



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 | <ul style="list-style-type: none">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) | EMA-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: -

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|-----------------------------------------------------------|---------------|
| 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.

| | |
|------------------|----------------------------|
| 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 |

Baseline characteristics

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 standard deviation | 67.5 ± 8 | 65 ± 9.4 | 67.7 ± 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 standard deviation | 59.5 ± 6.2 | 65 ± 7.9 | - |
| Gender categorical Units: Subjects | | | |
| Female | 89 | 91 | 2223 |
| Male | 81 | 92 | 2322 |

End points

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 $\geq 1:8$ - US Subjects

| | |
|-----------------|-----------------------------------------------------------|
| End point title | 1. Percentage of Subjects With hSBA Titer $\geq 1:8$ - 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 $\geq 1:8$ - US Subjects

| | |
|-----------------|-----------------------------------------------------------|
| End point title | 4. Percentage of Subjects With hSBA Titer $\geq 1:8$ - 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 $\geq 1:4$ - US Subjects

| | |
|-----------------|-----------------------------------------------------------|
| End point title | 5. Percentage of Subjects With hSBA Titer $\geq 1:4$ - 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 (GMT_{LA1}/GMT_{LA3}) 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 $\geq 1:8$; N=272, 271) | 0 (0 to 2) | 1 (0 to 4) | | |
| A (Post-vaccination hSBA titer $\geq 1:8$; N=277, 268) | 89 (85 to 93) | 74 (69 to 79) | | |
| C (Pre-vaccination hSBA titer $\geq 1:8$; N=273,272) | 4 (2 to 8) | 4 (2 to 7) | | |
| C (Post-vaccination hSBA titer $\geq 1:8$; N=277, 272) | 97 (94 to 99) | 94 (90 to 96) | | |
| W (Pre-vaccination hSBA titer $\geq 1:8$; N=263, 261) | 10 (7 to 14) | 16 (12 to 21) | | |
| W (Post-vaccination hSBA titer $\geq 1:8$; N=271,264) | 98 (96 to 100) | 99 (97 to 100) | | |
| Y (Pre-vaccination hSBA titer $\geq 1:8$; N=258, 260) | 3 (2 to 6) | 5 (3 to 9) | | |
| Y (Post-vaccination hSBA titer $\geq 1:8$; 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 $\geq 1:8$ and $\geq 1:4$ 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 $\geq 1:8$ and $\geq 1:4$ 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 $\geq 1:8$ and $\geq 1:4$ 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 $\geq 1:8$ and $\geq 1:4$ between the 2 dose and the 3 dose schedule (LA1 - LA3) is greater than -10%.

Secondary: 8. Percentage of Subjects With hSBA Titer $\geq 1:4$ - LA Subjects

| | |
|-----------------|--------------------------------------------------------------------|
| End point title | 8. Percentage of Subjects With hSBA Titer $\geq 1:4$ - 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 $\geq 1:4$; N=271, 272) | 1 (0 to 3) | 2 (1 to 5) | | |
| A (Post-vaccination hSBA titer $\geq 1:4$; N=268, 277) | 91 (87 to 94) | 78 (73 to 83) | | |
| C (Pre-vaccination hSBA titer $\geq 1:4$; N=272,273) | 10 (7 to 15) | 10 (7 to 14) | | |
| C (Post-vaccination hSBA titer $\geq 1:4$; N=272, 277) | 98 (96 to 99) | 96 (93 to 98) | | |
| W (Pre-vaccination hSBA titer $\geq 1:4$; N=261, 263) | 13 (9 to 17) | 17 (13 to 23) | | |
| W (Post-vaccination hSBA titer $\geq 1:4$; N=264,271) | 99 (97 to 100) | 100 (99 to 100) | | |
| Y (Pre-vaccination hSBA titer $\geq 1:4$; N=260, 258) | 8 (5 to 13) | 11 (8 to 16) | | |
| Y (Post-vaccination hSBA titer $\geq 1:4$; 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 ($\geq 1:8$) (N=98, 176) | 100 (96 to 100) | 99 (97 to 100) | | |
| Polio Type 2 ($\geq 1:8$) (N=98, 175) | 100 (96 to 100) | 100 (98 to 100) | | |
| Polio Type 3 ($\geq 1:8$) (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 μ g/mL) (N=101, 213) | 100 (96 to 100) | 99 (97 to 100) | | |
| Hib (≥ 1.0 μ g/mL) (N=101, 213) | 84 (76 to 91) | 89 (84 to 93) | | |
| PnC 4 (≥ 0.35 μ g/mL) (N=102, 181) | 100 (96 to 100) | 98 (95 to 100) | | |
| PnC 6B (≥ 0.35 μ g/mL) (N=102, 181) | 96 (90 to 99) | 88 (83 to 93) | | |
| PnC 9V (≥ 0.35 μ g/mL) (N=102, 181) | 98 (93 to 100) | 98 (94 to 99) | | |
| PnC 14 (≥ 0.35 μ g/mL) (N=102, 181) | 99 (95 to 100) | 100 (98 to 100) | | |
| PnC 18C (≥ 0.35 μ g/mL) (N=102, 181) | 100 (96 to 100) | 97 (94 to 99) | | |
| PnC 19F (≥ 0.35 μ g/mL) (N=102, 181) | 100 (96 to 100) | 99 (96 to 100) | | |
| PnC 23F (≥ 0.35 μ g/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 ($\geq 1:8$) (N=112,120,265,252) | 100 (97 to 100) | 98 (94 to 100) | 99 (97 to 100) | 98 (95 to 99) |
| Polio Type 2 ($\geq 1:8$) (N=112,120,265,252) | 99 (95 to 100) | 98 (93 to 99) | 98 (95 to 99) | 97 (95 to 99) |
| Polio Type 3 ($\geq 1:8$) (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 μ g/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 μ g/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 μ g/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 μ g/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 μ g/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 μ g/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 μ g/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 μ g/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 μ g/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 $\mu\text{g/mL}$) |
| 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 $\mu\text{g/mL}$) |
| 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 $\geq 1:4$ at 12 Months of Age- US Subjects

| | |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | 14. Percentage of Subjects With hSBA $\geq 1:4$ 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 $\geq 1:8$ at 12 Months of Age- US Subjects

| | |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | 15. Percentage of Subjects With hSBA $\geq 1:8$ 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 $\geq 1:4$ at 12 or 16 Months of Age- LA Subjects

| | |
|-----------------|--------------------------------------------------------------------------------------------------------|
| End point title | 17. Percentage of Subjects With hSBA $\geq 1:4$ 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 $\geq 1:8$ at 12 or 16 Months of Age- LA Subject

| | |
|-----------------|-------------------------------------------------------------------------------------------------------|
| End point title | 18. Percentage of Subjects With hSBA $\geq 1:8$ 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 \geq 1:4, at 1 Month After Toddler MenACWY Vaccination - US Subjects

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------|
| End point title | 20. Percentage of Subjects (95% CI) With hSBA \geq 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 \geq 1:8 at 1 Month After Toddler MenACWY Vaccination - US Subjects

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|
| End point title | 21. Percentage of Subjects (95% CI) With hSBA \geq 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 \geq 1:16 at 1 Month After Toddler MenACWY Vaccination - US Subjects

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------|
| End point title | 22. Percentage of Subjects (95% CI) With hSBA \geq 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 \geq 1:4 at 1 Month After Toddler MenACWY Vaccination - LA Subjects

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|
| End point title | 23. Percentage of Subjects (95% CI) With hSBA \geq 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 \geq 1:8 at 1 Month After Toddler MenACWY Vaccination - LA Subjects

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|
| End point title | 24. Percentage of Subjects (95% CI) With hSBA \geq 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 \geq 1:16 at 1 Month After Toddler MenACWY Vaccination - LA Subjects

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|
| End point title | 25. Percentage of Subjects With hSBA \geq 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 $\mu\text{g/mL}$ at 1 Month After Toddler Vaccination - US Subjects

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

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 $\mu\text{g/mL}$ at 1 Month After Toddler Vaccination - LA Subjects

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | 30. Percentage of Subjects With Pneumococcal Antibody Concentration ≥ 1.0 $\mu\text{g/mL}$ 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 $\geq 1:8$ at 1 Month After 1st (LA2) or 2nd (LA4) Toddler MenACWY Vaccination - LA Subjects

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | 33. Percentage of Subjects With hSBA $\geq 1:8$ 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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 |
|-----------------|----------------------------------------------------------|

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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}$ 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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. ($\geq 38^{\circ}\text{C}$) | 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

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 |
| GASTROESOPHAGEAL 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 |
| HAEMATOCHESIA | | | |
| 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 occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 301 (0.00%) 0 / 0 0 / 0 | 1 / 995 (0.10%) 1 / 1 0 / 0 | 0 / 203 (0.00%) 0 / 0 0 / 0 |
| Surgical and medical procedures INTESTINAL OPERATION subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 301 (0.00%) 0 / 0 0 / 0 | 0 / 995 (0.00%) 0 / 0 0 / 0 | 0 / 203 (0.00%) 0 / 0 0 / 0 |
| General disorders and administration site conditions OEDEMA subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 301 (0.00%) 0 / 0 0 / 0 | 1 / 995 (0.10%) 0 / 1 0 / 0 | 0 / 203 (0.00%) 0 / 0 0 / 0 |
| PYREXIA subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 301 (0.00%) 0 / 0 0 / 0 | 3 / 995 (0.30%) 0 / 3 0 / 0 | 0 / 203 (0.00%) 0 / 0 0 / 0 |
| Immune system disorders DRUG HYPERSENSITIVITY subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 301 (0.00%) 0 / 0 0 / 0 | 1 / 995 (0.10%) 0 / 1 0 / 0 | 0 / 203 (0.00%) 0 / 0 0 / 0 |
| FOOD ALLERGY subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 301 (0.00%) 0 / 0 0 / 0 | 1 / 995 (0.10%) 0 / 1 0 / 0 | 0 / 203 (0.00%) 0 / 0 0 / 0 |
| HYPOGAMMAGLOBULINAEMIA subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 301 (0.33%) 0 / 1 0 / 0 | 0 / 995 (0.00%) 0 / 0 0 / 0 | 0 / 203 (0.00%) 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 |
| GASTROESOPHAGEAL 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 |
| HAEMATOOCHEZIA | | | |
| 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 occurrences (all) | 154 / 301 (51.16%) 329 | 558 / 995 (56.08%) 1124 | 124 / 203 (61.08%) 276 |
| Gastrointestinal disorders | | | |
| DIARRHOEA subjects affected / exposed occurrences (all) | 91 / 301 (30.23%) 136 | 289 / 995 (29.05%) 521 | 78 / 203 (38.42%) 133 |
| FLATULENCE subjects affected / exposed occurrences (all) | 8 / 301 (2.66%) 10 | 23 / 995 (2.31%) 29 | 12 / 203 (5.91%) 12 |
| GASTROESOPHAGEAL REFLUX DISEASE subjects affected / exposed occurrences (all) | 11 / 301 (3.65%) 12 | 49 / 995 (4.92%) 51 | 12 / 203 (5.91%) 14 |
| TEETHING subjects affected / exposed occurrences (all) | 28 / 301 (9.30%) 40 | 83 / 995 (8.34%) 115 | 30 / 203 (14.78%) 41 |
| VOMITING subjects affected / exposed occurrences (all) | 69 / 301 (22.92%) 97 | 217 / 995 (21.81%) 326 | 61 / 203 (30.05%) 92 |
| Respiratory, thoracic and mediastinal disorders | | | |
| BRONCHOSPASM subjects affected / exposed occurrences (all) | 0 / 301 (0.00%) 0 | 15 / 995 (1.51%) 15 | 3 / 203 (1.48%) 3 |
| COUGH subjects affected / exposed occurrences (all) | 20 / 301 (6.64%) 24 | 64 / 995 (6.43%) 75 | 15 / 203 (7.39%) 18 |
| NASAL CONGESTION subjects affected / exposed occurrences (all) | 15 / 301 (4.98%) 16 | 60 / 995 (6.03%) 69 | 18 / 203 (8.87%) 18 |
| Skin and subcutaneous tissue disorders | | | |
| DERMATITIS ATOPIC subjects affected / exposed occurrences (all) | 9 / 301 (2.99%) 9 | 29 / 995 (2.91%) 29 | 13 / 203 (6.40%) 14 |
| DERMATITIS DIAPER subjects affected / exposed occurrences (all) | 21 / 301 (6.98%) 25 | 62 / 995 (6.23%) 74 | 13 / 203 (6.40%) 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 \geq 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 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>