporting group title	LA3B (MenACWY-CRM + Infant Vaccines)

Reporting group description:

LA infants received MenACWY at 2, 4 and 6 months of age; and as part of routine infant vaccination schedule received, DTaP-IPV-HBV, Hib, pneumococcal conjugate vaccine, and rotavirus vaccine. Around 12 months of age, received pneumococcal conjugate vaccine, HAV, and MMR-V. At 16 months of age, these subjects received DTaP and Hib. At 17 months of age, these subjects received the fourth dose of MenACWY.

Reporting group title	LA4 (Infant Vaccines Only)

Reporting group description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, pneumococcal conjugate vaccine, and rotavirus vaccine at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and a second dose of MenACWY along with DTaP and Hib vaccines at 15 months of age.

Reporting group title	LA5 (MenACWY-CRM + Infant Vaccines)

Reporting group description:

LA infants received MenACWY at 2, 4 and 6 months of age,; and as part of routine infant vaccination schedule received, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines. At 12 months of age, these subjects received the fourth dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V.

Reporting group title	LA6A (Infant Vaccines Only)

Reporting group description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 12 and a second dose of MenACWY at 15 months of age.

Reporting group title	LA6B (Infant Vaccines Only)

Reporting group description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 13 and a second dose of MenACWY at 15 months of age.

Reporting group title	LA6C (Infant Vaccines Only)

Reporting group description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 18 months of age.

Reporting group values	US1A (MenACWY-CRM + Infant Vaccines)	US1B (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)
Number of subjects	154	166	159
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0

Infants and toddlers (28 days-23 months)	154	166	159
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: days			
arithmetic mean	66.1	65.8	65.7
standard deviation	± 7.2	± 6.6	± 6.5
Gender categorical			
Units: Subjects			
Female	68	72	71
Male	86	94	88

Reporting group values	US3 (MenACWY-CRM + Infant Vaccines)	US4A (Infant Vaccines Only)	US4B (Infant Vaccines Only)
Number of subjects	680	76	70
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	680	76	70
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: days			
arithmetic mean	65	66.1	65
standard deviation	± 6	± 6.2	± 6.5
Gender categorical			
Units: Subjects			
Female	340	39	29
Male	340	37	41

Reporting group values	US4C (Infant Vaccines Only)	LA1A (MenACWY-CRM + Infant Vaccines)	LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects	203	151	150
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	203	151	150
Children (2-11 years)	0	0	0

Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: days			
arithmetic mean	65.9	68	68.6
standard deviation	± 6.5	± 7.7	± 8.9
Gender categorical			
Units: Subjects			
Female	103	79	82
Male	100	72	68

Reporting group values	LA2 (Infant Vaccines Only)	LA3A (MenACWY-CRM + Infant Vaccines)	LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects	148	151	150
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	148	151	150
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: days			
arithmetic mean	67.8	67.1	68.4
standard deviation	± 8.3	± 7.9	± 8.7
Gender categorical			
Units: Subjects			
Female	72	72	75
Male	76	79	75

Reporting group values	LA4 (Infant Vaccines Only)	LA5 (MenACWY-CRM + Infant Vaccines)	LA6A (Infant Vaccines Only)
Number of subjects	150	1426	358
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	150	1426	358
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0

85 years and over	0	0	0

Age continuous			
Units: days			
arithmetic mean	67.5	65	67.7
standard deviation	± 8	± 9.4	± 9.7
Gender categorical			
Units: Subjects			
Female	81	682	178
Male	69	744	180

Reporting group values	LA6B (Infant Vaccines Only)	LA6C (Infant Vaccines Only)	Total
Number of subjects	170	183	4545
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	170	183	4545
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: days			
arithmetic mean	59.5	65	
standard deviation	± 6.2	± 7.9	-
Gender categorical			
Units: Subjects			
Female	89	91	2223
Male	81	92	2322

End points reporting groups

Reporting group title	US1A (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccine. These infants received a fourth dose of MenACWY concomitantly with pneumococcal, HAV, and MMR-V vaccines at 12 months of age.	
Reporting group title	US1B (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines. These infants received pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a fourth dose of MenACWY at 13 months of age.	
Reporting group title	US2 (Infant Vaccines Only)
Reporting group description:	
US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age.	
Reporting group title	US3 (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccine. These infants received fourth dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months of age.	
Reporting group title	US4A (Infant Vaccines Only)
Reporting group description:	
US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age.	
Reporting group title	US4B (Infant Vaccines Only)
Reporting group description:	
US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These subjects received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 13 and a second dose of MenACWY at 15 months of age.	
Reporting group title	US4C (Infant Vaccines Only)
Reporting group description:	
US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These subjects received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and one dose of MenACWY at 18 months of age.	
Reporting group title	LA1A (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
Latin American LA infants received MenACWY at 2 and 6 months of age; and as part of routine infant vaccination schedule, received, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These subjects received a third dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months of age.	
Reporting group title	LA1B (MenACWY-CRM + Infant Vaccines)
Reporting group description:	
LA infants received MenACWY at 2 and 6 months of age and as part of routine infant vaccination schedule, received, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These subjects received pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and a third dose of MenACWY at 13 months of age.	
Reporting group title	LA2 (Infant Vaccines Only)
Reporting group description:	
LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received one dose of	

MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age.

Reporting group title	LA3A (MenACWY-CRM + Infant Vaccines)

Reporting group description:

LA infants received MenACWY at 2, 4 and 6 months of age; and as part of routine infant vaccination schedule received, DTaP-IPV-HBV, Hib, pneumococcal conjugate vaccine, and rotavirus vaccine. Around 12 months of age, these infants were recommended to receive pneumococcal conjugate vaccine, HAV, and MMR-V. At 16 months of age, these subjects received the fourth dose of MenACWY along with concomitant DTaP and Hib.

Reporting group title	LA3B (MenACWY-CRM + Infant Vaccines)

Reporting group description:

LA infants received MenACWY at 2, 4 and 6 months of age; and as part of routine infant vaccination schedule received, DTaP-IPV-HBV, Hib, pneumococcal conjugate vaccine, and rotavirus vaccine. Around 12 months of age, received pneumococcal conjugate vaccine, HAV, and MMR-V. At 16 months of age, these subjects received DTaP and Hib. At 17 months of age, these subjects received the fourth dose of MenACWY.

Reporting group title	LA4 (Infant Vaccines Only)

Reporting group description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, pneumococcal conjugate vaccine, and rotavirus vaccine at 2, 4 and 6 months of age. These infants received one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and a second dose of MenACWY along with DTaP and Hib vaccines at 15 months of age.

Reporting group title	LA5 (MenACWY-CRM + Infant Vaccines)

Reporting group description:

LA infants received MenACWY at 2, 4 and 6 months of age,; and as part of routine infant vaccination schedule received, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines. At 12 months of age, these subjects received the fourth dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V.

Reporting group title	LA6A (Infant Vaccines Only)

Reporting group description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 12 and a second dose of MenACWY at 15 months of age.

Reporting group title	LA6B (Infant Vaccines Only)

Reporting group description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 13 and a second dose of MenACWY at 15 months of age.

Reporting group title	LA6C (Infant Vaccines Only)

Reporting group description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 18 months of age.

Subject analysis set title	Exposed population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All enrolled subjects who actually received a study vaccination.

Subject analysis set title	Enrolled population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects who signed an informed consent, underwent screening procedures, and were randomized

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed population who provided post-baseline safety data.

Subject analysis set title	Concomitant Infant US subjects

Subject analysis set type	Per protocol

Subject analysis set description:

US infant subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	MenACWY Infant US subjects
Subject analysis set type	Per protocol

Subject analysis set description:

US infant subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	Pertussis Infant US subjects
Subject analysis set type	Per protocol

Subject analysis set description:

US infant subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	MenACWY Infant LA subjects
Subject analysis set type	Per protocol

Subject analysis set description:

LA infant subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	MenACWY Toddler US subjects
Subject analysis set type	Per protocol

Subject analysis set description:

US toddler subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations

Subject analysis set title	Pneumococcal Toddler US subjects
Subject analysis set type	Per protocol

Subject analysis set description:

US toddler subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	Concomitant Infant LA subjects
Subject analysis set type	Per protocol

Subject analysis set description:

LA infant subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	Pertussis Infant LA subjects
Subject analysis set type	Per protocol

Subject analysis set description:

LA infant subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	MenACWY Toddler LA subjects
Subject analysis set type	Per protocol

Subject analysis set description:

LA toddler subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	Concomitant Toddler LA subjects
Subject analysis set type	Per protocol

Subject analysis set description:

LA toddler subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	Pertussis Toddler LA subjects
Subject analysis set type	Per protocol

Subject analysis set description:

LA toddler subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	Pneumococcal Toddler LA subjects

Subject analysis set type	Per protocol

Subject analysis set description:

LA toddler subjects who received all the relevant doses of vaccine correctly; provided evaluable serum samples at the relevant time points; had no major protocol deviations.

Subject analysis set title	US4B+US4C Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed US4B and US4C population who provided post-baseline safety data.

Subject analysis set title	US1A + US3 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed US1A and US3 population who provided post-baseline safety data.

Subject analysis set title	US2+US4A Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed US2 and US4A population who provided post-baseline safety data.

Subject analysis set title	LA3 Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

All LA3 subjects who received doses of vaccine correctly, and provided evaluable serum samples at the relevant time points.

Subject analysis set title	LA1 Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

All LA1 subjects who received doses of vaccine correctly, and provided evaluable serum samples at the relevant time points.

Subject analysis set title	LA2+LA4+LA6A Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed LA2, LA4 and LA6A population who provided post-baseline safety data.

Subject analysis set title	LA6B+LA6C Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed LA6B and LA6C population who provided post-baseline safety data.

Subject analysis set title	US1 Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

All US1 subjects who received doses of vaccine correctly, and provided evaluable serum samples at the relevant time points.

Subject analysis set title	US4 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed US4 population who provided post-baseline safety data.

Subject analysis set title	LA6 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed LA6 population who provided post-baseline safety data.

Subject analysis set title	US1 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed US1 population who provided post-baseline safety data.

Subject analysis set title	LA1 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed LA1 population who provided post-baseline safety data.

Subject analysis set title	LA3 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed LA3 population who provided post-baseline safety data.

Subject analysis set title	US1+US3 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed US1 and US3 population who provided post-baseline safety data.

Subject analysis set title	US2+US4 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed US2 and US4 population who provided post-baseline safety data.

Subject analysis set title	LA3+LA5 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed LA3 and LA5 population who provided post-baseline safety data.

Subject analysis set title	LA4+LA6 Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed LA4 and LA6 population who provided post-baseline safety data.

Primary: 1. Percentage of Subjects With hSBA Titer >=1:8 - US Subjects

End point title	1. Percentage of Subjects With hSBA Titer >=1:8 - US

End point description:

End point type	Primary

End point timeframe:

13 months of age (one month post-toddler 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: No statistical analysis is associated to this Endpoint. Analyses were run descriptively.

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

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	74		
Units: Percentages of subjects				
number (confidence interval 95%)				
A (84, 74)	94 (87 to 98)	72 (60 to 81)		
C (86, 73)	98 (92 to 100)	90 (81 to 96)		
W (85, 73)	100 (96 to 100)	58 (45 to 69)		
Y (84, 68)	100 (96 to 100)	56 (43 to 68)		

Statistical analyses

No statistical analyses for this end point

Primary: 2. Geometric Mean hSBA Titers – US Subjects

End point title	2. Geometric Mean hSBA Titers – US Subjects[3]

End point description:

End point type	Primary

End point timeframe:

13 months of age (one month post-toddler vaccination)

Notes:

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

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	74		
Units: Titers				
geometric mean (confidence interval 95%)				
A Pre-vaccination (84, 74)	2.51 (2.14 to 2.96)	2.14 (1.8 to 2.54)		
A Post-vaccination (84, 74)	77 (55 to 109)	17 (12 to 25)		
C Pre-vaccination (86, 73)	7.72 (5.9 to 10)	2.26 (1.69 to 3.03)		
C Post-vaccination (86, 73)	227 (155 to 332)	35 (23 to 54)		
W Pre-vaccination (85, 73)	14 (11 to 18)	2.21 (1.69 to 2.9)		
W Post-vaccination (85, 73)	416 (288 to 602)	11 (7.59 to 17)		
Y Pre-vaccination (84, 68)	11 (8.76 to 15)	2.14 (1.6 to 2.86)		
Y Post-vaccination (84, 68)	395 (269 to 580)	10 (6.72 to 16)		

Statistical analyses

Statistical analysis title	A (Post-vaccination GMT; group ratio US1A:US2)

Statistical analysis description:

Using the MenACWY GMTs in sero group A, immunogenicity of the fourth dose at 1 month after the 12-month vaccination in those subjects receiving MenACWY at 2, 4, and 6 months was considered superior

to the immune response of a single dose given at 12-months of age if the lower limit of the two-sided 95% CI of the ratio of the two GMTs was >= 2.0.

Comparison groups	US2 (Infant Vaccines Only) v US1A (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	Ratio of GMTs
Point estimate	4.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.04
upper limit	6.74

Statistical analysis title	C (Post-vaccination GMT; group ratio US1A:US2)

Statistical analysis description:

Using the MenACWY GMTs in sero group C, immunogenicity of the fourth dose at 1 month after the 12-month vaccination in those subjects receiving MenACWY at 2, 4, and 6 months was considered superior to the immune response of a single dose given at 12-months of age if the lower limit of the two-sided 95% CI of the ratio of the two GMTs was >= 2.0.

Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US2 (Infant Vaccines Only)
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	Ratio of GMTs
Point estimate	6.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.16
upper limit	9.79

Statistical analysis title	W (Post-vaccination GMT; group ratio US1A:US2)

Statistical analysis description:

Using the MenACWY GMTs in sero group W, immunogenicity of the fourth dose at 1 month after the 12-month vaccination in those subjects receiving MenACWY at 2, 4, and 6 months was considered superior to the immune response of a single dose given at 12-months of age if the lower limit of the two-sided 95% CI of the ratio of the two GMTs was >= 2.0.

Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US2 (Infant Vaccines Only)

Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	Ratio of GMTs
Point estimate	37
Confidence interval	
level	95 %
sides	2-sided
lower limit	24
upper limit	58

Statistical analysis title	Y (Post-vaccination GMT; group ratio US1A:US2)

Statistical analysis description:

Using the MenACWY GMTs in sero group Y, immunogenicity of the fourth dose at 1 month after the 12-month vaccination in those subjects receiving MenACWY at 2, 4, and 6 months was considered superior to the immune response of a single dose given at 12-months of age if the lower limit of the two-sided 95% CI of the ratio of the two GMTs was >= 2.0.

Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US2 (Infant Vaccines Only)
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	Ratio of GMTs
Point estimate	38
Confidence interval	
level	95 %
sides	2-sided
lower limit	24
upper limit	60

Secondary: 3. Geometric Mean hSBA Titers Post-infant Series - US Subjects

End point title	3. Geometric Mean hSBA Titers Post-infant Series - US Subjects[4]

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post infant series)

Notes:

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

End point values	US2 (Infant Vaccines Only)	US1 Per Protocol Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	90	212		
Units: Titers				
geometric mean (confidence interval 95%)				
A (Pre-vaccination GMT; N= 65, 177)	2.1 (1.92 to 2.29)	2.11 (2 to 2.23)		
A (Post-vaccination GMT; N= 80, 212)	2.03 (1.53 to 2.7)	13 (11 to 16)		
C (Pre-vaccination GMT; N= 64, 168)	2.17 (1.83 to 2.57)	2.48 (2.23 to 2.75)		
C (Post-vaccination GMT; N= 84, 204)	2.12 (1.64 to 2.74)	108 (92 to 127)		
W (Pre-vaccination GMT; N= 66, 165)	2.71 (2.2 to 3.33)	3.07 (2.7 to 3.5)		
W (Post-vaccination GMT; N=90, 197)	2.08 (1.67 to 2.6)	100 (86 to 116)		
Y (Pre-vaccination GMT; N=62, 150)	2.13 (1.85 to 2.45)	2.53 (2.31 to 2.77)		
Y (Post-vaccination GMT; N=84, 182)	2.03 (1.6 to 2.57)	73 (62 to 86)		

Statistical analyses

No statistical analyses for this end point

Secondary: 4. Percentage of Subjects With hSBA Titer >=1:8 - US Subjects

End point title	4. Percentage of Subjects With hSBA Titer >=1:8 - US

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post-infant series)

Notes:

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

End point values	US2 (Infant Vaccines Only)	US1 Per Protocol Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	90	212		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A (Pre-vaccination GMT; N= 65, 177)	3 (0 to 11)	2 (0 to 5)		
A (Post-vaccination GMT; N= 80, 212)	1 (0.032 to 7)	67 (61 to 74)		
C (Pre-vaccination GMT; N= 64, 168)	5 (1 to 13)	7 (3 to 11)		
C (Post-vaccination GMT; N= 84, 204)	1 (0.03 to 6)	97 (93 to 99)		
W (Pre-vaccination GMT; N= 66, 165)	11 (4 to 21)	17 (12 to 24)		
W (Post-vaccination GMT; N=90, 197)	2 (0 to 8)	96 (93 to 99)		
Y (Pre-vaccination GMT; N=62, 150)	3 (0 to 11)	5 (2 to 10)		

Y (Post-vaccination GMT; N=84, 182)	0 (0 to 4)	96 (92 to 98)		

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Percentage of Subjects With hSBA Titer >=1:4 - US Subjects

End point title	5. Percentage of Subjects With hSBA Titer >=1:4 - US

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post-infant series)

Notes:

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

End point values	US2 (Infant Vaccines Only)	US1 Per Protocol Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	90	212		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A (Pre-vaccination GMT; N= 65, 177)	3 (0 to 11)	2 (1 to 6)		
A (Post-vaccination GMT; N= 80, 212)	1 (0.03 to 7)	71 (65 to 77)		
C (Pre-vaccination GMT; N= 64, 168)	5 (1 to 13)	10 (6 to 16)		
C (Post-vaccination GMT; N= 84, 204)	2 (0 to 8)	99 (96 to 100)		
W (Pre-vaccination GMT; N= 66, 165)	15 (8 to 26)	22 (16 to 30)		
W (Post-vaccination GMT; N=90, 197)	2 (0 to 8)	99 (96 to 100)		
Y (Pre-vaccination GMT; N=62, 150)	5 (1 to 13)	17 (11 to 24)		
Y (Post-vaccination GMT; N=84, 182)	1 (0.03 to 6)	98 (95 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Geometric Mean hSBA Titers Post-infant Series - LA Subjects

End point title	6. Geometric Mean hSBA Titers Post-infant Series - LA Subjects

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post-infant series)

End point values	LA3 Per Protocol Set	LA1 Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	272	277		
Units: Titers				
geometric mean (confidence interval 95%)				
A (Pre-vaccination GMT; N= 271, 272)	2.03 (1.97 to 2.09)	2.09 (2.03 to 2.16)		
A (Post-vaccination GMT; N= 268, 277)	43 (36 to 52)	31 (26 to 38)		
C (Pre-vaccination GMT; N= 272, 273)	2.34 (2.19 to 2.49)	2.32 (2.18 to 2.47)		
C (Post-vaccination GMT; N= 272, 277)	150 (127 to 177)	155 (131 to 183)		
W (Pre-vaccination GMT; N= 261, 263)	2.54 (2.31 to 2.79)	2.9 (2.64 to 3.18)		
W (Post-vaccination GMT; N=264,271)	182 (159 to 208)	259 (227 to 296)		
Y (Pre-vaccination GMT; N=260, 258)	2.26 (2.14 to 2.39)	2.35 (2.22 to 2.49)		
Y (Post-vaccination GMT; N=263,272)	125 (107 to 146)	159 (136 to 185)		

Statistical analyses

Statistical analysis title	Serogroup A
Comparison groups	LA1 Per Protocol Set v LA3 Per Protocol Set
Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Method	ANOVA
Parameter estimate	Ratio of GMTs
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.95

Notes:

[7] - LA1 was noninferior to LA3, if the lower limit of the two-sided 95% CI for the ratio of GMTs between the 2 dose and the 3 dose schedule (GMTLA1/GMTLA3) is > 0.5.

Statistical analysis title	Serogroup C
Comparison groups	LA3 Per Protocol Set v LA1 Per Protocol Set

Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Method	ANOVA
Parameter estimate	Ratio of GMTs
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.31

Notes:

[8] - LA1 was noninferior to LA3, if the lower limit of the two-sided 95% CI for the ratio of GMTs between the 2 dose and the 3 dose schedule (GMTLA1/GMTLA3) is > 0.5.

Statistical analysis title	Serogroup W
Comparison groups	LA3 Per Protocol Set v LA1 Per Protocol Set
Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Method	ANOVA
Parameter estimate	Ratio of GMTs
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	1.72

Notes:

[9] - LA1 was noninferior to LA3, if the lower limit of the two-sided 95% CI for the ratio of GMTs between the 2 dose and the 3 dose schedule (GMTLA1/GMTLA3) is > 0.5.

Statistical analysis title	Serogroup Y
Comparison groups	LA3 Per Protocol Set v LA1 Per Protocol Set
Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Method	ANOVA
Parameter estimate	Ratio of GMTs
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.58

Notes:

[10] - LA1 was noninferior to LA3, if the lower limit of the two-sided 95% CI for the ratio of GMTs between the 2 dose and the 3 dose schedule (GMTLA1/GMTLA3) is > 0.5.

Secondary: 7. Percentage of Subjects With hSBA Titer >=1:8 - LA Subjects

End point title	7. Percentage of Subjects With hSBA Titer >=1:8 - LA Subjects

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post-infant series)

End point values	LA3 Per Protocol Set	LA1 Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	272	277		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A (Pre-vaccination hSBA titer ≥1:8; N= 272, 271)	0 (0 to 2)	1 (0 to 4)		
A (Post-vaccination hSBA titer ≥1:8; N= 277, 268)	89 (85 to 93)	74 (69 to 79)		
C (Pre-vaccination hSBA titer ≥1:8; N= 273,272)	4 (2 to 8)	4 (2 to 7)		
C (Post-vaccination hSBA titer ≥1:8; N= 277, 272)	97 (94 to 99)	94 (90 to 96)		
W (Pre-vaccination hSBA titer ≥1:8; N= 263, 261)	10 (7 to 14)	16 (12 to 21)		
W (Post-vaccination hSBA titer ≥1:8; N=271,264)	98 (96 to 100)	99 (97 to 100)		
Y (Pre-vaccination hSBA titer ≥1:8; N=258, 260)	3 (2 to 6)	5 (3 to 9)		
Y (Post-vaccination hSBA titer ≥1:8; N=272,263)	98 (96 to 99)	97 (94 to 99)		

Statistical analyses

Statistical analysis title	Serogroup A
Comparison groups	LA1 Per Protocol Set v LA3 Per Protocol Set
Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage (hSBA titers >=8) difference
Point estimate	-15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.2
upper limit	-8.5

Notes:

[11] - LA1 was noninferior to LA3, if the lower limit of the two-sided 95% CI for the difference in percentage of subjects with hSBA ≥ 1:8 and ≥1:4 between the 2 dose and the 3 dose schedule (LA1 - LA3) is greater than -10%.

Statistical analysis title	Serogroup C
Comparison groups	LA1 Per Protocol Set v LA3 Per Protocol Set

Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage (hSBA titers >=8) difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	0.3

Notes:

[12] - LA1 was noninferior to LA3, if the lower limit of the two-sided 95% CI for the difference in percentage of subjects with hSBA ≥ 1:8 and ≥1:4 between the 2 dose and the 3 dose schedule (LA1 - LA3) is greater than -10%.

Statistical analysis title	Serogroup W
Comparison groups	LA1 Per Protocol Set v LA3 Per Protocol Set
Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage (hSBA titers >=8) difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	3.1

Notes:

[13] - LA1 was noninferior to LA3, if the lower limit of the two-sided 95% CI for the difference in percentage of subjects with hSBA ≥ 1:8 and ≥1:4 between the 2 dose and the 3 dose schedule (LA1 - LA3) is greater than -10%.

Statistical analysis title	Serogroup Y
Comparison groups	LA1 Per Protocol Set v LA3 Per Protocol Set
Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage (hSBA titers >=8) difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	1.7

Notes:

[14] - LA1 was noninferior to LA3, if the lower limit of the two-sided 95% CI for the difference in percentage of subjects with hSBA ≥ 1:8 and ≥1:4 between the 2 dose and the 3 dose schedule (LA1 - LA3) is greater than -10%.

Secondary: 8. Percentage of Subjects With hSBA Titer >=1:4 - LA Subjects

End point title	8. Percentage of Subjects With hSBA Titer >=1:4 - LA Subjects

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post-infant series)

End point values	LA3 Per Protocol Set	LA1 Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	272	277		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A (Pre-vaccination hSBA titer ≥1:4; N= 271, 272)	1 (0 to 3)	2 (1 to 5)		
A (Post-vaccination hSBA titer ≥1:4; N= 268, 277)	91 (87 to 94)	78 (73 to 83)		
C (Pre-vaccination hSBA titer ≥1:4; N= 272,273)	10 (7 to 15)	10 (7 to 14)		
C (Post-vaccination hSBA titer ≥1:4; N= 272, 277)	98 (96 to 99)	96 (93 to 98)		
W (Pre-vaccination hSBA titer ≥1:4; N= 261, 263)	13 (9 to 17)	17 (13 to 23)		
W (Post-vaccination hSBA titer ≥1:4; N=264,271)	99 (97 to 100)	100 (99 to 100)		
Y (Pre-vaccination hSBA titer ≥1:4; N=260, 258)	8 (5 to 13)	11 (8 to 16)		
Y (Post-vaccination hSBA titer ≥1:4; N=263,272)	99 (97 to 100)	98 (96 to 99)		

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Geometric Mean Concentrations or Titers of DTaP, HBV, Hib, Pneumococcal and Polio Antigens at 1 Month After Infant Series Vaccination - US Subjects

End point title	9. Geometric Mean Concentrations or Titers of DTaP, HBV, Hib, Pneumococcal and Polio Antigens at 1 Month After Infant Series Vaccination - US Subjects[15]

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post-infant series)

Notes:

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

End point values	US2 (Infant Vaccines Only)	US1 Per Protocol Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	102	214		
Units: Titers				
geometric mean (confidence interval 95%)				
Diphtheria (N=102, 214)	2.88 (2.5 to 3.32)	2.52 (2.28 to 2.78)		
Tetanus (N=102, 214)	2.31 (2.01 to 2.64)	2.5 (2.28 to 2.74)		
PT (N=83, 174)	54 (44 to 66)	54 (48 to 62)		
FHA (N=83, 174)	114 (97 to 134)	118 (106 to 132)		
Pertactin (N=83, 174)	110 (90 to 134)	114 (100 to 130)		
Polio Type 1 (N=98, 176)	441 (361 to 540)	422 (363 to 491)		
Polio Type 2 (N=98, 175)	290 (235 to 358)	348 (297 to 408)		
Polio Type 3 (N=98, 176)	635 (493 to 818)	733 (607 to 885)		
Hepatitis B (N=98, 148)	2112 (1668 to 2674)	1863 (1538 to 2257)		
Hib (N=101, 213)	3.56 (2.77 to 4.58)	4.64 (3.9 to 5.53)		
PnC 4 (N=102, 181)	2 (1.73 to 2.3)	1.67 (1.5 to 1.86)		
PnC 6B (N=102, 181)	2.55 (1.99 to 3.27)	1.94 (1.61 to 2.34)		
PnC 9V (N=102, 181)	2.15 (1.83 to 2.53)	1.83 (1.62 to 2.06)		
PnC 14 (N=102, 181)	6.79 (5.78 to 7.96)	6.97 (6.18 to 7.86)		
PnC 18C (N=102, 181)	2.54 (2.18 to 2.95)	1.96 (1.75 to 2.19)		
PnC 19F (N=102, 181)	2.73 (2.39 to 3.13)	2.24 (2.02 to 2.48)		
PnC 23F (N=102, 181)	2.15 (1.76 to 2.62)	1.71 (1.47 to 1.98)		

Statistical analyses

Statistical analysis title	Diphtheria

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	0.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.04

Statistical analysis title	Tetanus

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.28

Statistical analysis title	PT

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.26

Statistical analysis title	FHA

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs

(US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.25

Statistical analysis title	Pertactin

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.32

Statistical analysis title	Polio Type 1

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	0.96

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.23

Statistical analysis title	Polio Type 2

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.55

Statistical analysis title	Polio Type 3

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.56

Statistical analysis title	Hepatitis B

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs

(US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.2

Statistical analysis title	HIb

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.77

Statistical analysis title	PnC 4

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	0.84

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1

Statistical analysis title	PnC 6B

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.03

Statistical analysis title	PnC 9V

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.04

Statistical analysis title	PnC 14

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs

(US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.26

Statistical analysis title	PnC 18C

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.93

Statistical analysis title	PnC 19F

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.97

Statistical analysis title	PnC 23F

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the ratio of pertussis GMCs (US1 /US2) must be greater than 0.67; the lower limit of 95% CI for the ratio of all other GMCs (GMCUS1 / GMCUS2) must be greater than 0.50.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.02

Secondary: 10. Seroresponse Rates to DTaP, HBV, Hib, Pneumococcal and Polio Antigens at 1 Month After Infant Series Vaccination - US Subjects

End point title	10. Seroresponse Rates to DTaP, HBV, Hib, Pneumococcal and Polio Antigens at 1 Month After Infant Series Vaccination - US Subjects[16]

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post-infant series)

Notes:

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

End point values	US2 (Infant Vaccines Only)	US1 Per Protocol Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	102	214		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Diphtheria (≥ 0.1 IU/mL) (N=102, 214)	100 (96 to 100)	100 (97 to 100)		

Tetanus (≥ 0.1 IU/mL) (N=102, 214)	100 (96 to 100)	100 (98 to 100)		
PT(≥ 4-fold rise) (N=83, 174)	86 (76 to 92)	87 (81 to 92)		
FHA (≥ 4-fold rise) (N=83, 174)	80 (69 to 88)	85 (79 to 90)		
Pertactin (≥ 4-fold rise) (N=83, 174)	78 (68 to 87)	76 (69 to 83)		
Polio Type 1 (≥1:8) (N=98, 176)	100 (96 to 100)	99 (97 to 100)		
Polio Type 2 (≥1:8) (N=98, 175)	100 (96 to 100)	100 (98 to 100)		
Polio Type 3 (≥1:8)(N=98, 176)	100 (96 to 100)	99 (97 to 100)		
Hepatitis B (≥10 mIU/mL) (N=98, 148)	100 (96 to 100)	99 (96 to 100)		
Hib (≥ 0.15 µg/mL) (N=101, 213)	100 (96 to 100)	99 (97 to 100)		
Hib (≥1.0 µg/mL) (N=101, 213)	84 (76 to 91)	89 (84 to 93)		
PnC 4 (≥ 0.35 µg/mL) (N=102, 181)	100 (96 to 100)	98 (95 to 100)		
PnC 6B (≥ 0.35 µg/mL) (N=102, 181)	96 (90 to 99)	88 (83 to 93)		
PnC 9V (≥ 0.35 µg/mL) (N=102, 181)	98 (93 to 100)	98 (94 to 99)		
PnC 14 (≥ 0.35 µg/mL) (N=102, 181)	99 (95 to 100)	100 (98 to 100)		
PnC 18C (≥ 0.35 µg/mL) (N=102, 181)	100 (96 to 100)	97 (94 to 99)		
PnC 19F (≥ 0.35 µg/mL) (N=102, 181)	100 (96 to 100)	99 (96 to 100)		
PnC 23F (≥ 0.35 µg/mL) (N=102, 181)	94 (88 to 98)	92 (87 to 95)		

Statistical analyses

Statistical analysis title	Diphtheria

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	3

Statistical analysis title	Tetanus

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	4

Statistical analysis title	PT
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	12

Statistical analysis title	FHA
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	17

Statistical analysis title	Pertactin
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	10

Statistical analysis title	Polio Type 1
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	3

Statistical analysis title	Polio Type 2
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set

Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	4

Statistical analysis title	Polio Type 3

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	3

Statistical analysis title	Hepatitis B

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3

Statistical analysis title	Hib (≥ 0.15 µg/mL)
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	3

Statistical analysis title	Hib (≥1.0 µg/mL)
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	14

Statistical analysis title	PnC 4
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set

Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	2

Statistical analysis title	PnC 6B

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	-1

Statistical analysis title	PnC 9V

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	5

Statistical analysis title	PnC 14
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	5

Statistical analysis title	PnC 18C
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	1

Statistical analysis title	PnC 19F
Statistical analysis description:	
To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.	
Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set

Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3

Statistical analysis title	PnC 23F

Statistical analysis description:

To assess non-inferiority of US1 over US2, the lower limit of 95% CI for the difference in seroresponse rates (US1 - US2) must be greater than -5% for polio and -10% for all others.

Comparison groups	US2 (Infant Vaccines Only) v US1 Per Protocol Set
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	5

Secondary: 11. Geometric Mean Concentrations or Titers of DTaP, HBV, Hib, Pneumococcal and Polio Antigens at 1 Month After Infant Series Vaccination - LA Subjects

End point title	11. Geometric Mean Concentrations or Titers of DTaP, HBV, Hib, Pneumococcal and Polio Antigens at 1 Month After Infant Series Vaccination - LA Subjects[17]

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post-infant series)

Notes:

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

End point values	LA2 (Infant Vaccines Only)	LA4 (Infant Vaccines Only)	LA3 Per Protocol Set	LA1 Per Protocol Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	123	137	283	287
Units: Titers				
geometric mean (confidence interval 95%)				
Diphtheria (N=123, 137, 283, 287)	1.54 (1.32 to 1.81)	1.77 (1.52 to 2.05)	1.45 (1.31 to 1.61)	1.8 (1.62 to 1.99)
Tetanus (N=123, 137, 283, 287)	2.19 (1.94 to 2.46)	2.65 (2.37 to 2.96)	2.51 (2.33 to 2.71)	2.41 (2.33 to 2.6)
PT (N=123, 135, 281, 285)	45 (39 to 53)	49 (42 to 56)	45 (41 to 50)	47 (43 to 52)
FHA (N=123, 135, 281, 286)	97 (85 to 112)	112 (99 to 128)	99 (91 to 109)	102 (93 to 112)
Pertactin (N=123, 135, 281, 286)	124 (105 to 146)	149 (127 to 175)	119 (106 to 133)	123 (110 to 137)
Polio Type 1 (N=112, 120, 252, 265)	598 (477 to 749)	684 (550 to 850)	533 (458 to 619)	535 (462 to 620)
Polio Type 2 (N=112, 120, 252, 265)	366 (289 to 463)	385 (306 to 483)	318 (271 to 372)	353 (302 to 411)
Polio Type 3 (N=112, 120, 252, 265)	747 (571 to 977)	813 (627 to 1054)	656 (548 to 785)	710 (596 to 846)
Hepatitis B (N=104, 118, 237, 243)	2045 (1682 to 2485)	1993 (1660 to 2394)	1900 (1670 to 2162)	2273 (2001 to 2583)
Hib (N=123, 137, 283, 287)	6.01 (4.84 to 7.47)	6.74 (5.49 to 8.28)	7.19 (6.23 to 8.29)	7.64 (6.63 to 8.8)
PnC 4 (N=116, 126, 256, 268)	2.24 (1.94 to 2.58)	2.39 (2.08 to 2.74)	1.91 (1.74 to 2.1)	2.07 (1.88 to 2.27)
PnC 6B (N=116, 124, 255, 264)	2.21 (1.76 to 2.77)	2.4 (1.93 to 2.98)	2.09 (1.8 to 2.44)	2.15 (1.85 to 2.49)
PnC 9V (N=116, 126, 256, 268)	2.21 (1.89 to 2.6)	2.19 (1.88 to 2.55)	1.81 (1.63 to 2.02)	1.89 (1.71 to 2.1)
PnC 14 (N=116, 126, 256, 268)	8.06 (6.63 to 9.78)	9.18 (7.62 to 11)	7.69 (6.75 to 8.77)	7.29 (6.42 to 8.29)
PnC 18C (N=116, 126, 256, 268)	2.09 (1.78 to 2.44)	2.26 (1.94 to 2.62)	1.7 (1.53 to 1.89)	1.86 (1.68 to 2.07)
PnC 19F (N=116, 126, 254, 268)	2.6 (2.2 to 3.06)	2.53 (2.16 to 2.96)	2.3 (2.06 to 2.57)	2.34 (2.1 to 2.6)
PnC 23F (N=115, 125, 256, 267)	2.46 (1.99 to 3.03)	2.42 (1.98 to 2.96)	2.12 (1.84 to 2.44)	1.88 (1.64 to 2.16)

Statistical analyses

Statistical analysis title	Diphtheria
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.4

Notes:

[18] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	Tetanus
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.27

Notes:

[19] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	PT
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.25

Notes:

[20] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	FHA
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.23

Notes:

[21] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	Pertactin
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.21

Notes:

[22] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	Polio Type 1
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.17

Notes:

[23] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	Polio Type 2
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.28

Notes:

[24] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	Polio Type 3
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.31

Notes:

[25] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	Hepatitis B
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.4

Notes:

[26] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	Hib
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.65

Notes:

[27] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	PnC 4
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.09

Notes:

[28] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	PnC 6B
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[29]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.27

Notes:

[29] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	PnC 9V
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.04

Notes:

[30] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	PnC 14
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[31]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.14

Notes:

[31] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	PnC 18C
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[32]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.08

Notes:

[32] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	PnC 19F
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[33]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.1

Notes:

[33] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	PnC 23F
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority[34]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	0.99

Notes:

[34] - To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the ratio of pertussis GMCs (LA1 / LA2) must be greater than 0.67; the lower limit of the 95% CI for the ratio of all other GMCs (LA1 / LA2) must be greater than 0.50.

Statistical analysis title	Diphtheria
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[35]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.99

Notes:

[35] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	Tetanus

Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[36]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.09

Notes:

[36] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	PT
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[37]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.1

Notes:

[37] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	FHA
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[38]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.03

Notes:

[38] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	Pertactin
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[39]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.97

Notes:

[39] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	Polio Type 1
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[40]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.02

Notes:

[40] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	Polio Type 2
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[41]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.09

Notes:

[41] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	Polio Type 3
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[42]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.11

Notes:

[42] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	Hepatitis B
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[43]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.19

Notes:

[43] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	Hib
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set

Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[44]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.37

Notes:

[44] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	PnC 4
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[45]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.95

Notes:

[45] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	PnC 6B
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[46]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.14

Notes:

[46] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	PnC 9V
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[47]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1

Notes:

[47] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	PnC 14
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[48]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.05

Notes:

[48] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	PnC 18C
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[49]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.9

Notes:

[49] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	PnC 19F
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[50]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.1

Notes:

[50] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Statistical analysis title	PnC 23F
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[51]
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.12

Notes:

[51] - To assess non-inferiority of LA3 over LA4, the lower limit of two-sided 95% CI for the ratio of pertussis GMCs (LA3 / LA4) must be greater than 0.67; the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3 / LA4) or GMTs (poliovirus antigens) for the other antigens must be greater than 0.50.

Secondary: 13. Seroresponse Rates to DTaP, HBV, Hib, Pneumococcal and Polio Antigens at 1 Month After Infant Series Vaccination - LA Subjects

End point title	13. Seroresponse Rates to DTaP, HBV, Hib, Pneumococcal and Polio Antigens at 1 Month After Infant Series Vaccination - LA Subjects[52]

End point description:

End point type	Secondary

End point timeframe:

7 months of age (one month post-infant series)

Notes:

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

Justification: No statistical analysis is associated to this Endpoint. Analyses were run descriptively.

End point values	LA2 (Infant Vaccines Only)	LA4 (Infant Vaccines Only)	LA3 Per Protocol Set	LA1 Per Protocol Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	123	137	283	287
Units: Percentage of Subjects				
geometric mean (confidence interval 95%)				
Diphtheria(≥ 0.1 IU/mL) (N=123, 137, 287, 283)	98 (94 to 100)	99 (95 to 100)	99 (96 to 100)	99 (96 to 100)
Tetanus (≥ 0.1 IU/mL) (N=123,137,287,283)	100 (97 to 100)	100 (97 to 100)	100 (99 to 100)	100 (98 to 100)
PT(≥ 4-fold rise) (N=123,135,285,281)	86 (79 to 92)	82 (75 to 88)	85 (80 to 89)	85 (81 to 89)
FHA (≥ 4-fold rise) (N=123,135,286,281)	86 (79 to 92)	81 (74 to 88)	82 (77 to 86)	84 (79 to 88)
Pertactin(≥ 4-fold rise)(N=123,135,286,281)	87 (80 to 92)	88 (81 to 93)	86 (82 to 90)	81 (76 to 85)
Polio Type 1 (≥1:8) (N=112,120,265,252)	100 (97 to 100)	98 (94 to 100)	99 (97 to 100)	98 (95 to 99)
Polio Type 2 (≥1:8) (N=112,120,265,252)	99 (95 to 100)	98 (93 to 99)	98 (95 to 99)	97 (95 to 99)
Polio Type 3 (≥1:8) (N=112,120,265,252)	97 (92 to 99)	97 (92 to 99)	96 (93 to 98)	97 (95 to 99)
Hepatitis B(≥10 mIU/mL)(N=104,118,243,237)	100 (97 to 100)	100 (97 to 100)	100 (98 to 100)	100 (98 to 100)
Hib (≥0.15 µg/mL) (N=123,137,287,283)	98 (94 to 100)	99 (96 to 100)	97 (94 to 99)	99 (98 to 100)
Hib (≥1.0 µg/mL) (N=123,137,287,283)	93 (88 to 97)	96 (91 to 98)	93 (90 to 96)	95 (92 to 97)
PnC 4 (≥ 0.35 µg/mL) (N=116,126,268,256)	99 (95 to 100)	98 (94 to 100)	97 (94 to 99)	99 (96 to 100)
PnC 6B (≥ 0.35 µg/mL) (N=116,124,264,255)	86 (79 to 92)	90 (83 to 94)	91 (87 to 95)	91 (86 to 94)
PnC 9V (≥ 0.35 µg/mL) (N=116,126,268,256)	98 (94 to 100)	96 (91 to 99)	97 (94 to 99)	97 (95 to 99)
PnC 14 (≥ 0.35 µg/mL) (N=116,126,268,256)	97 (93 to 99)	98 (94 to 100)	98 (95 to 99)	99 (97 to 100)
PnC 18C(≥ 0.35 µg/mL) (N=116,126,268,256)	98 (94 to 100)	98 (94 to 100)	95 (91 to 97)	97 (94 to 98)
PnC 19F (≥ 0.35 µg/mL)(N=116,126,268,254)	98 (94 to 100)	96 (91 to 99)	98 (96 to 100)	97 (94 to 98)
PnC 23F (≥ 0.35 µg/mL)(N=115,125,267,256)	97 (91 to 99)	94 (88 to 97)	95 (91 to 97)	93 (89 to 96)

Statistical analyses

Statistical analysis title	Diphtheria

Statistical analysis description:

To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	4.4

Statistical analysis title	Tetanus

Statistical analysis description:

To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	2.6

Statistical analysis title	PT

Statistical analysis description:

To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.7
upper limit	7.1

Statistical analysis title	FHA
Statistical analysis description:	
To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.2
upper limit	5.8

Statistical analysis title	Pertactin
Statistical analysis description:	
To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.9
upper limit	2.2

Statistical analysis title	Polio Type 1
Statistical analysis description:	
To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	1

Statistical analysis title	Polio Type 2

Statistical analysis description:

To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	2.3

Statistical analysis title	Polio Type 3

Statistical analysis description:

To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	5.1

Statistical analysis title	Hepatitis B
Statistical analysis description:	
To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	3.5

Statistical analysis title	Hib(≥ 0.15 µg/mL)
Statistical analysis description:	
To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	5

Statistical analysis title	Hib (≥1.0 µg/mL)
Statistical analysis description:	
To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	7.7

Statistical analysis title	PnC 4

Statistical analysis description:

To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	3.3

Statistical analysis title	PnC 6B

Statistical analysis description:

To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	12.3

Statistical analysis title	PnC 9V
Statistical analysis description:	
To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	3.6

Statistical analysis title	PnC 14
Statistical analysis description:	
To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	6.2

Statistical analysis title	PnC 18C
Statistical analysis description:	
To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2.9

Statistical analysis title	PnC 19F

Statistical analysis description:

To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2.9

Statistical analysis title	PnC 23F

Statistical analysis description:

To assess non-inferiority of LA1 to LA2, the lower limit of the 95% CI for the difference in seroresponse rates (LA1 - LA2) must be greater than -5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA2 (Infant Vaccines Only) v LA1 Per Protocol Set
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	1.9

Statistical analysis title	Diphtheria
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	3.8

Statistical analysis title	Tetanus
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	2.7

Statistical analysis title	PT
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set

Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	10.7

Statistical analysis title	FHA

Statistical analysis description:

To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.1
upper limit	8.8

Statistical analysis title	Pertactin

Statistical analysis description:

To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	5.7

Statistical analysis title	Polio Type 1
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	4.7

Statistical analysis title	Polio Type 2
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	4.8

Statistical analysis title	Polio Type 3
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set

Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	4.5

Statistical analysis title	Hepatitis B

Statistical analysis description:

To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	2.7

Statistical analysis title	Hib (≥ 0.15 µg/mL)

Statistical analysis description:

To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	1

Statistical analysis title	Hib (≥1.0 µg/mL)
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	3

Statistical analysis title	PnC 4
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	3

Statistical analysis title	PnC 6B
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set

Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	9

Statistical analysis title	PnC 9V

Statistical analysis description:

To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	6

Statistical analysis title	PnC 14

Statistical analysis description:

To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.

Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	3.4

Statistical analysis title	PnC 18C
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	0.8

Statistical analysis title	PnC 19F
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	7.5

Statistical analysis title	PnC 23F
Statistical analysis description:	
To assess non-inferiority of LA3 over LA4, the lower limit of the two-sided 95% CI for the difference in seroresponse rates (LA3 - LA4) must be greater than 5% for poliovirus and greater than -10% for all other antigens.	
Comparison groups	LA4 (Infant Vaccines Only) v LA3 Per Protocol Set

Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	7

Secondary: 14. Percentage of Subjects With hSBA ≥1:4 at 12 Months of Age- US Subjects

End point title	14. Percentage of Subjects With hSBA ≥1:4 at 12 Months of Age- US Subjects[53]

End point description:

End point type	Secondary

End point timeframe:

12 Months of Age (before toddler vaccination)

Notes:

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

End point values	US2 (Infant Vaccines Only)	US1 Per Protocol Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	74	169		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A (74, 167)	3 (0 to 9)	16 (11 to 23)		
C (73, 169)	8 (3 to 17)	57 (50 to 65)		
W (73, 166)	4 (1 to 12)	81 (74 to 86)		
Y (68, 154)	1 (0.0037 to 8)	73 (65 to 80)		

Statistical analyses

No statistical analyses for this end point

Secondary: 15. Percentage of Subjects With hSBA ≥1:8 at 12 Months of Age- US Subjects

End point title	15. Percentage of Subjects With hSBA ≥1:8 at 12 Months of Age- US Subjects[54]

End point description:

End point type	Secondary

End point timeframe:

12 Months of Age (before toddler vaccination)

Notes:

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

End point values	US2 (Infant Vaccines Only)	US1 Per Protocol Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	74	169		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A (74, 167)	1 (0.034 to 7)	12 (7 to 18)		
C (73, 169)	7 (2 to 15)	52 (44 to 60)		
W (73, 166)	4 (1 to 12)	69 (62 to 76)		
Y (68, 154)	1 (0.0037 to 8)	60 (52 to 68)		

Statistical analyses

No statistical analyses for this end point

Secondary: 16. Geometric Mean Titers – US Subjects

End point title	16. Geometric Mean Titers – US Subjects[55]

End point description:

End point type	Secondary

End point timeframe:

12 Months of Age (before toddler vaccination)

Notes:

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

End point values	US2 (Infant Vaccines Only)	US1 Per Protocol Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	74	169		
Units: Titers				
geometric mean (confidence interval 95%)				
A (74, 167)	2.14 (1.8 to 2.54)	2.78 (2.48 to 3.12)		
C (73, 169)	2.26 (1.69 to 3.03)	8.07 (6.66 to 9.77)		
W (73, 166)	2.21 (1.69 to 2.9)	14 (12 to 17)		
Y (68, 154)	2.14 (1.6 to 2.86)	11 (8.98 to 13)		

Statistical analyses

No statistical analyses for this end point

Secondary: 17. Percentage of Subjects With hSBA ≥1:4 at 12 or 16 Months of Age- LA Subjects

End point title	17. Percentage of Subjects With hSBA ≥1:4 at 12 or 16 Months of Age- LA Subjects[56]

End point description:

End point type	Secondary

End point timeframe:

12 or 16 Months of Age (before toddler vaccination)

Notes:

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

End point values	LA2 (Infant Vaccines Only)	LA4 (Infant Vaccines Only)	LA3 Per Protocol Set	LA1 Per Protocol Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	78	102	229	206
Units: Percentage of Subjects				
number (confidence interval 95%)				
A (N=78, 101, 205, 229)	1 (0.032 to 7)	1 (0.025 to 5)	18 (14 to 24)	29 (23 to 36)
C (N=78, 102, 206, 229)	4 (1 to 11)	2 (0 to 7)	32 (26 to 38)	62 (55 to 68)
W (N=70, 98, 198, 218)	4 (1 to 12)	5 (2 to 12)	72 (66 to 78)	95 (92 to 98)
Y (N=71, 95, 195, 212)	3 (0 to 10)	2 (0 to 7)	65 (58 to 71)	82 (76 to 87)

Statistical analyses

No statistical analyses for this end point

Secondary: 18. Percentage of Subjects With hSBA ≥1:8 at 12 or 16 Months of Age- LA Subject

End point title	18. Percentage of Subjects With hSBA ≥1:8 at 12 or 16 Months of Age- LA Subject[57]

End point description:

End point type	Secondary

End point timeframe:

12 or 16 Months of Age (before-toddler vaccination)

Notes:

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

End point values	LA2 (Infant Vaccines Only)	LA4 (Infant Vaccines Only)	LA3 Per Protocol Set	LA1 Per Protocol Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	78	102	229	206
Units: Percentage of Subjects				
number (confidence interval 95%)				
A (N=78, 101, 205, 229)	0 (0 to 5)	0 (0 to 4)	15 (11 to 20)	25 (20 to 32)
C (N=78, 102, 206, 229)	4 (1 to 11)	1 (0.025 to 5)	26 (20 to 32)	57 (50 to 64)
W (N=70, 98, 198, 218)	4 (1 to 12)	5 (2 to 12)	63 (56 to 69)	85 (79 to 90)
Y (N=71, 95, 195, 212)	3 (0 to 10)	0 (0 to 4)	52 (45 to 59)	72 (65 to 78)

Statistical analyses

No statistical analyses for this end point

Secondary: 19. Geometric Mean Titers - LA Subjects

End point title	19. Geometric Mean Titers - LA Subjects[58]

End point description:

End point type	Secondary

End point timeframe:

12 or 16 Months of Age (before pre-toddler vaccination)

Notes:

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

End point values	LA2 (Infant Vaccines Only)	LA4 (Infant Vaccines Only)	LA3 Per Protocol Set	LA1 Per Protocol Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	78	102	229	206
Units: Titers				
geometric mean (confidence interval 95%)				
A (N=78, 101, 205, 229)	2.02 (1.7 to 2.4)	2.02 (1.74 to 2.35)	2.96 (2.63 to 3.33)	4.26 (3.55 to 5.11)
C (N=78, 102, 206, 229)	2.18 (1.73 to 2.74)	2.05 (1.68 to 2.51)	4.14 (3.54 to 4.84)	12 (9.33 to 15)
W (N=70, 98, 198, 218)	2.34 (1.79 to 3.05)	2.33 (1.86 to 2.91)	14 (12 to 18)	31 (26 to 37)
Y (N=71, 95, 195, 212)	2.2 (1.7 to 2.84)	2.04 (1.64 to 2.55)	9.45 (7.81 to 11)	18 (15 to 22)

Statistical analyses

No statistical analyses for this end point

Secondary: 20. Percentage of Subjects (95% CI) With hSBA ≥ 1:4, at 1 Month After Toddler MenACWY Vaccination - US Subjects

End point title	20. Percentage of Subjects (95% CI) With hSBA ≥ 1:4, at 1 Month After Toddler MenACWY Vaccination - US Subjects[59]

End point description:

End point type	Secondary

End point timeframe:

13 months of age (one month post-toddler vaccination)

Notes:

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

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	74		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A Pre-vaccination (84, 74)	12 (6 to 21)	3 (0 to 9)		
A Post-vaccination (84, 74)	94 (87 to 98)	78 (67 to 87)		
C Pre-vaccination (86, 73)	53 (42 to 64)	8 (3 to 17)		
C Post-vaccination (86, 73)	99 (94 to 100)	95 (87 to 98)		
W Pre-vaccination (85, 73)	80 (70 to 88)	4 (1 to 12)		
W Post-vaccination (85, 73)	100 (96 to 100)	73 (61 to 82)		
Y Pre-vaccination (84, 68)	74 (63 to 83)	1 (0.037 to 8)		
Y Post-vaccination (84, 68)	100 (96 to 100)	62 (49 to 73)		

Statistical analyses

No statistical analyses for this end point

Secondary: 21. Percentage of Subjects (95% CI) With hSBA ≥ 1:8 at 1 Month After Toddler MenACWY Vaccination - US Subjects

End point title	21. Percentage of Subjects (95% CI) With hSBA ≥ 1:8 at 1 Month After Toddler MenACWY Vaccination - US Subjects[60]

End point description:

End point type	Secondary

End point timeframe:

13 months of age (one month post-toddler vaccination)

Notes:

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

Justification: No statistical analysis is associated to this Endpoint. Analyses were run descriptively.

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	74		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A Pre-vaccination (84, 74)	10 (4 to 18)	1 (0.034 to 7)		
A Post-vaccination (84, 74)	94 (87 to 98)	72 (60 to 81)		
C Pre-vaccination (86, 73)	50 (39 to 61)	7 (2 to 15)		
C Post-vaccination (86, 73)	98 (92 to 100)	90 (81 to 96)		
W Pre-vaccination (85, 73)	71 (60 to 80)	4 (1 to 12)		
W Post-vaccination (85, 73)	100 (96 to 100)	58 (45 to 69)		
Y Pre-vaccination (84, 68)	61 (49 to 71)	1 (0.037 to 8)		
Y Post-vaccination (84, 68)	100 (96 to 100)	56 (43 to 68)		

Statistical analyses

No statistical analyses for this end point

Secondary: 22. Percentage of Subjects (95% CI) With hSBA ≥ 1:16 at 1 Month After Toddler MenACWY Vaccination - US Subjects

End point title	22. Percentage of Subjects (95% CI) With hSBA ≥ 1:16 at 1 Month After Toddler MenACWY Vaccination - US Subjects[61]

End point description:

End point type	Secondary

End point timeframe:

13 months of age (one month post-toddler vaccination)

Notes:

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

Justification: No statistical analysis is associated to this Endpoint. Analyses were run descriptively.

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	74		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A Pre-vaccination (84, 74)	5 (1 to 12)	1 (0.034 to 7)		

A Post-vaccination (84, 74)	90 (82 to 96)	55 (43 to 67)		
C Pre-vaccination (86, 73)	35 (25 to 46)	0 (0 to 5)		
C Post-vaccination (86, 73)	95 (89 to 99)	78 (67 to 87)		
W Pre-vaccination (85, 73)	48 (37 to 59)	3 (0 to 10)		
W Post-vaccination (85, 73)	100 (96 to 100)	38 (27 to 50)		
Y Pre-vaccination (84, 68)	45 (34 to 56)	1 (0.037 to 8)		
Y Post-vaccination (84, 68)	100 (96 to 100)	41 (29 to 54)		

Statistical analyses

No statistical analyses for this end point

Secondary: 23. Percentage of Subjects (95% CI) With hSBA ≥1:4 at 1 Month After Toddler MenACWY Vaccination - LA Subjects

End point title	23. Percentage of Subjects (95% CI) With hSBA ≥1:4 at 1 Month After Toddler MenACWY Vaccination - LA Subjects[62]

End point description:

End point type	Secondary

End point timeframe:

13 or 17 Months of Age (one month post-toddler vaccination)

Notes:

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

End point values	LA1A (MenACWY-CRM + Infant Vaccines)	LA3A (MenACWY-CRM + Infant Vaccines)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	122		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A Pre-vaccination (103, 120)	28 (20 to 38)	18 (12 to 26)		
A Post-vaccination (103,120)	94 (88 to 98)	95 (89 to 98)		
C Pre-vaccination (102,122)	61 (51 to 70)	30 (22 to 38)		
C Post-vaccination (102,122)	98 (93 to 100)	98 (94 to 100)		
W Pre-vaccination (98,112)	97 (91 to 99)	71 (61 to 79)		
W Post-vaccination (98,112)	100 (96 to 100)	100 (97 to 100)		
Y Pre-vaccination (98,109)	78 (68 to 85)	61 (52 to 71)		
Y Post-vaccination (98,109)	99 (94 to 100)	99 (95 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 24. Percentage of Subjects (95% CI) With hSBA ≥1:8 at 1 Month After Toddler MenACWY Vaccination - LA Subjects

End point title	24. Percentage of Subjects (95% CI) With hSBA ≥1:8 at 1 Month After Toddler MenACWY Vaccination - LA Subjects[63]

End point description:

End point type	Secondary

End point timeframe:

13 or 17 Months of Age (one month post-toddler vaccination)

Notes:

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

End point values	LA1A (MenACWY-CRM + Infant Vaccines)	LA3A (MenACWY-CRM + Infant Vaccines)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	122		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A Pre-vaccination (103, 120)	23 (16 to 33)	13 (8 to 21)		
A Post-vaccination (103,120)	94 (88 to 98)	95 (89 to 98)		
C Pre-vaccination (102,122)	57 (47 to 67)	22 (15 to 31)		
C Post-vaccination (102,122)	97 (92 to 99)	98 (94 to 100)		
W Pre-vaccination (98,112)	84 (75 to 90)	62 (52 to 71)		
W Post-vaccination (98,112)	99 (94 to 100)	100 (97 to 100)		
Y Pre-vaccination (98,109)	67 (57 to 76)	47 (37 to 57)		
Y Post-vaccination (98,109)	99 (94 to 100)	99 (95 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 25. Percentage of Subjects With hSBA ≥ 1:16 at 1 Month After Toddler MenACWY Vaccination - LA Subjects

End point title	25. Percentage of Subjects With hSBA ≥ 1:16 at 1 Month After Toddler MenACWY Vaccination - LA Subjects[64]

End point description:

End point type	Secondary

End point timeframe:

13 or 17 Months of Age (one month post-toddler vaccination)

Notes:

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

Justification: No statistical analysis is associated to this Endpoint. Analyses were run descriptively.

End point values	LA1A (MenACWY-CRM + Infant Vaccines)	LA3A (MenACWY-CRM + Infant Vaccines)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	122		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A Pre-vaccination (103, 120)	16 (9 to 24)	9 (5 to 16)		
A Post-vaccination (103,120)	93 (86 to 97)	94 (88 to 98)		
C Pre-vaccination (102,122)	47 (37 to 57)	18 (12 to 26)		
C Post-vaccination (102,122)	95 (89 to 98)	96 (91 to 99)		
W Pre-vaccination (98,112)	64 (54 to 74)	50 (40 to 60)		
W Post-vaccination (98,112)	99 (94 to 100)	100 (97 to 100)		
Y Pre-vaccination (98,109)	53 (43 to 63)	32 (23 to 42)		
Y Post-vaccination (98,109)	99 (94 to 100)	98 (94 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 26. Geometric Mean hSBA Titers at 1 Month After Toddler MenACWY Vaccination - LA Subjects

End point title	26. Geometric Mean hSBA Titers at 1 Month After Toddler MenACWY Vaccination - LA Subjects[65]

End point description:

End point type	Secondary

End point timeframe:

13 or 17 Months of Age (one month post-toddler vaccination)

Notes:

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

End point values	LA1A (MenACWY-CRM + Infant Vaccines)	LA3A (MenACWY-CRM + Infant Vaccines)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	122		
Units: Titers				
geometric mean (confidence interval 95%)				
A Pre-vaccination (103, 120)	3.83 (3.3 to 4.45)	2.95 (2.57 to 3.39)		

A Post-vaccination (103,120)	112 (85 to 148)	146 (113 to 188)		
C Pre-vaccination (102,122)	11 (8.91 to 13)	3.83 (3.2 to 4.6)		
C Post-vaccination (102,122)	279 (218 to 358)	283 (225 to 355)		
W Pre-vaccination (98,112)	28 (22 to 34)	13 (11 to 16)		
W Post-vaccination (98,112)	762 (604 to 960)	727 (586 to 903)		
Y Pre-vaccination (98,109)	16 (13 to 20)	8.1 (6.58 to 9.96)		
Y Post-vaccination (98,109)	550 (426 to 710)	590 (463 to 751)		

Statistical analyses

No statistical analyses for this end point

Secondary: 27. Geometric Mean Concentrations of Pneumococcal Antibodies at 1 Month After Toddler Vaccination - US Subjects

End point title	27. Geometric Mean Concentrations of Pneumococcal Antibodies at 1 Month After Toddler Vaccination - US Subjects[66]

End point description:

End point type	Secondary

End point timeframe:

13 months of age (one month post-toddler vaccination)

Notes:

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

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US1B (MenACWY-CRM + Infant Vaccines)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	99		
Units: Titers				
geometric mean (confidence interval 95%)				
PnC 4 (N=86, N=99)	2.9 (2.33 to 3.61)	3.24 (2.64 to 3.97)		
PnC 6B (N=86, N=99)	6.82 (5.67 to 8.21)	8.58 (7.22 to 10)		
PnC 9V (N=86, N=99)	2.8 (2.26 to 3.47)	3.13 (2.56 to 3.82)		
PnC 14 (N=86, N=99)	12 (9.74 to 14)	15 (12 to 17)		
PnC 18C (N=87, N=98)	2.76 (2.26 to 3.38)	2.71 (2.24 to 3.27)		
PnC 19F(N=86, N=99)	3.63 (3 to 4.39)	3.48 (2.92 to 4.16)		
PnC 23F (N=87, N=99)	5.31 (4.2 to 6.71)	5.63 (4.52 to 7.01)		

Statistical analyses

Statistical analysis title	PnC 4
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the ratio of pneumococcal GMCs (US1A / US1B) had to be greater than 0.50.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.2

Statistical analysis title	PnC 6B
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the ratio of pneumococcal GMCs (US1A / US1B) had to be greater than 0.50.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.02

Statistical analysis title	PnC 9V
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the ratio of pneumococcal GMCs (US1A / US1B) had to be greater than 0.50.	

Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.2

Statistical analysis title	PnC 14

Statistical analysis description:

To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the ratio of pneumococcal GMCs (US1A / US1B) had to be greater than 0.50.

Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.03

Statistical analysis title	PnC 18C

Statistical analysis description:

To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the ratio of pneumococcal GMCs (US1A / US1B) had to be greater than 0.50.

Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.34

Statistical analysis title	PnC 19F
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the ratio of pneumococcal GMCs (US1A / US1B) had to be greater than 0.50.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.34

Statistical analysis title	PnC 23F
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the ratio of pneumococcal GMCs (US1A / US1B) had to be greater than 0.50.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.29

Secondary: 28. Percentage of Subjects With Pneumococcal Antibody GMCs ≥1.0 µg/mL at 1 Month After Toddler Vaccination - US Subjects

End point title	28. Percentage of Subjects With Pneumococcal Antibody GMCs

	≥1.0 µg/mL at 1 Month After Toddler Vaccination - US

End point description:

End point type	Secondary

End point timeframe:

13 months of age (one month post-toddler vaccination)

Notes:

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

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US1B (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	99	81	
Units: Percentage of Subjects				
number (confidence interval 95%)				
PnC 4 (N=86, N=99, N=81)	91 (82 to 96)	90 (82 to 95)	84 (74 to 91)	
PnC 6B (N=86, N=99, N=80)	100 (96 to 100)	96 (90 to 99)	99 (93 to 100)	
PnC 9V (N=86, N=99, N=80)	87 (78 to 93)	91 (83 to 96)	86 (77 to 93)	
PnC 14 (N=86, N=99, N=81)	99 (94 to 100)	100 (96 to 100)	100 (96 to 100)	
PnC 18C (N=87, N=98, N=81)	86 (77 to 93)	92 (85 to 96)	94 (86 to 98)	
PnC 19F(N=86, N=99, N=80)	97 (90 to 99)	93 (86 to 97)	99 (93 to 100)	
PnC 23F (N=87, N=99, N=80)	93 (86 to 97)	95 (89 to 98)	99 (93 to 100)	

Statistical analyses

Statistical analysis title	PnC 4

Statistical analysis description:

To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the difference in rates (US1A - US1B) had to be greater than -10%.

Comparison groups	US1B (MenACWY-CRM + Infant Vaccines) v US1A (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	10

Statistical analysis title	PnC 6B
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the difference in rates (US1A - US1B) had to be greater than -10%.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	10

Statistical analysis title	PnC 9V
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the difference in rates (US1A - US1B) had to be greater than -10%.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	5

Statistical analysis title	PnC 14
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the difference in rates (US1A - US1B) had to be greater than -10%.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)

Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	3

Statistical analysis title	PnC 18C
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the difference in rates (US1A - US1B) had to be greater than -10%.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	3

Statistical analysis title	PnC 19F
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the difference in rates (US1A - US1B) had to be greater than -10%.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	11

Statistical analysis title	PnC 23F
Statistical analysis description:	
To assess non-inferiority of US1A over US1B, the lower limit of 95% CI for the difference in rates (US1A - US1B) had to be greater than -10%.	
Comparison groups	US1A (MenACWY-CRM + Infant Vaccines) v US1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	5

Secondary: 29. Geometric Mean Concentrations of Pneumococcal Antibodies at 1 Month After Toddler Vaccination – LA Subjects

End point title	29. Geometric Mean Concentrations of Pneumococcal Antibodies at 1 Month After Toddler Vaccination – LA Subjects[68]
End point description:	
End point type	Secondary
End point timeframe:	
13 months of age (one month post-toddler vaccination)	

Notes:

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

End point values	LA1A (MenACWY-CRM + Infant Vaccines)	LA1B (MenACWY-CRM + Infant Vaccines)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	97		
Units: Concentrations (µg/mL)				
geometric mean (confidence interval 95%)				
PnC 4 (N=97, N=97)	3.16 (2.63 to 3.8)	4.02 (3.34 to 4.83)		
PnC 6B (N=96, N=97)	4.52 (3.42 to 5.97)	5.61 (4.25 to 7.4)		
PnC 9V (N=97, N=97)	2.79 (2.34 to 3.31)	3.77 (3.17 to 4.48)		

PnC 14(N=97, N=97)	8.91 (7.52 to 11)	14 (12 to 16)		
PnC 18C (N=97, N=97)	2.15 (1.79 to 2.58)	2.77 (2.31 to 3.32)		
PnC 19F (N=97, N=97)	3.26 (2.62 to 4.05)	4.26 (3.43 to 5.29)		
PnC 23F (N=97, N=97)	4.38 (3.51 to 5.48)	5.92 (4.74 to 7.4)		

Statistical analyses

Statistical analysis title	PnC 4
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the ratio of pneumococcal GMCs (LA1A / LA1B) had to be greater than 0.50.	
Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.02

Statistical analysis title	PnC 6B
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the ratio of pneumococcal GMCs (LA1A / LA1B) had to be greater than 0.50.	
Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.2

Statistical analysis title	PnC 9V
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the ratio of pneumococcal GMCs (LA1A / LA1B) had to be greater than 0.50.	
Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.94

Statistical analysis title	PnC 14
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the ratio of pneumococcal GMCs (LA1A / LA1B) had to be greater than 0.50.	
Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.82

Statistical analysis title	PnC 18C
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the ratio of pneumococcal GMCs (LA1A / LA1B) had to be greater than 0.50.	
Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)

Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.01

Statistical analysis title	PnC 19F
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the ratio of pneumococcal GMCs (LA1A / LA1B) had to be greater than 0.50.	
Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.04

Statistical analysis title	PnC 23F
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the ratio of pneumococcal GMCs (LA1A / LA1B) had to be greater than 0.50.	
Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.01

Secondary: 30. Percentage of Subjects With Pneumococcal Antibody Concentration ≥1.0 µg/mL at 1 Month After Toddler Vaccination - LA Subjects

End point title	30. Percentage of Subjects With Pneumococcal Antibody Concentration ≥1.0 µg/mL at 1 Month After Toddler Vaccination - LA Subjects[69]

End point description:

End point type	Secondary

End point timeframe:

13 months of age (one month post-toddler vaccination)

Notes:

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

End point values	LA1A (MenACWY-CRM + Infant Vaccines)	LA1B (MenACWY-CRM + Infant Vaccines)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	97		
Units: Percentage of Subjects				
number (confidence interval 95%)				
PnC 4 (N=97, N=97)	93 (86 to 97)	95 (88 to 98)		
PnC 6B (N=96, N=97)	86 (78 to 93)	89 (81 to 94)		
PnC 9V (N=97, N=97)	92 (84 to 96)	95 (88 to 98)		
PnC 14(N=97, N=97)	99 (94 to 100)	100 (96 to 100)		
PnC 18C (N=97, N=97)	80 (71 to 88)	95 (88 to 98)		
PnC 19F (N=97, N=97)	90 (82 to 95)	93 (86 to 97)		
PnC 23F (N=97, N=97)	95 (88 to 98)	95 (88 to 98)		

Statistical analyses

Statistical analysis title	PnC 4

Statistical analysis description:

To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the difference in rates (LA1A - LA1B) had to be greater than -10%.

Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	5.2

Statistical analysis title	PnC 6B
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the difference in rates (LA1A - LA1B) had to be greater than -10%.	
Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.9
upper limit	7.3

Statistical analysis title	PnC 9V
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the difference in rates (LA1A - LA1B) had to be greater than -10%.	
Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.9
upper limit	4.3

Statistical analysis title	PnC 14
Statistical analysis description:	
To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the difference	

in rates (LA1A - LA1B) had to be greater than -10%.

Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	2.7

Statistical analysis title	PnC 18C

Statistical analysis description:

To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the difference in rates (LA1A - LA1B) had to be greater than -10%.

Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.1
upper limit	-5.6

Statistical analysis title	PnC 19F

Statistical analysis description:

To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the difference in rates (LA1A - LA1B) had to be greater than -10%.

Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.6
upper limit	5.2

Statistical analysis title	PnC 23F

Statistical analysis description:

To assess non-inferiority of LA1A over LA1B, the lower limit of the two-sided 95% CI for the difference in rates (LA1A - LA1B) had to be greater than -10%.

Comparison groups	LA1A (MenACWY-CRM + Infant Vaccines) v LA1B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	7

Secondary: 31. Geometric Mean Concentrations or Titers of DTaP and Hib Antigens at 1 Month After Toddler Vaccination - LA Subjects

End point title	31. Geometric Mean Concentrations or Titers of DTaP and Hib Antigens at 1 Month After Toddler Vaccination - LA Subjects[70]

End point description:

End point type	Secondary

End point timeframe:

17 months of age (one month post-toddler vaccination)

Notes:

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

End point values	LA3A (MenACWY-CRM + Infant Vaccines)	LA3B (MenACWY-CRM + Infant Vaccines)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	101		
Units: Titers				
geometric mean (confidence interval 95%)				
Diphtheria (N=118, N=101)	5.4 (4.74 to 6.15)	5.16 (4.48 to 5.94)		

Tetanus (N=118, N=101)	6.17 (5.29 to 7.2)	6.58 (5.57 to 7.77)		
PT (N=113, N=99)	68 (58 to 80)	62 (52 to 73)		
FHA (N=113, N=99)	245 (208 to 288)	215 (181 to 256)		
Pertactin (N=113, N=99)	238 (198 to 286)	197 (161 to 240)		
Hib (N=117, N=101)	35 (28 to 43)	41 (32 to 51)		

Statistical analyses

Statistical analysis title	Diphtheria

Statistical analysis description:

To assess non-inferiority of LA3A over LA3B, the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3A/LA3B) had to be greater than 0.67 for PT, FHA and pertactin and greater than 0.50 for Hib, diphtheria and tetanus.

Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.27

Statistical analysis title	Tetanus

Statistical analysis description:

To assess non-inferiority of LA3A over LA3B, the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3A/LA3B) had to be greater than 0.67 for PT, FHA and pertactin and greater than 0.50 for Hib, diphtheria and tetanus.

Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.18

Statistical analysis title	PT
Statistical analysis description:	
To assess non-inferiority of LA3A over LA3B, the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3A/LA3B) had to be greater than 0.67 for PT, FHA and pertactin and greater than 0.50 for Hib, diphtheria and tetanus.	
Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.4

Statistical analysis title	FHA
Statistical analysis description:	
To assess non-inferiority of LA3A over LA3B, the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3A/LA3B) had to be greater than 0.67 for PT, FHA and pertactin and greater than 0.50 for Hib, diphtheria and tetanus.	
Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.44

Statistical analysis title	Pertactin
Statistical analysis description:	
To assess non-inferiority of LA3A over LA3B, the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3A/LA3B) had to be greater than 0.67 for PT, FHA and pertactin and greater than 0.50 for Hib, diphtheria and tetanus.	
Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)

Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.59

Statistical analysis title	Hib

Statistical analysis description:

To assess non-inferiority of LA3A over LA3B, the lower limit of the two-sided 95% CI for the ratio of GMCs (LA3A/LA3B) had to be greater than 0.67 for PT, FHA and pertactin and greater than 0.50 for Hib, diphtheria and tetanus.

Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANOVA
Parameter estimate	Ratio of GMCs
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.16

Secondary: 32. Seroresponse Rates to DTaP and Hib Antigens at 1 Month After Toddler Vaccination - LA Subjects

End point title	32. Seroresponse Rates to DTaP and Hib Antigens at 1 Month After Toddler Vaccination - LA Subjects[71]

End point description:

End point type	Secondary

End point timeframe:

17 months of age (one month post-toddler vaccination)

Notes:

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

End point values	LA3A (MenACWY-CRM + Infant Vaccines)	LA3B (MenACWY-CRM + Infant Vaccines)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	101		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Diphtheria (≥1.0 IU/mL) (N=118, N=101)	98 (94 to 100)	98 (93 to 100)		
Tetanus (≥1.0 IU/mL) (N=118, N=101)	98 (94 to 100)	98 (93 to 100)		
PT (≥4 fold rise) (N=113, N=99)	89 (82 to 94)	84 (75 to 90)		
FHA (≥4-fold rise) (N=113, N=99)	87 (79 to 92)	88 (80 to 94)		
Pertactin (≥4-fold rise) (N=113, N=99)	89 (82 to 94)	88 (80 to 94)		
Hib (≥0.15 µg/mL) (N=117, N=101)	100 (97 to 100)	100 (96 to 100)		
Hib (≥1.0 µg/mL) (N=117, N=101)	100 (97 to 100)	99 (95 to 100)		

Statistical analyses

Statistical analysis title	Diphtheria
Statistical analysis description:	
To assess non-inferiority of LA3A over LA3B, The lower limit of the two-sided 95% CI for the difference (LA3A-LA3B) in percentages of subjects with seroresponse against diphtheria, tetanus, Hib and pertussis antigens (except FHA for ≥4 fold rise) was greater than -10%	
Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	5.4

Statistical analysis title	Tetanus
Statistical analysis description:	
To assess non-inferiority of LA3A over LA3B, The lower limit of the two-sided 95% CI for the difference (LA3A-LA3B) in percentages of subjects with seroresponse against diphtheria, tetanus, Hib and pertussis antigens (except FHA for ≥4 fold rise) was greater than -10%	
Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)

Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	5.4

Statistical analysis title	PT

Statistical analysis description:

To assess non-inferiority of LA3A over LA3B, The lower limit of the two-sided 95% CI for the difference (LA3A-LA3B) in percentages of subjects with seroresponse against diphtheria, tetanus, Hib and pertussis antigens (except FHA for ≥4 fold rise) was greater than -10%

Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	15.2

Statistical analysis title	FHA

Statistical analysis description:

To assess non-inferiority of LA3A over LA3B, The lower limit of the two-sided 95% CI for the difference (LA3A-LA3B) in percentages of subjects with seroresponse against diphtheria, tetanus, Hib and pertussis antigens (except FHA for ≥4 fold rise) was greater than -10%

Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	8.2

Statistical analysis title	Pertactin

Statistical analysis description:

To assess non-inferiority of LA3A over LA3B, The lower limit of the two-sided 95% CI for the difference (LA3A-LA3B) in percentages of subjects with seroresponse against diphtheria, tetanus, Hib and pertussis antigens (except FHA for ≥4 fold rise) was greater than -10%

Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	10.6

Statistical analysis title	Hib (≥ 0.15 µg/mL)

Statistical analysis description:

To assess non-inferiority of LA3A over LA3B, The lower limit of the two-sided 95% CI for the difference (LA3A-LA3B) in percentages of subjects with seroresponse against diphtheria, tetanus, Hib and pertussis antigens (except FHA for ≥4 fold rise) was greater than -10%

Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	3.6

Statistical analysis title	Hib (≥1.0 µg/mL)

Statistical analysis description:

To assess non-inferiority of LA3A over LA3B, The lower limit of the two-sided 95% CI for the difference (LA3A-LA3B) in percentages of subjects with seroresponse against diphtheria, tetanus, Hib and pertussis antigens (except FHA for ≥4 fold rise) was greater than -10%

Comparison groups	LA3A (MenACWY-CRM + Infant Vaccines) v LA3B (MenACWY-CRM + Infant Vaccines)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen CI
Parameter estimate	Percentage Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	5.3

Secondary: 33. Percentage of Subjects With hSBA ≥1:8 at 1 Month After 1st (LA2) or 2nd (LA4) Toddler MenACWY Vaccination - LA Subjects

End point title	33. Percentage of Subjects With hSBA ≥1:8 at 1 Month After 1st (LA2) or 2nd (LA4) Toddler MenACWY Vaccination - LA Subjects[72]

End point description:

End point type	Secondary

End point timeframe:

13 or 16 months of age (one month post 1st or 2nd toddler vaccination)

Notes:

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

End point values	LA2 (Infant Vaccines Only)	LA4 (Infant Vaccines Only)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	102		
Units: Percentage of Subjects				
number (confidence interval 95%)				
A Pre-vaccination (78, 101)	0 (0 to 5)	0 (0 to 4)		
A Post-vaccination ((78, 101)	74 (63 to 84)	97 (92 to 99)		
C Pre-vaccination (78, 102)	4 (1 to 11)	1 (0.025 to 5)		
C Post-vaccination (78, 102)	91 (82 to 96)	100 (96 to 100)		
W Pre-vaccination (70, 98)	4 (1 to 12)	5 (2 to 12)		
W Post-vaccination (70, 98)	79 (67 to 87)	100 (96 to 100)		
Y Pre-vaccination (71, 95)	3 (0 to 10)	0 (0 to 4)		
Y Post-vaccination (71, 95)	72 (60 to 82)	100 (96 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 34. Geometric Mean hSBA Titers at 1 Month After 1st (LA2) or 2nd (LA4) Toddler MenACWY Vaccination - LA Subjects

End point title	34. Geometric Mean hSBA Titers at 1 Month After 1st (LA2) or 2nd (LA4) Toddler MenACWY Vaccination - LA Subjects[73]

End point description:

End point type	Secondary

End point timeframe:

13 or 16 months of age (one month post 1st or 2nd toddler vaccination)

Notes:

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

End point values	LA2 (Infant Vaccines Only)	LA4 (Infant Vaccines Only)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	102		
Units: Titers				
geometric mean (confidence interval 95%)				
A Pre-vaccination (78, 101)	2.02 (1.7 to 2.4)	2.02 (1.74 to 2.35)		
A Post-vaccination (78, 101)	25 (18 to 34)	128 (97 to 169)		
C Pre-vaccination (78, 102)	2.18 (1.73 to 2.74)	2.05 (1.68 to 2.51)		
C Post-vaccination (78, 102)	45 (34 to 60)	501 (391 to 643)		
W Pre-vaccination (70, 98)	2.34 (1.79 to 3.05)	2.33 (1.86 to 2.91)		
W Post-vaccination (70, 98)	22 (16 to 28)	394 (313 to 497)		
Y Pre-vaccination (71, 95)	2.2 (1.7 to 2.84)	2.04 (1.64 to 2.55)		
Y Post-vaccination (71, 95)	15 (11 to 20)	329 (254 to 426)		

Statistical analyses

No statistical analyses for this end point

Secondary: 35. Number of Subjects With Solicited Local and Systemic Reactions Post First Vaccination – Infant Series

End point title	35. Number of Subjects With Solicited Local and Systemic Reactions Post First Vaccination – Infant Series[74]

End point description:

End point type	Secondary

End point timeframe:

7 days after vaccination

Notes:

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

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US1B (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)	US3 (MenACWY-CRM + Infant Vaccines)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	153	165	159	677
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	10	17	23	66
Erythema (mm) - Severe	0	0	2	0
Induration (mm) - Any	10	14	25	61
Induration (mm) - Severe	0	0	0	0
Tenderness - Any	64	76	69	324
Tenderness - Severe	3	4	6	25
Body Temp. (>= 38° C)	13	6	7	32
Change in Eating Habits - Any	42	46	34	171
Change in Eating Habits - Severe	1	1	1	8
Diarrhea - Any	24	23	17	107
Diarrhea - Severe	2	0	1	3
Irritability - Any	82	107	96	419
Irritability - Severe	6	2	4	24
Persistent Crying - Any	43	74	49	252
Persistent Crying - Severe	1	2	5	11
Rash - Any	6	9	5	16
Rash - Severe	3	4	3	4
Sleepiness - Any	83	104	76	354
Sleepiness - Severe	2	3	0	14
Vomiting - Any	15	18	14	67
Vomiting - Severe	0	0	0	0
Analgesic / Antipyretic medication used	105	120	110	447

End point values	LA2 (Infant Vaccines Only)	LA4 (Infant Vaccines Only)	LA5 (MenACWY-CRM + Infant Vaccines)	US4 Safety Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	148	150	1424	345

Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	62	65	542	54
Erythema (mm) - Severe	0	1	1	4
Induration (mm) - Any	56	53	249	44
Induration (mm) - Severe	0	0	2	1
Tenderness - Any	96	95	916	161
Tenderness - Severe	19	20	92	19
Body Temp. (>= 38° C)	12	5	211	21
Change in Eating Habits - Any	30	16	250	96
Change in Eating Habits - Severe	0	1	6	2
Diarrhea - Any	20	22	222	46
Diarrhea - Severe	0	0	2	1
Irritability - Any	62	59	508	211
Irritability - Severe	2	2	22	12
Persistent Crying - Any	53	43	479	125
Persistent Crying - Severe	3	8	29	8
Rash - Any	6	4	98	11
Rash - Severe	2	1	54	3
Sleepiness - Any	53	52	727	173
Sleepiness - Severe	2	4	21	3
Vomiting - Any	9	17	215	36
Vomiting - Severe	0	1	2	1
Analgesic / Antipyretic medication used	75	80	996	223

End point values	LA6 Safety Set	US1 Safety Set	LA1 Safety Set	LA3 Safety Set
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	709	318	301	301
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	273	27	86	86
Erythema (mm) - Severe	4	0	0	1
Induration (mm) - Any	126	24	74	72
Induration (mm) - Severe	0	0	1	0
Tenderness - Any	501	140	154	170
Tenderness - Severe	74	7	30	22
Body Temp. (>= 38° C)	97	19	15	18
Change in Eating Habits - Any	127	88	37	44
Change in Eating Habits - Severe	4	2	2	0
Diarrhea - Any	96	47	42	44
Diarrhea - Severe	2	2	1	1
Irritability - Any	240	189	121	99
Irritability - Severe	2	8	7	4
Persistent Crying - Any	258	117	95	87
Persistent Crying - Severe	21	3	5	11
Rash - Any	55	15	11	12
Rash - Severe	26	7	7	4
Sleepiness - Any	381	187	106	93
Sleepiness - Severe	14	5	8	6

Vomiting - Any	100	33	25	29
Vomiting - Severe	1	0	0	1
Analgesic / Antipyretic medication used	510	225	155	159

Statistical analyses

No statistical analyses for this end point

Secondary: 36. Number of Subjects With Solicited Local and Systemic Reactions Post Second Vaccination – Infant Series

End point title	36. Number of Subjects With Solicited Local and Systemic Reactions Post Second Vaccination – Infant Series[75]

End point description:

End point type	Secondary

End point timeframe:

7 days after vaccination

Notes:

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

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US1B (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)	US3 (MenACWY-CRM + Infant Vaccines)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	141	150	151	645
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	14	19	35	75
Erythema (mm) - Severe	0	0	0	0
Induration (mm) - Any	16	16	27	45
Induration (mm) - Severe	1	0	0	0
Tenderness - Any	59	59	56	230
Tenderness - Severe	1	0	2	13
Body Temp. (>= 38° C)	17	6	15	49
Change in Eating Habits - Any	25	21	20	122
Change in Eating Habits - Severe	0	0	0	3
Diarrhea - Any	16	10	11	53
Diarrhea - Severe	0	1	1	1
Irritability - Any	83	80	83	342
Irritability - Severe	2	0	3	14
Persistent Crying - Any	42	41	34	178
Persistent Crying - Severe	0	0	0	5
Rash - Any	3	5	4	24
Rash - Severe	3	1	1	6
Sleepiness - Any	69	56	47	238
Sleepiness - Severe	0	0	1	3
Vomiting - Any	8	9	7	49

Vomiting - Severe	0	0	0	0
Analgesic / Antipyretic medication used	94	91	96	385

End point values	LA4 (Infant Vaccines Only)	LA5 (MenACWY-CRM + Infant Vaccines)	US4 Safety Set	LA6 Safety Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	150	1424	325	709
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	45	583	60	311
Erythema (mm) - Severe	0	0	2	0
Induration (mm) - Any	36	194	48	126
Induration (mm) - Severe	0	0	3	0
Tenderness - Any	59	726	137	401
Tenderness - Severe	5	49	11	45
Body Temp. (>= 38° C)	13	223	28	122
Change in Eating Habits - Any	12	160	64	90
Change in Eating Habits - Severe	0	6	0	5
Diarrhea - Any	14	149	35	90
Diarrhea - Severe	0	4	2	1
Irritability - Any	41	414	182	209
Irritability - Severe	0	13	9	5
Persistent Crying - Any	22	294	107	187
Persistent Crying - Severe	1	14	4	10
Rash - Any	2	97	13	46
Rash - Severe	1	52	4	29
Sleepiness - Any	26	485	131	237
Sleepiness - Severe	1	13	2	7
Vomiting - Any	10	136	27	75
Vomiting - Severe	0	3	1	0
Analgesic / Antipyretic medication used	61	857	201	430

End point values	US1 Safety Set	LA3 Safety Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	291	301		
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	33	92		
Erythema (mm) - Severe	0	0		
Induration (mm) - Any	32	73		
Induration (mm) - Severe	1	0		
Tenderness - Any	118	115		
Tenderness - Severe	1	13		
Body Temp. (>= 38° C)	23	23		
Change in Eating Habits - Any	46	28		

Change in Eating Habits - Severe	0	3		
Diarrhea - Any	26	28		
Diarrhea - Severe	1	1		
Irritability - Any	163	82		
Irritability - Severe	2	3		
Persistent Crying - Any	83	42		
Persistent Crying - Severe	0	4		
Rash - Any	8	13		
Rash - Severe	4	5		
Sleepiness - Any	125	62		
Sleepiness - Severe	0	4		
Vomiting - Any	17	20		
Vomiting - Severe	0	1		
Analgesic / Antipyretic medication used	185	131		

Statistical analyses

No statistical analyses for this end point

Secondary: 37. Number of Subjects With Solicited Local and Systemic Reactions Post Third Vaccination – Infant Series

End point title	37. Number of Subjects With Solicited Local and Systemic Reactions Post Third Vaccination – Infant Series[76]

End point description:

End point type	Secondary

End point timeframe:

7 days after vaccination

Notes:

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

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US1B (MenACWY-CRM + Infant Vaccines)	US2 (Infant Vaccines Only)	US3 (MenACWY-CRM + Infant Vaccines)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	138	145	143	627
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	16	18	28	92
Erythema (mm) - Severe	0	0	1	0
Induration (mm) - Any	15	15	29	59
Induration (mm) - Severe	0	0	2	0
Tenderness - Any	37	45	45	189
Tenderness - Severe	0	0	1	1
Body Temp. (>= 38° C)	4	9	14	33
Change in Eating Habits - Any	19	22	18	94
Change in Eating Habits - Severe	0	0	1	3

Diarrhea - Any	13	9	9	41
Diarrhea - Severe	0	0	0	2
Irritability - Any	58	73	70	285
Irritability - Severe	1	1	0	4
Persistent Crying - Any	28	26	24	135
Persistent Crying - Severe	0	0	0	4
Rash - Any	2	9	4	14
Rash - Severe	1	4	3	2
Sleepiness - Any	37	41	39	179
Sleepiness - Severe	0	0	0	6
Vomiting - Any	6	6	9	31
Vomiting - Severe	0	0	0	0
Analgesic / Antipyretic medication used	75	82	96	349

End point values	LA2 (Infant Vaccines Only)	LA4 (Infant Vaccines Only)	LA5 (MenACWY-CRM + Infant Vaccines)	US4 Safety Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	131	147	1357	311
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	27	38	485	67
Erythema (mm) - Severe	0	0	1	1
Induration (mm) - Any	25	32	125	53
Induration (mm) - Severe	0	0	0	1
Tenderness - Any	40	50	504	92
Tenderness - Severe	2	1	21	7
Body Temp. (>= 38° C)	10	14	164	20
Change in Eating Habits - Any	11	9	126	39
Change in Eating Habits - Severe	1	0	5	2
Diarrhea - Any	8	11	97	26
Diarrhea - Severe	1	0	2	1
Irritability - Any	29	28	311	157
Irritability - Severe	1	0	5	6
Persistent Crying - Any	15	12	181	74
Persistent Crying - Severe	2	0	11	4
Rash - Any	1	1	62	8
Rash - Severe	0	1	29	1
Sleepiness - Any	15	17	317	91
Sleepiness - Severe	0	0	6	1
Vomiting - Any	9	12	104	20
Vomiting - Severe	1	0	1	1
Analgesic / Antipyretic medication used	38	51	592	178

End point values	LA6 Safety Set	US1 Safety Set	LA1 Safety Set	LA3 Safety Set

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	679	283	297	290
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	273	34	69	64
Erythema (mm) - Severe	1	0	0	1
Induration (mm) - Any	73	30	54	64
Induration (mm) - Severe	0	0	0	1
Tenderness - Any	306	82	92	78
Tenderness - Severe	14	0	6	2
Body Temp. (>= 38° C)	101	13	13	26
Change in Eating Habits - Any	66	41	25	23
Change in Eating Habits - Severe	3	0	1	1
Diarrhea - Any	58	22	17	12
Diarrhea - Severe	3	0	1	0
Irritability - Any	164	131	57	62
Irritability - Severe	2	2	0	2
Persistent Crying - Any	118	54	28	27
Persistent Crying - Severe	2	0	2	0
Rash - Any	29	11	8	6
Rash - Severe	10	5	5	3
Sleepiness - Any	164	78	38	45
Sleepiness - Severe	3	0	1	1
Vomiting - Any	52	12	16	11
Vomiting - Severe	1	0	2	1
Analgesic / Antipyretic medication used	342	157	93	90

Statistical analyses

No statistical analyses for this end point

Secondary: 38. Number of Subjects With Solicited Local and Systemic Reactions After Vaccination at 12 Months of Age

End point title	38. Number of Subjects With Solicited Local and Systemic Reactions After Vaccination at 12 Months of Age[77]

End point description:

End point type	Secondary

End point timeframe:

7 days after vaccination

Notes:

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

Justification: No statistical analysis is associated to this Endpoint. Analyses were run descriptively.

End point values	US1A (MenACWY-CRM + Infant Vaccines)	US1B (MenACWY-CRM + Infant Vaccines)	US3 (MenACWY-CRM + Infant Vaccines)	LA1A (MenACWY-CRM + Infant Vaccines)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	122	124	582	145
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	11	16	70	36
Erythema (mm) - Severe	0	0	2	0
Induration (mm) - Any	10	13	34	32
Induration (mm) - Severe	0	0	0	0
Tenderness - Any	28	31	149	35
Tenderness - Severe	0	0	2	6
Body Temp. (>= 38° C)	14	10	35	16
Change in Eating Habits - Any	21	17	80	10
Change in Eating Habits - Severe	1	2	6	1
Diarrhea - Any	5	14	56	9
Diarrhea - Severe	0	0	4	0
Irritability - Any	53	53	218	29
Irritability - Severe	2	2	6	1
Persistent Crying - Any	21	21	99	7
Persistent Crying - Severe	0	0	6	0
Rash - Any	8	4	23	3
Rash - Severe	1	1	2	2
Sleepiness - Any	38	29	111	18
Sleepiness - Severe	0	1	3	0
Vomiting - Any	6	4	21	3
Vomiting - Severe	0	0	1	0
Analgesic / Antipyretic medication used	60	56	260	48

End point values	LA1B (MenACWY-CRM + Infant Vaccines)	LA5 (MenACWY-CRM + Infant Vaccines)	US4B+US4C Safety Set	US1A + US3 Safety Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	143	1275	261	704
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	33	309	49	81
Erythema (mm) - Severe	1	0	1	2
Induration (mm) - Any	28	84	39	44
Induration (mm) - Severe	1	0	1	0
Tenderness - Any	32	392	75	177
Tenderness - Severe	2	8	1	2
Body Temp. (>= 38° C)	12	188	20	49
Change in Eating Habits - Any	11	138	29	101
Change in Eating Habits - Severe	0	5	1	7
Diarrhea - Any	10	123	14	61
Diarrhea - Severe	0	7	1	4
Irritability - Any	23	289	103	271

Irritability - Severe	2	3	1	8
Persistent Crying - Any	12	134	55	120
Persistent Crying - Severe	1	2	1	6
Rash - Any	1	65	12	31
Rash - Severe	0	36	3	3
Sleepiness - Any	15	211	50	149
Sleepiness - Severe	0	3	3	3
Vomiting - Any	5	82	11	27
Vomiting - Severe	0	4	0	1
Analgesic / Antipyretic medication used	43	406	120	320

End point values	US2+US4A Safety Set	LA2+LA4+LA6 A Safety Set	LA6B+LA6C Safety Set	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	137	564	349	
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	18	166	67	
Erythema (mm) - Severe	1	2	0	
Induration (mm) - Any	12	72	43	
Induration (mm) - Severe	0	1	0	
Tenderness - Any	38	184	100	
Tenderness - Severe	0	2	3	
Body Temp. (>= 38° C)	12	84	40	
Change in Eating Habits - Any	20	56	46	
Change in Eating Habits - Severe	1	4	0	
Diarrhea - Any	16	51	37	
Diarrhea - Severe	1	5	1	
Irritability - Any	62	130	74	
Irritability - Severe	4	5	0	
Persistent Crying - Any	24	52	28	
Persistent Crying - Severe	1	0	0	
Rash - Any	5	20	17	
Rash - Severe	3	8	10	
Sleepiness - Any	22	81	53	
Sleepiness - Severe	1	1	2	
Vomiting - Any	8	35	12	
Vomiting - Severe	0	3	0	
Analgesic / Antipyretic medication used	78	204	87	

Statistical analyses

No statistical analyses for this end point

Secondary: 39. Number of Subjects With Solicited Local and Systemic Reactions Post First Vaccination – Toddler Series

End point title	39. Number of Subjects With Solicited Local and Systemic

	Reactions Post First Vaccination – Toddler Series[78]

End point description:

End point type	Secondary

End point timeframe:

7 days post vaccination

Notes:

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

End point values	US1B (MenACWY-CRM + Infant Vaccines)	US4B (Infant Vaccines Only)	US4C (Infant Vaccines Only)	LA1A (MenACWY-CRM + Infant Vaccines)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	120	59	179	145
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	7	9	28	36
Erythema (mm) - Severe	0	0	1	0
Induration (mm) - Any	1	3	14	32
Induration (mm) - Severe	0	0	0	0
Tenderness - Any	16	10	38	35
Tenderness - Severe	0	1	1	6
Body Temp. (>= 38° C)	5	0	5	16
Change in Eating Habits - Any	9	5	14	10
Change in Eating Habits - Severe	0	0	1	1
Diarrhea - Any	8	5	13	9
Diarrhea - Severe	0	2	1	0
Irritability - Any	39	17	52	29
Irritability - Severe	1	1	1	1
Persistent Crying - Any	16	10	17	7
Persistent Crying - Severe	0	1	1	0
Rash - Any	1	2	5	3
Rash - Severe	0	0	2	2
Sleepiness - Any	25	6	21	18
Sleepiness - Severe	1	0	0	0
Vomiting - Any	2	2	6	3
Vomiting - Severe	0	0	0	0
Analgesic / Antipyretic medication used	37	16	45	48

End point values	LA1B (MenACWY-CRM + Infant Vaccines)	LA3A (MenACWY-CRM + Infant Vaccines)	LA3B (MenACWY-CRM + Infant Vaccines)	LA5 (MenACWY-CRM + Infant Vaccines)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	143	142	137	1275
Units: Subjects				
number (not applicable)				

Erythema (mm) - Any	17	36	19	309
Erythema (mm) - Severe	1	1	1	0
Induration (mm) - Any	9	33	16	84
Induration (mm) - Severe	1	1	1	0
Tenderness - Any	21	36	18	392
Tenderness - Severe	1	2	2	8
Body Temp. (>= 38° C)	5	4	2	188
Change in Eating Habits - Any	4	6	6	138
Change in Eating Habits - Severe	1	1	0	5
Diarrhea - Any	4	8	2	123
Diarrhea - Severe	0	0	1	7
Irritability - Any	10	13	9	289
Irritability - Severe	0	0	0	3
Persistent Crying - Any	5	4	5	134
Persistent Crying - Severe	0	0	0	2
Rash - Any	1	2	1	65
Rash - Severe	1	2	0	36
Sleepiness - Any	3	6	7	211
Sleepiness - Severe	1	0	0	3
Vomiting - Any	0	1	3	82
Vomiting - Severe	0	0	0	4
Analgesic / Antipyretic medication used	15	20	8	406

End point values	LA6B (Infant Vaccines Only)	LA6C (Infant Vaccines Only)	US1A + US3 Safety Set	US2+US4A Safety Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	160	175	704	136
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	24	52	81	18
Erythema (mm) - Severe	0	7	2	1
Induration (mm) - Any	5	35	44	12
Induration (mm) - Severe	0	5	0	0
Tenderness - Any	34	45	177	38
Tenderness - Severe	0	5	2	0
Body Temp. (>= 38° C)	7	8	49	12
Change in Eating Habits - Any	9	17	101	20
Change in Eating Habits - Severe	0	0	7	1
Diarrhea - Any	6	12	61	16
Diarrhea - Severe	0	0	4	1
Irritability - Any	25	28	271	62
Irritability - Severe	1	0	8	4
Persistent Crying - Any	9	15	120	24
Persistent Crying - Severe	1	0	6	1
Rash - Any	2	2	31	5
Rash - Severe	0	1	3	3
Sleepiness - Any	14	20	149	22
Sleepiness - Severe	1	1	3	1
Vomiting - Any	4	3	27	8

Vomiting - Severe	0	0	1	0
Analgesic / Antipyretic medication used	14	34	320	77

End point values	LA2+LA4+LA6 A Safety Set			
Subject group type	Subject analysis set			
Number of subjects analysed	564			
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	166			
Erythema (mm) - Severe	2			
Induration (mm) - Any	72			
Induration (mm) - Severe	1			
Tenderness - Any	184			
Tenderness - Severe	2			
Body Temp. (>= 38° C)	84			
Change in Eating Habits - Any	56			
Change in Eating Habits - Severe	4			
Diarrhea - Any	51			
Diarrhea - Severe	5			
Irritability - Any	130			
Irritability - Severe	5			
Persistent Crying - Any	52			
Persistent Crying - Severe	0			
Rash - Any	20			
Rash - Severe	8			
Sleepiness - Any	81			
Sleepiness - Severe	1			
Vomiting - Any	35			
Vomiting - Severe	3			
Analgesic / Antipyretic medication used	204			

Statistical analyses

No statistical analyses for this end point

Secondary: 40. Number of Subjects With Solicited Local and Systemic Reactions Post Second Vaccination – Toddler Series

End point title	40. Number of Subjects With Solicited Local and Systemic Reactions Post Second Vaccination – Toddler Series[79]

End point description:

End point type	Secondary

End point timeframe:

7 days post vaccination

Notes:

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

Justification: No statistical analysis is associated to this Endpoint. Analyses were run descriptively.

End point values	US4B (Infant Vaccines Only)	LA6B (Infant Vaccines Only)	US2+US4A Safety Set	LA2+LA4+LA6 A Safety Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	55	153	120	539
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	6	28	14	143
Erythema (mm) - Severe	1	0	0	2
Induration (mm) - Any	2	2	10	51
Induration (mm) - Severe	1	0	0	1
Tenderness - Any	16	33	19	128
Tenderness - Severe	0	1	0	5
Body Temp. (>= 38° C)	1	15	5	30
Change in Eating Habits - Any	2	11	7	18
Change in Eating Habits - Severe	0	1	0	0
Diarrhea - Any	3	9	4	28
Diarrhea - Severe	0	0	1	1
Irritability - Any	22	32	31	71
Irritability - Severe	0	1	0	2
Persistent Crying - Any	10	6	9	37
Persistent Crying - Severe	0	2	0	3
Rash - Any	1	3	4	9
Rash - Severe	0	3	0	4
Sleepiness - Any	8	12	12	36
Sleepiness - Severe	0	2	0	1
Vomiting - Any	2	7	5	12
Vomiting - Severe	0	0	0	0
Analgesic / Antipyretic medication used	14	21	40	85

Statistical analyses

No statistical analyses for this end point

Secondary: 41. Number of Subjects With Solicited Local and Systemic Reactions Post First Vaccination – Infant Series

End point title	41. Number of Subjects With Solicited Local and Systemic Reactions Post First Vaccination – Infant Series

End point description:

End point type	Secondary

End point timeframe:

7 days post vaccination

End point values	US1+US3 Safety Set	US2+US4 Safety Set	LA3+LA5 Safety Set	LA4+LA6 Safety Set
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	989	503	1724	859
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	93	77	628	338
Erythema (mm) - Severe	0	6	2	5
Induration (mm) - Any	85	69	321	179
Induration (mm) - Severe	0	1	2	0
Tenderness - Any	464	230	1086	596
Tenderness - Severe	32	25	114	94
Body Temp. (>= 38° C)	51	28	229	102
Change in Eating Habits - Any	259	130	294	143
Change in Eating Habits - Severe	10	3	6	5
Diarrhea - Any	154	63	266	118
Diarrhea - Severe	5	2	3	2
Irritability - Any	608	307	607	299
Irritability - Severe	32	16	26	4
Persistent Crying - Any	369	174	566	301
Persistent Crying - Severe	14	13	40	29
Rash - Any	31	16	110	59
Rash - Severe	11	6	58	27
Sleepiness - Any	541	249	820	433
Sleepiness - Severe	19	3	27	18
Vomiting - Any	100	50	244	117
Vomiting - Severe	0	1	3	2
Analgesic / Antipyretic medication used	672	333	1155	590

Statistical analyses

No statistical analyses for this end point

Secondary: 42. Number of Subjects With Solicited Local and Systemic Reactions Post Second Vaccination – Infant Series

End point title	42. Number of Subjects With Solicited Local and Systemic Reactions Post Second Vaccination – Infant Series

End point description:

End point type	Secondary

End point timeframe:

7 days post vaccination

End point values	US1+US3 Safety Set	US2+US4 Safety Set	LA3+LA5 Safety Set	LA4+LA6 Safety Set
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	936	476	1672	824
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	108	95	675	356
Erythema (mm) - Severe	0	2	0	0
Induration (mm) - Any	77	75	267	162
Induration (mm) - Severe	1	3	0	0
Tenderness - Any	348	193	841	460
Tenderness - Severe	14	13	62	50
Body Temp. (>= 38° C)	72	43	246	135
Change in Eating Habits - Any	168	84	188	102
Change in Eating Habits - Severe	3	0	9	5
Diarrhea - Any	79	46	177	104
Diarrhea - Severe	2	3	5	1
Irritability - Any	505	265	496	250
Irritability - Severe	16	12	16	5
Persistent Crying - Any	261	141	336	209
Persistent Crying - Severe	5	4	18	11
Rash - Any	32	17	110	48
Rash - Severe	10	5	57	30
Sleepiness - Any	363	178	547	263
Sleepiness - Severe	3	3	17	8
Vomiting - Any	66	34	156	85
Vomiting - Severe	0	1	4	0
Analgesic / Antipyretic medication used	570	297	988	491

Statistical analyses

No statistical analyses for this end point

Secondary: 43. Number of Subjects With Solicited Local and Systemic Reactions Post Third Vaccination – Infant Series

End point title	43. Number of Subjects With Solicited Local and Systemic Reactions Post Third Vaccination – Infant Series

End point description:

End point type	Secondary

End point timeframe:

7 days post vaccination

End point values	US1+US3 Safety Set	US2+US4 Safety Set	LA3+LA5 Safety Set	LA4+LA6 Safety Set
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	910	454	1646	826
Units: Subjects				
number (not applicable)				
Erythema (mm) - Any	126	95	549	311
Erythema (mm) - Severe	0	2	2	1
Induration (mm) - Any	89	82	189	105
Induration (mm) - Severe	0	3	1	0
Tenderness - Any	271	137	582	356
Tenderness - Severe	1	8	23	15
Body Temp. (>= 38° C)	46	34	190	115
Change in Eating Habits - Any	135	57	149	75
Change in Eating Habits - Severe	3	3	6	3
Diarrhea - Any	63	35	109	69
Diarrhea - Severe	2	1	2	3
Irritability - Any	416	227	373	192
Irritability - Severe	6	6	7	2
Persistent Crying - Any	189	98	208	130
Persistent Crying - Severe	4	4	11	2
Rash - Any	25	12	68	30
Rash - Severe	7	4	32	11
Sleepiness - Any	257	130	362	181
Sleepiness - Severe	6	1	7	3
Vomiting - Any	43	29	115	64
Vomiting - Severe	0	1	2	1
Analgesic / Antipyretic medication used	506	274	682	393

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Throughout the study

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	LA2+4+6AB

Reporting group description:

Groups Infant Vaccines only (LA2, LA4, LA6A and LA6B) pooled. In all groups LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants either received: one dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and a second dose of MenACWY at 15 months of age (LA2 and LA4), or received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and one dose each of MenACWY at 12 and 15 months of age (LA6A); or one dose each of MenACWY at 13 and 15 months of age (LA6B).

Reporting group title	LA1+LA3+LA5

Reporting group description:

Groups Men ACWY-CRM + Infant Vaccines (LA1, LA3 and LA5) pooled
LA1 infants received MenACWY at 2 and 6 months of age; and DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received at 12 months of age pneumococcal conjugate vaccine, HAV, and MMR-V and concomitant third dose of MenACWY (LA1A) or a third dose of MenACWY at 13 months of age (LA1B).
LA 3 and LA5 infants received MenACWY, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. At 12 months of age these infants received pneumococcal conjugate vaccine, HAV, and MMR-V and received:
1. Fourth dose of MenACWY concomitantly with DTaP and Hib at 16 months of age (LA3A)
2. DTaP and Hib at 16 months and fourth dose of MenACWY at 17 months of age (LA3B).
3. Concomitantly the fourth dose of MenACWY (LA5).

Reporting group title	LA6C

Reporting group description:

LA infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus, and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These infants received concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and one dose of MenACWY at 18 months of age.

Reporting group title	US2+US4A+US4B

Reporting group description:

Groups Infant Vaccines only (US2, US4A, and US4B) pooled.
In both groups US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines at 2, 4 and 6 months of age. These infants received:
1. One dose of MenACWY concomitantly with pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months; and a second dose of MenACWY at 15 months of age (US2 and US4A).
2. Concomitant pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and one dose of MenACWY at 13 and a second dose of MenACWY at 15 months of age (US4B).

Reporting group title	US1+US3

Reporting group description:

Groups MenACWY-CRM + Infant Vaccines (US1 +US3) pooled. US infants received MenACWY at 2, 4 and 6 months of age along with routine infant vaccines, DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccine. These infants either received a fourth dose of MenACWY concomitantly with pneumococcal, HAV, and MMR-V vaccines at 12 months of age (US1A and US3) or received pneumococcal conjugate vaccine, HAV, and MMR-V at 12 months and a fourth dose of MenACWY at 13 months of age(US1B).

Reporting group title	US4C

Reporting group description:

US infants received as part of routine infant vaccination schedule DTaP-IPV-HBV, Hib, rotavirus and pneumococcal conjugate vaccines, at 2, 4 and 6 months of age. These subjects received concomitant

Serious adverse events	LA2+4+6AB	LA1+LA3+LA5	LA6C
Total subjects affected by serious adverse events			
subjects affected / exposed	84 / 824 (10.19%)	173 / 2026 (8.54%)	12 / 183 (6.56%)
number of deaths (all causes)	0	3	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
BRAIN NEOPLASM			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
Vascular disorders			
KAWASAKI'S DISEASE			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
Surgical and medical procedures			
INTESTINAL OPERATION			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
OEDEMA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
PYREXIA			

subjects affected / exposed	5 / 824 (0.61%)	5 / 2026 (0.25%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
FOOD ALLERGY			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
HYPOGAMMAGLOBULINAEMIA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
APNOEA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
ASTHMA			
subjects affected / exposed	3 / 824 (0.36%)	6 / 2026 (0.30%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHIAL HYPERREACTIVITY			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOSPASM			
subjects affected / exposed	2 / 824 (0.24%)	5 / 2026 (0.25%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CHOKING			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
HYPOXIA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
LARYNGOSPASM			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
PULMONARY HYPERTENSION			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY DISORDER			
subjects affected / exposed	0 / 824 (0.00%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
STATUS ASTHMATICUS			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
TACHYPNOEA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
WHEEZING			

subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ACCIDENTAL DRUG INTAKE BY CHILD			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
ACCIDENTAL EXPOSURE			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
BURNS SECOND DEGREE			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
FOREIGN BODY			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
HEAD INJURY			
subjects affected / exposed	0 / 824 (0.00%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIMB TRAUMATIC AMPUTATION			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
RIB FRACTURE			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
ROAD TRAFFIC ACCIDENT			

subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
SKULL FRACTURE			
subjects affected / exposed	0 / 824 (0.00%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THERMAL BURN			
subjects affected / exposed	0 / 824 (0.00%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRAUMATIC BRAIN INJURY			
subjects affected / exposed	0 / 824 (0.00%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER LIMB FRACTURE			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
FOREIGN BODY ASPIRATION			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
Congenital, familial and genetic disorders			
ATRIAL SEPTAL DEFECT			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
FALLOT'S TETRALOGY			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
HYPOSPADIAS			

subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
OPTIC NERVE HYPOPLASIA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
PYLORIC STENOSIS			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
Cardiac disorders			
CYANOSIS			
subjects affected / exposed	1 / 824 (0.12%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY VALVE STENOSIS			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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			
COMPLEX PARTIAL SEIZURES			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
CONVULSION			
subjects affected / exposed	0 / 824 (0.00%)	5 / 2026 (0.25%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE CONVULSION			
subjects affected / exposed	4 / 824 (0.49%)	13 / 2026 (0.64%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 4	2 / 13	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GRAND MAL CONVULSION			

subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
PSYCHOMOTOR SKILLS IMPAIRED			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
TONIC CONVULSION			
subjects affected / exposed	2 / 824 (0.24%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHADENITIS			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
Ear and labyrinth disorders			
HAEMATOTYMPANUM			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
Eye disorders			
BLEPHARITIS			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	4 / 824 (0.49%)	8 / 2026 (0.39%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA HAEMORRHAGIC			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
GASTRITIS			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	2 / 824 (0.24%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATOCHEZIA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGUINAL HERNIA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
INTUSSUSCEPTION			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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

NAUSEA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
PERITONITIS			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STOMATITIS			
subjects affected / exposed	1 / 824 (0.12%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	3 / 824 (0.36%)	4 / 2026 (0.20%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URTICARIA			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
Renal and urinary disorders			
NEPHROTIC SYNDROME			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
SYNOSTOSIS			

subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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			
ABSCESS LIMB			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
ABSCESS NECK			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
ACARODERMATITIS			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS ORAL			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
ACUTE SINUSITIS			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
BACTERAEMIA			
subjects affected / exposed	0 / 824 (0.00%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL DIARRHOEA			

subjects affected / exposed	6 / 824 (0.73%)	3 / 2026 (0.15%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BOTULISM			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
BRONCHIOLITIS			
subjects affected / exposed	16 / 824 (1.94%)	32 / 2026 (1.58%)	6 / 183 (3.28%)
occurrences causally related to treatment / all	0 / 18	0 / 33	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	1 / 824 (0.12%)	6 / 2026 (0.30%)	2 / 183 (1.09%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS VIRAL			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
BRONCHOPNEUMONIA			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CROUP INFECTIOUS			
subjects affected / exposed	0 / 824 (0.00%)	3 / 2026 (0.15%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DENGUE FEVER			

subjects affected / exposed	2 / 824 (0.24%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS INFECTIOUS			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
EXANTHEMA SUBITUM			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
FEBRILE INFECTION			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	4 / 824 (0.49%)	14 / 2026 (0.69%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 14	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPETIGO			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
INFECTIOUS MONONUCLEOSIS			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
INFLUENZA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
LOWER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
LUNG INFECTION			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
OSTEOMYELITIS			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
OTITIS MEDIA			
subjects affected / exposed	4 / 824 (0.49%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OTITIS MEDIA ACUTE			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
PERIORBITAL CELLULITIS			
subjects affected / exposed	2 / 824 (0.24%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERTUSSIS			
subjects affected / exposed	2 / 824 (0.24%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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	9 / 824 (1.09%)	37 / 2026 (1.83%)	2 / 183 (1.09%)
occurrences causally related to treatment / all	0 / 9	0 / 37	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	2 / 824 (0.24%)	5 / 2026 (0.25%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA PRIMARY ATYPICAL			
subjects affected / exposed	0 / 824 (0.00%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA RESPIRATORY SYNCYTIAL VIRAL			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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 VIRAL			
subjects affected / exposed	1 / 824 (0.12%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 824 (0.00%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
RESPIRATORY TRACT INFECTION			

VIRAL			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
SINUSITIS			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
STAPHYLOCOCCAL ABSCESS			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
STAPHYLOCOCCAL SKIN INFECTION			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (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
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 824 (0.00%)	4 / 2026 (0.20%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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	8 / 824 (0.97%)	9 / 2026 (0.44%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VARICELLA			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
VIRAL DIARRHOEA			
subjects affected / exposed	1 / 824 (0.12%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			
subjects affected / exposed	2 / 824 (0.24%)	1 / 2026 (0.05%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (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
VULVAL ABSCESS			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
Metabolism and nutrition disorders			
COW'S MILK INTOLERANCE			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
DEHYDRATION			

subjects affected / exposed	1 / 824 (0.12%)	1 / 2026 (0.05%)	2 / 183 (1.09%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETES MELLITUS			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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
HYPONATRAEMIA			
subjects affected / exposed	0 / 824 (0.00%)	1 / 2026 (0.05%)	0 / 183 (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

Serious adverse events	US2+US4A+US4B	US1+US3	US4C
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 301 (5.98%)	58 / 995 (5.83%)	14 / 203 (6.90%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN NEOPLASM			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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

Vascular disorders			
KAWASAKI'S DISEASE			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
INTESTINAL OPERATION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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			
OEDEMA			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
PYREXIA			
subjects affected / exposed	0 / 301 (0.00%)	3 / 995 (0.30%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
FOOD ALLERGY			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
HYPOGAMMAGLOBULINAEMIA			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
APNOEA			

subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
ASTHMA			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
BRONCHIAL HYPERREACTIVITY			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
BRONCHOSPASM			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
CHOKING			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
HYPOXIA			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
LARYNGOSPASM			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
PULMONARY HYPERTENSION			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY DISORDER			

subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
STATUS ASTHMATICUS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TACHYPNOEA			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (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
WHEEZING			
subjects affected / exposed	0 / 301 (0.00%)	2 / 995 (0.20%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ACCIDENTAL DRUG INTAKE BY CHILD			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
ACCIDENTAL EXPOSURE			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
BURNS SECOND DEGREE			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
FOREIGN BODY			

subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (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
HEAD INJURY			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
LIMB TRAUMATIC AMPUTATION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
RIB FRACTURE			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
SKULL FRACTURE			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THERMAL BURN			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRAUMATIC BRAIN INJURY			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
UPPER LIMB FRACTURE			

subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
FOREIGN BODY ASPIRATION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
Congenital, familial and genetic disorders			
ATRIAL SEPTAL DEFECT			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (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
FALLOT'S TETRALOGY			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
HYPOSPADIAS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
OPTIC NERVE HYPOPLASIA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYLORIC STENOSIS			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
Cardiac disorders			
CYANOSIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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

PULMONARY VALVE STENOSIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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			
COMPLEX PARTIAL SEIZURES			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONVULSION			
subjects affected / exposed	1 / 301 (0.33%)	2 / 995 (0.20%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE CONVULSION			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GRAND MAL CONVULSION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
PSYCHOMOTOR SKILLS IMPAIRED			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
TONIC CONVULSION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
LYMPHADENITIS			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (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
Ear and labyrinth disorders			
HAEMATOTYMPANUM			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
Eye disorders			
BLEPHARITIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
DIARRHOEA HAEMORRHAGIC			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
GASTRITIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
GASTROOESOPHAGEAL REFLUX DISEASE			

subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
HAEMATOCHEZIA			
subjects affected / exposed	1 / 301 (0.33%)	1 / 995 (0.10%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGUINAL HERNIA			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (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
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTUSSUSCEPTION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
NAUSEA			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
PERITONITIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
STOMATITIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
VOMITING			

subjects affected / exposed	1 / 301 (0.33%)	1 / 995 (0.10%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
URTICARIA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
NEPHROTIC SYNDROME			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
SYNOSTOSIS			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABSCESS LIMB			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS NECK			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
ACARODERMATITIS			

subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
ABSCESS ORAL			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
ACUTE SINUSITIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
BACTERAEMIA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
BACTERIAL DIARRHOEA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
BOTULISM			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
BRONCHIOLITIS			
subjects affected / exposed	3 / 301 (1.00%)	10 / 995 (1.01%)	2 / 203 (0.99%)
occurrences causally related to treatment / all	0 / 3	0 / 10	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			

subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
BRONCHITIS VIRAL			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
BRONCHOPNEUMONIA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
CELLULITIS			
subjects affected / exposed	0 / 301 (0.00%)	3 / 995 (0.30%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CROUP INFECTIOUS			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DENGUE FEVER			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
ENTERITIS INFECTIOUS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EXANTHEMA SUBITUM			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
FEBRILE INFECTION			

subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	0 / 301 (0.00%)	2 / 995 (0.20%)	2 / 203 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPETIGO			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
INFECTIOUS MONONUCLEOSIS			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
INFLUENZA			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
LUNG INFECTION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
OSTEOMYELITIS			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OTITIS MEDIA			

subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
OTITIS MEDIA ACUTE			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
PERIORBITAL CELLULITIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERTUSSIS			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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
PHARYNGITIS			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	2 / 301 (0.66%)	4 / 995 (0.40%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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 PRIMARY ATYPICAL			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (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 VIRAL			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS			
subjects affected / exposed	4 / 301 (1.33%)	4 / 995 (0.40%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 301 (0.00%)	3 / 995 (0.30%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
SINUSITIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
STAPHYLOCOCCAL ABSCESS			

subjects affected / exposed	0 / 301 (0.00%)	2 / 995 (0.20%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 301 (0.00%)	2 / 995 (0.20%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SKIN INFECTION			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (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	1 / 301 (0.33%)	1 / 995 (0.10%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VARICELLA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL DIARRHOEA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			

subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL PHARYNGITIS			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (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
VULVAL ABSCESS			
subjects affected / exposed	0 / 301 (0.00%)	1 / 995 (0.10%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 301 (0.33%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
COW'S MILK INTOLERANCE			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
DEHYDRATION			
subjects affected / exposed	1 / 301 (0.33%)	5 / 995 (0.50%)	2 / 203 (0.99%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETES MELLITUS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
HYPOGLYCAEMIA			

subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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
HYPONATRAEMIA			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (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	LA2+4+6AB	LA1+LA3+LA5	LA6C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	740 / 824 (89.81%)	1853 / 2026 (91.46%)	171 / 183 (93.44%)
Nervous system disorders			
SOMNOLENCE			
subjects affected / exposed	513 / 824 (62.26%)	1198 / 2026 (59.13%)	110 / 183 (60.11%)
occurrences (all)	1119	2412	235
General disorders and administration site conditions			
INJECTION SITE ERYTHEMA			
subjects affected / exposed	548 / 824 (66.50%)	1245 / 2026 (61.45%)	117 / 183 (63.93%)
occurrences (all)	1361	2589	262
INJECTION SITE INDURATION			
subjects affected / exposed	333 / 824 (40.41%)	745 / 2026 (36.77%)	90 / 183 (49.18%)
occurrences (all)	597	1230	197
INJECTION SITE PAIN			
subjects affected / exposed	698 / 824 (84.71%)	1592 / 2026 (78.58%)	164 / 183 (89.62%)
occurrences (all)	1765	3532	422
MALAISE			
subjects affected / exposed	73 / 824 (8.86%)	136 / 2026 (6.71%)	5 / 183 (2.73%)
occurrences (all)	92	178	5
PYREXIA			
subjects affected / exposed	341 / 824 (41.38%)	748 / 2026 (36.92%)	74 / 183 (40.44%)
occurrences (all)	584	1173	115
CRYING			

subjects affected / exposed	419 / 824 (50.85%)	927 / 2026 (45.76%)	98 / 183 (53.55%)
occurrences (all)	749	1560	197
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	287 / 824 (34.83%)	597 / 2026 (29.47%)	57 / 183 (31.15%)
occurrences (all)	527	1040	114
FLATULENCE			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	29 / 824 (3.52%)	53 / 2026 (2.62%)	1 / 183 (0.55%)
occurrences (all)	30	55	1
TEETHING			
subjects affected / exposed	2 / 824 (0.24%)	11 / 2026 (0.54%)	0 / 183 (0.00%)
occurrences (all)	2	13	0
VOMITING			
subjects affected / exposed	228 / 824 (27.67%)	486 / 2026 (23.99%)	39 / 183 (21.31%)
occurrences (all)	365	798	66
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
subjects affected / exposed	7 / 824 (0.85%)	38 / 2026 (1.88%)	15 / 183 (8.20%)
occurrences (all)	8	58	27
COUGH			
subjects affected / exposed	24 / 824 (2.91%)	41 / 2026 (2.02%)	4 / 183 (2.19%)
occurrences (all)	24	41	5
NASAL CONGESTION			
subjects affected / exposed	1 / 824 (0.12%)	6 / 2026 (0.30%)	1 / 183 (0.55%)
occurrences (all)	1	8	1
Skin and subcutaneous tissue disorders			
DERMATITIS ATOPIC			
subjects affected / exposed	16 / 824 (1.94%)	26 / 2026 (1.28%)	1 / 183 (0.55%)
occurrences (all)	18	27	1
DERMATITIS DIAPER			
subjects affected / exposed	4 / 824 (0.49%)	8 / 2026 (0.39%)	0 / 183 (0.00%)
occurrences (all)	5	8	0

ECZEMA			
subjects affected / exposed	0 / 824 (0.00%)	0 / 2026 (0.00%)	0 / 183 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	136 / 824 (16.50%)	323 / 2026 (15.94%)	32 / 183 (17.49%)
occurrences (all)	221	500	43
Psychiatric disorders			
IRRITABILITY			
subjects affected / exposed	474 / 824 (57.52%)	1120 / 2026 (55.28%)	110 / 183 (60.11%)
occurrences (all)	1080	2329	267
EATING DISORDERS			
subjects affected / exposed	263 / 824 (31.92%)	607 / 2026 (29.96%)	69 / 183 (37.70%)
occurrences (all)	475	991	129
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	28 / 824 (3.40%)	68 / 2026 (3.36%)	9 / 183 (4.92%)
occurrences (all)	31	74	10
BRONCHIOLITIS			
subjects affected / exposed	52 / 824 (6.31%)	180 / 2026 (8.88%)	36 / 183 (19.67%)
occurrences (all)	67	211	51
BRONCHITIS			
subjects affected / exposed	95 / 824 (11.53%)	219 / 2026 (10.81%)	17 / 183 (9.29%)
occurrences (all)	140	297	28
CROUP INFECTIOUS			
subjects affected / exposed	1 / 824 (0.12%)	2 / 2026 (0.10%)	0 / 183 (0.00%)
occurrences (all)	1	2	0
GASTROENTERITIS			
subjects affected / exposed	35 / 824 (4.25%)	48 / 2026 (2.37%)	3 / 183 (1.64%)
occurrences (all)	39	51	3
NASOPHARYNGITIS			
subjects affected / exposed	192 / 824 (23.30%)	375 / 2026 (18.51%)	27 / 183 (14.75%)
occurrences (all)	267	486	13
OTITIS MEDIA			
subjects affected / exposed	17 / 824 (2.06%)	26 / 2026 (1.28%)	2 / 183 (1.09%)
occurrences (all)	23	27	3

OTITIS MEDIA ACUTE			
subjects affected / exposed	15 / 824 (1.82%)	37 / 2026 (1.83%)	7 / 183 (3.83%)
occurrences (all)	17	40	7
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	71 / 824 (8.62%)	163 / 2026 (8.05%)	5 / 183 (2.73%)
occurrences (all)	86	198	10
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 824 (0.49%)	16 / 2026 (0.79%)	0 / 183 (0.00%)
occurrences (all)	4	16	0
VIRAL INFECTION			
subjects affected / exposed	28 / 824 (3.40%)	44 / 2026 (2.17%)	1 / 183 (0.55%)
occurrences (all)	30	44	1

Non-serious adverse events	US2+US4A+US4B	US1+US3	US4C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	279 / 301 (92.69%)	957 / 995 (96.18%)	202 / 203 (99.51%)
Nervous system disorders			
SOMNOLENCE			
subjects affected / exposed	184 / 301 (61.13%)	676 / 995 (67.94%)	141 / 203 (69.46%)
occurrences (all)	391	1513	360
General disorders and administration site conditions			
INJECTION SITE ERYTHEMA			
subjects affected / exposed	108 / 301 (35.88%)	280 / 995 (28.14%)	100 / 203 (49.26%)
occurrences (all)	202	440	201
INJECTION SITE INDURATION			
subjects affected / exposed	101 / 301 (33.55%)	204 / 995 (20.50%)	78 / 203 (38.42%)
occurrences (all)	169	332	156
INJECTION SITE PAIN			
subjects affected / exposed	196 / 301 (65.12%)	651 / 995 (65.43%)	147 / 203 (72.41%)
occurrences (all)	433	1350	351
MALAISE			
subjects affected / exposed	0 / 301 (0.00%)	0 / 995 (0.00%)	0 / 203 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	94 / 301 (31.23%)	296 / 995 (29.75%)	74 / 203 (36.45%)
occurrences (all)	134	442	129

CRYING			
subjects affected / exposed	154 / 301 (51.16%)	558 / 995 (56.08%)	124 / 203 (61.08%)
occurrences (all)	329	1124	276
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	91 / 301 (30.23%)	289 / 995 (29.05%)	78 / 203 (38.42%)
occurrences (all)	136	521	133
FLATULENCE			
subjects affected / exposed	8 / 301 (2.66%)	23 / 995 (2.31%)	12 / 203 (5.91%)
occurrences (all)	10	29	12
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	11 / 301 (3.65%)	49 / 995 (4.92%)	12 / 203 (5.91%)
occurrences (all)	12	51	14
TEETHING			
subjects affected / exposed	28 / 301 (9.30%)	83 / 995 (8.34%)	30 / 203 (14.78%)
occurrences (all)	40	115	41
VOMITING			
subjects affected / exposed	69 / 301 (22.92%)	217 / 995 (21.81%)	61 / 203 (30.05%)
occurrences (all)	97	326	92
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
subjects affected / exposed	0 / 301 (0.00%)	15 / 995 (1.51%)	3 / 203 (1.48%)
occurrences (all)	0	15	3
COUGH			
subjects affected / exposed	20 / 301 (6.64%)	64 / 995 (6.43%)	15 / 203 (7.39%)
occurrences (all)	24	75	18
NASAL CONGESTION			
subjects affected / exposed	15 / 301 (4.98%)	60 / 995 (6.03%)	18 / 203 (8.87%)
occurrences (all)	16	69	18
Skin and subcutaneous tissue disorders			
DERMATITIS ATOPIC			
subjects affected / exposed	9 / 301 (2.99%)	29 / 995 (2.91%)	13 / 203 (6.40%)
occurrences (all)	9	29	14
DERMATITIS DIAPER			
subjects affected / exposed	21 / 301 (6.98%)	62 / 995 (6.23%)	13 / 203 (6.40%)
occurrences (all)	25	74	14

ECZEMA			
subjects affected / exposed	32 / 301 (10.63%)	105 / 995 (10.55%)	21 / 203 (10.34%)
occurrences (all)	34	109	25
RASH			
subjects affected / exposed	33 / 301 (10.96%)	154 / 995 (15.48%)	39 / 203 (19.21%)
occurrences (all)	52	207	59
Psychiatric disorders			
IRRITABILITY			
subjects affected / exposed	240 / 301 (79.73%)	800 / 995 (80.40%)	171 / 203 (84.24%)
occurrences (all)	714	2293	566
EATING DISORDERS			
subjects affected / exposed	122 / 301 (40.53%)	425 / 995 (42.71%)	93 / 203 (45.81%)
occurrences (all)	196	759	183
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	30 / 301 (9.97%)	93 / 995 (9.35%)	29 / 203 (14.29%)
occurrences (all)	40	123	35
BRONCHIOLITIS			
subjects affected / exposed	34 / 301 (11.30%)	108 / 995 (10.85%)	25 / 203 (12.32%)
occurrences (all)	45	139	26
BRONCHITIS			
subjects affected / exposed	6 / 301 (1.99%)	10 / 995 (1.01%)	5 / 203 (2.46%)
occurrences (all)	7	10	7
CROUP INFECTIOUS			
subjects affected / exposed	12 / 301 (3.99%)	44 / 995 (4.42%)	15 / 203 (7.39%)
occurrences (all)	12	56	16
GASTROENTERITIS			
subjects affected / exposed	18 / 301 (5.98%)	49 / 995 (4.92%)	6 / 203 (2.96%)
occurrences (all)	19	55	6
NASOPHARYNGITIS			
subjects affected / exposed	9 / 301 (2.99%)	41 / 995 (4.12%)	11 / 203 (5.42%)
occurrences (all)	9	43	12
OTITIS MEDIA			
subjects affected / exposed	76 / 301 (25.25%)	258 / 995 (25.93%)	62 / 203 (30.54%)
occurrences (all)	112	413	96
OTITIS MEDIA ACUTE			

subjects affected / exposed	15 / 301 (4.98%)	42 / 995 (4.22%)	13 / 203 (6.40%)
occurrences (all)	33	66	34
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 301 (0.00%)	2 / 995 (0.20%)	0 / 203 (0.00%)
occurrences (all)	0	2	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	108 / 301 (35.88%)	340 / 995 (34.17%)	74 / 203 (36.45%)
occurrences (all)	159	459	103
VIRAL INFECTION			
subjects affected / exposed	22 / 301 (7.31%)	82 / 995 (8.24%)	20 / 203 (9.85%)
occurrences (all)	24	94	23

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 April 2007	Inclusion of a second primary endpoint to assess the response to what was described initially as a "boost" dose of MenACWY
03 December 2007	Testing for MMR-V antigens was removed from the planned testing.
27 May 2008	Revision of the primary objective and endpoints for all serogroups to evaluate the percentage of subjects with hSBA ≥ 1:8 one month post-4th dose instead of one month post-3rd dose
07 August 2008	To require subjects in groups US4 and LA6 (receiving MenACWY for the first time at 13 months of age) to delay their MenACWY vaccination until 18 months of age in order to serve as a control for the 4-dose MenACWY groups up to 6 months post the final MenACWY dose.
15 June 2009	To provide an a additional concomitant vaccine (2nd dose of Hepatitis A vaccine) in the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/22094635