



Clinical trial results:

A Phase 4, Randomized, Open-Label Trial to Describe The Safety, Tolerability, And Immunogenicity of 13-Valent Pneumococcal Conjugate Vaccine Formulated In Multidose Vials When Given With Routine Pediatric Vaccines in Healthy Infants in India

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2016-005134-29 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 20 December 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 25 June 2020 |
| First version publication date | 25 June 2020 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | B4671004 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03548337 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 06 February 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 December 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To describe the safety profile of 13-valent pneumococcal conjugate (13vPnC) with 2-phenoxyethanol (2-PE) in the multidose vial (MDV) group and without 2-PE in the single dose pre-filled syringe (PFS) group.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 31 December 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | India: 300 |
| Worldwide total number of subjects | 300 |
| 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) | 300 |
| 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: -

Pre-assignment

Screening details:

A total of 301 subjects were enrolled in the study. Out of 301 subjects, 300 were randomized and received the study vaccination.

Period 1

| | |
|------------------------------|--------------------------------------|
| Period 1 title | Infant Series (duration of 3 months) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | 13vPnC: Multi-dose Vial (With Preservative) |

Arm description:

Infant series: subjects were randomized to receive a single 0.5 milliliter (mL) dose of 13-valent pneumococcal conjugate vaccine (13vPnC) with preservative 2-phenoxyethanol (2-PE) from a multi-dose vial (MDV), intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) along with 2 routine vaccines: 1) diphtheria, tetanus, and pertussis; Haemophilus influenzae type b; and hepatitis B virus (DTP-Hib-HBV) vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Infant series was followed by toddler dose. Toddler dose: subjects were administered with a single 0.5 mL dose of 13vPnC vaccine with preservative 2-PE from MDV, intramuscularly at age of 12 months (Vaccination 4) along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice).

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | 13vPnC |
| Investigational medicinal product code | B467 |
| Other name | 13vPnC |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of 13vPnC from a MDV with preservative 2-PE, intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3).

| | |
|--|-------------------|
| Investigational medicinal product name | DTP-Hib-HBV |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of DTP-Hib-HBV intramuscularly at age of 6 weeks, 10 weeks and 14 weeks.

| | |
|--|-------------------|
| Investigational medicinal product name | Rotavirus vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of rotavirus vaccine intramuscularly at age of 6 weeks, 10 weeks and 14 weeks.

| | |
|---|--|
| Arm title | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) |
| Arm description: | |
| Infant series: subjects were randomized to receive a single 0.5 mL dose of 13vPnC without preservative 2-PE from a single-dose prefilled syringe (PFS), intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) along with 2 routine vaccines: 1) DTP-Hib-HBV vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Infant series was followed by toddler dose. Toddler dose: subjects were administered with a single 0.5 mL dose of 13vPnC vaccine without preservative 2-PE from single dose PFS, intramuscularly at age of 12 months (Vaccination 4) along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice). | |
| Arm type | Active comparator |
| Investigational medicinal product name | 13vPnC |
| Investigational medicinal product code | B467 |
| Other name | 13vPnC |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of 13vPnC from single dose PFS without preservative 2-PE, intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3).

| | |
|--|-------------------|
| Investigational medicinal product name | DTP-Hib-HBV |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of DTP-Hib-HBV intramuscularly at age of 6 weeks, 10 weeks and 14 weeks.

| | |
|--|-------------------|
| Investigational medicinal product name | Rotavirus vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of rotavirus vaccine intramuscularly at age of 6 weeks, 10 weeks and 14 weeks.

| Number of subjects in period 1 | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) |
|------------------------------------|---|--|
| | | |
| Started | 150 | 150 |
| Vaccination 1 | 150 | 150 |
| Vaccination 2 | 144 | 144 |
| Vaccination 3 | 144 | 141 |
| Completed | 139 | 139 |
| Not completed | 11 | 11 |
| Adverse event, non-fatal | - | 2 |
| No Longer Met Eligibility Criteria | 1 | - |
| Lost to follow-up | 2 | 1 |

| | | |
|-------------------------------|---|---|
| Withdrawal by parent/guardian | 8 | 8 |
|-------------------------------|---|---|

Period 2

| | |
|------------------------------|------------------------------------|
| Period 2 title | Toddler dose (duration of 1 month) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | 13vPnC: Multi-dose Vial (With Preservative) |

Arm description:

Infant series: subjects were randomized to receive a single 0.5 mL dose of 13vPnC from a MDV with preservative 2-PE, intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) respectively along with 2 routine vaccines: 1) diphtheria, tetanus, and pertussis; Haemophilus influenzae type b; and hepatitis B virus (DTP- Hib-HBV) vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Toddler dose followed infant series. Toddler dose: subjects were administered a single 0.5 mL dose of 13vPnC vaccine from MDV with preservative 2-PE (Vaccination 4), at age of 12 months along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice).

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | 13vPnC |
| Investigational medicinal product code | B467 |
| Other name | 13vPnC |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of 13vPnC from a MDV with preservative 2-PE, intramuscularly at age of 12 months (Vaccination 4).

| | |
|--|---------------------------|
| Investigational medicinal product name | Hepatitis A virus vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of hepatitis A virus vaccine intramuscularly at age of 12 months.

| | |
|------------------|--|
| Arm title | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) |
|------------------|--|

Arm description:

Infant series: subjects were randomized to receive a single 0.5 mL dose of 13vPnC from a single-dose PFS without preservative 2-PE, intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) respectively along with 2 routine vaccines: 1) DTP-Hib-HBV vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Toddler dose followed infant series. Toddler dose: subjects were administered a single 0.5 mL dose of 13vPnC vaccine from single-dose PFS without preservative 2-PE (Vaccination 4), at age of 12 months along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice).

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | 13vPnC |
| Investigational medicinal product code | B467 |
| Other name | 13vPnC |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of 13vPnC from single dose PFS without preservative 2-PE, intramuscularly at age of 12 months (Vaccination 4).

| | |
|--|---------------------------|
| Investigational medicinal product name | Hepatitis A virus vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single 0.5 mL dose of hepatitis A virus vaccine intramuscularly at age of 12 months.

| Number of subjects in period 2 | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) |
|--------------------------------|---|--|
| | | |
| Started | 139 | 139 |
| Vaccination 4 | 139 | 139 |
| Completed | 138 | 138 |
| Not completed | 1 | 1 |
| Withdrawal by parent/guardian | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | 13vPnC: Multi-dose Vial (With Preservative) |
| Reporting group description: | |
| <p>Infant series: subjects were randomized to receive a single 0.5 milliliter (mL) dose of 13-valent pneumococcal conjugate vaccine (13vPnC) with preservative 2-phenoxylethanol (2-PE) from a multi-dose vial (MDV), intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) along with 2 routine vaccines: 1) diphtheria, tetanus, and pertussis; Haemophilus influenzae type b; and hepatitis B virus (DTP-Hib-HBV) vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Infant series was followed by toddler dose. Toddler dose: subjects were administered with a single 0.5 mL dose of 13vPnC vaccine with preservative 2-PE from MDV, intramuscularly at age of 12 months (Vaccination 4) along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice).</p> | |
| Reporting group title | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) |
| Reporting group description: | |
| <p>Infant series: subjects were randomized to receive a single 0.5 mL dose of 13vPnC without preservative 2-PE from a single-dose prefilled syringe (PFS), intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) along with 2 routine vaccines: 1) DTP-Hib-HBV vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Infant series was followed by toddler dose. Toddler dose: subjects were administered with a single 0.5 mL dose of 13vPnC vaccine without preservative 2-PE from single dose PFS, intramuscularly at age of 12 months (Vaccination 4) along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice).</p> | |

| Reporting group values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | Total |
|--|---|--|-------|
| Number of subjects | 150 | 150 | 300 |
| 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 | 150 | 300 |
| 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: Weeks | | | |
| arithmetic mean | 6.9 | 6.9 | - |
| standard deviation | ± 0.95 | ± 0.99 | - |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 74 | 67 | 141 |
| Male | 76 | 83 | 159 |

| | | | |
|---|-----|-----|-----|
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 150 | 150 | 300 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 0 | 0 | 0 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not Hispanic or Latino | 150 | 150 | 300 |
| Unknown or Not Reported | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | 13vPnC: Multi-dose Vial (With Preservative) |
| Reporting group description: | |
| Infant series: subjects were randomized to receive a single 0.5 milliliter (mL) dose of 13-valent pneumococcal conjugate vaccine (13vPnC) with preservative 2-phenoxyethanol (2-PE) from a multi-dose vial (MDV), intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) along with 2 routine vaccines: 1) diphtheria, tetanus, and pertussis; Haemophilus influenzae type b; and hepatitis B virus (DTP-Hib-HBV) vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Infant series was followed by toddler dose. Toddler dose: subjects were administered with a single 0.5 mL dose of 13vPnC vaccine with preservative 2-PE from MDV, intramuscularly at age of 12 months (Vaccination 4) along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice). | |
| Reporting group title | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) |
| Reporting group description: | |
| Infant series: subjects were randomized to receive a single 0.5 mL dose of 13vPnC without preservative 2-PE from a single-dose prefilled syringe (PFS), intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) along with 2 routine vaccines: 1) DTP-Hib-HBV vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Infant series was followed by toddler dose. Toddler dose: subjects were administered with a single 0.5 mL dose of 13vPnC vaccine without preservative 2-PE from single dose PFS, intramuscularly at age of 12 months (Vaccination 4) along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice). | |
| Reporting group title | 13vPnC: Multi-dose Vial (With Preservative) |
| Reporting group description: | |
| Infant series: subjects were randomized to receive a single 0.5 mL dose of 13vPnC from a MDV with preservative 2-PE, intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) respectively along with 2 routine vaccines: 1) diphtheria, tetanus, and pertussis; Haemophilus influenzae type b; and hepatitis B virus (DTP- Hib-HBV) vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Toddler dose followed infant series. Toddler dose: subjects were administered a single 0.5 mL dose of 13vPnC vaccine from MDV with preservative 2-PE (Vaccination 4), at age of 12 months along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice). | |
| Reporting group title | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) |
| Reporting group description: | |
| Infant series: subjects were randomized to receive a single 0.5 mL dose of 13vPnC from a single-dose PFS without preservative 2-PE, intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) respectively along with 2 routine vaccines: 1) DTP-Hib-HBV vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Toddler dose followed infant series. Toddler dose: subjects were administered a single 0.5 mL dose of 13vPnC vaccine from single-dose PFS without preservative 2-PE (Vaccination 4), at age of 12 months along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice). | |

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 1

| | |
|--|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 1 ^[1] |
| End point description: | |
| Local reactions were recorded daily using an daily electronic diary(e-diary). Local reactions included redness, swelling and pain at injection site. Redness and swelling were graded as mild (0.5 to 2.5 centimeters [cm]), moderate (2.5 to 7.0 cm) and, severe (greater than [>] 7 cm). Pain at injection site was graded as mild (hurts if gently touched (example, whimpers, winces, protests, or withdraws), moderate (hurts if gently touched [with crying]), and severe (causes limitation of limb movement). Subjects may be represented in more than 1 row. Here, "Any" for each of 3 local reactions represents | |

any grade of local reaction among mild, moderate or severe. Safety population for infant series included all subjects who received at least 1 dose of study vaccine during infant series. Here, "Overall Number of Subjects analyzed, N" signifies subjects who were evaluable for this outcome measure.

| | |
|-----------------------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Within 7 days after Vaccination 1 | |

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: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 147 | 148 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Any | 19.7 (13.6 to 27.1) | 16.9 (11.2 to 23.9) | | |
| Redness: Mild | 17.7 (11.9 to 24.8) | 12.8 (7.9 to 19.3) | | |
| Redness: Moderate | 2.0 (0.4 to 5.8) | 4.1 (1.5 to 8.6) | | |
| Redness: Severe | 0 (0.0 to 2.5) | 0 (0.0 to 2.5) | | |
| Swelling: Any | 27.9 (20.8 to 35.9) | 33.8 (26.2 to 42.0) | | |
| Swelling: Mild | 21.8 (15.4 to 29.3) | 23.6 (17.1 to 31.3) | | |
| Swelling: Moderate | 6.1 (2.8 to 11.3) | 10.1 (5.8 to 16.2) | | |
| Swelling: Severe | 0 (0.0 to 2.5) | 0 (0.0 to 2.5) | | |
| Pain at injection site: Any | 61.9 (53.5 to 69.8) | 67.6 (59.4 to 75.0) | | |
| Pain at injection site: Mild | 28.6 (21.4 to 36.6) | 31.1 (25.6 to 41.3) | | |
| Pain at injection site: Moderate | 30.6 (23.3 to 38.7) | 29.1 (21.9 to 37.1) | | |
| Pain at injection site: Severe | 2.7 (0.7 to 6.8) | 5.4 (2.4 to 10.4) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events (SE) Within 7 Days After Vaccination 1

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Systemic Events (SE) Within 7 Days After Vaccination 1 ^[2] |
|-----------------|---|

End point description:

Systemic Events:recorded daily using an daily e-diary. Systemic events:Fever graded 1)less than(<)38.0 degrees Celsius[C],2)greater than or equal to(>=)38.0 degree C to 38.4 degree C,3)38.5 degree C to 38.9 degree C,4)39.0 degree C to 40.0 degree C,5)>40.0 degree C; Decreased appetite graded:mild(decreased interest in eating),moderate(decreased oral intake), severe(refusal to

graded:mild(increased or prolonged sleeping bouts),moderate(lightly subdued; interfering with daily activity),severe(disabling;not interested in usual daily activity); Irritability graded:mild(easily consolable),moderate(required increased attention),severe(inconsolable;crying could not be comforted). Subjects may be represented in >1 row."Any" for decreased appetite,increased sleep,irritability:any grade of these systemic events. Safety population for infant series:all subjects who received at least 1 dose of study vaccine during infant series. "N":subjects who were evaluable for this measure.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Within 7 days after Vaccination 1

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 147 | 148 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: <38.0 degree C | 15.0 (9.6 to 21.8) | 10.8 (6.3 to 17.0) | | |
| Fever: >=38.0 degree C to 38.4 degree C | 10.9 (6.4 to 17.1) | 8.1 (4.3 to 13.7) | | |
| Fever: 38.5 degree C to 38.9 degree C | 1.4 (0.2 to 4.8) | 2.7 (0.7 to 6.8) | | |
| Fever: 39.0 degree C to 40.0 degree C | 1.4 (0.2 to 4.8) | 0 (0.0 to 2.5) | | |
| Fever: >40.0 degree C | 1.4 (0.2 to 4.8) | 0 (0.0 to 2.5) | | |
| Decreased appetite: Any | 42.2 (34.1 to 50.6) | 53.4 (45.0 to 61.6) | | |
| Decreased appetite: Mild | 23.8 (17.2 to 31.5) | 30.4 (23.1 to 38.5) | | |
| Decreased appetite: Moderate | 17.7 (11.9 to 24.8) | 21.6 (15.3 to 29.1) | | |
| Decreased appetite: Severe | 0.7 (0.0 to 3.7) | 1.4 (0.2 to 4.8) | | |
| Drowsiness: Any | 55.1 (46.7 to 63.3) | 66.2 (58.0 to 73.8) | | |
| Drowsiness: Mild | 29.3 (22.0 to 37.3) | 33.1 (25.6 to 41.3) | | |
| Drowsiness: Moderate | 25.2 (18.4 to 33.0) | 31.1 (23.7 to 39.2) | | |
| Drowsiness: Severe | 0.7 (0.0 to 3.7) | 2.0 (0.4 to 5.8) | | |
| Irritability: Any | 64.6 (56.3 to 72.3) | 65.5 (57.3 to 73.2) | | |
| Irritability: Mild | 37.4 (29.6 to 45.8) | 32.4 (25.0 to 40.6) | | |
| Irritability: Moderate | 21.8 (15.4 to 29.3) | 26.4 (19.5 to 34.2) | | |
| Irritability: Severe | 5.4 (2.4 to 10.4) | 6.8 (3.3 to 12.1) | | |

Statistical analyses

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 2

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 2 ^[3] |
|-----------------|--|

End point description:

Local reactions were recorded daily using an electronic diary. Local reactions included redness, swelling and pain at injection site. Redness and swelling were graded as mild (0.5 to 2.5 cm), moderate (2.5 to 7.0 cm) and, severe (> 7 cm). Pain at injection site was graded as mild (hurts if gently touched (example, whimpers, winces, protests, or withdraws), moderate (hurts if gently touched [with crying]), and severe (causes limitation of limb movement). Subjects may be represented in more than 1 row. Here, "Any" for each of 3 local reactions represents any grade of local reaction among mild, moderate or severe. Safety population for infant series included all subjects who received at least 1 dose of study vaccine during infant series. Here, "N": number subjects who were evaluable for this outcome measure.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Within 7 days after Vaccination 2

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 141 | 140 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Any | 17.0 (11.2 to 24.3) | 19.3 (13.1 to 26.8) | | |
| Redness: Mild | 16.3 (10.6 to 23.5) | 17.9 (11.9 to 25.2) | | |
| Redness: Moderate | 0.7 (0.0 to 3.9) | 1.4 (0.2 to 5.1) | | |
| Redness: Severe | 0 (0.0 to 2.6) | 0 (0.0 to 2.6) | | |
| Swelling: Any | 24.8 (17.9 to 32.8) | 27.9 (20.6 to 36.1) | | |
| Swelling: Mild | 21.3 (14.8 to 29.0) | 22.9 (16.2 to 30.7) | | |
| Swelling: Moderate | 3.5 (1.2 to 8.1) | 5.0 (2.0 to 10.0) | | |
| Swelling: Severe | 0 (0.0 to 2.6) | 0 (0.0 to 2.6) | | |
| Pain at injection site: Any | 59.6 (51.0 to 67.7) | 62.1 (53.6 to 70.2) | | |
| Pain at injection site: Mild | 32.6 (25.0 to 41.0) | 29.3 (21.9 to 37.6) | | |
| Pain at injection site: Moderate | 20.6 (14.2 to 28.2) | 26.4 (19.3 to 34.5) | | |
| Pain at injection site: Severe | 6.4 (3.0 to 11.8) | 6.4 (3.0 to 11.9) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 2

| | |
|---|--|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 2 ^[4] |
| End point description: | |
| Systemic Events:recorded daily using an daily e-diary. Systemic events:Fever graded 1)< 38.0 degrees C,2) >= 38.0 degree C to 38.4 degree C,3)38.5 degree C to 38.9 degree C,4)39.0 degree C to 40.0 degree C,5)>40.0 degree C; Decreased appetite graded: mild(decreased interest in eating),moderate(decreased oral intake), severe(refusal to feed);Drowsiness graded: mild(increased or prolonged sleeping bouts),moderate(lightly subdued; interfering with daily activity),severe (disabling;not interested in usual daily activity); Irritability graded: mild(easily consolable),moderate(required increased attention),severe(inconsolable;crying could not be comforted). Subjects may be represented in >1 row. "Any" for decreased appetite,increased sleep,irritability:any grade of these systemic events. Safety population for infant series:all subjects who received at least 1 dose of study vaccine during infant series. "N":subjects who were evaluable for this measure. | |
| End point type | Primary |

End point timeframe:

Within 7 days after Vaccination 2

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 141 | 140 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: <38.0 degree C | 8.5 (4.5 to 14.4) | 8.6 (4.5 to 14.5) | | |
| Fever: >=38.0 degree C to 38.4 degree C | 6.4 (3.0 to 11.8) | 5.7 (2.5 to 10.9) | | |
| Fever: 38.5 degree C to 38.9 degree C | 2.1 (0.4 to 6.1) | 2.1 (0.4 to 6.1) | | |
| Fever: 39.0 degree C to 40.0 degree C | 0 (0.0 to 2.6) | 0 (0.0 to 2.6) | | |
| Fever: >40.0 degree C | 0 (0.0 to 2.6) | 0.7 (0.0 to 3.9) | | |
| Decreased appetite: Any | 40.4 (32.3 to 49.0) | 38.6 (30.5 to 47.2) | | |
| Decreased appetite: Mild | 27.0 (19.8 to 35.1) | 25.0 (18.1 to 33.0) | | |
| Decreased appetite: Moderate | 12.1 (7.2 to 18.6) | 12.1 (7.2 to 18.7) | | |
| Decreased appetite: Severe | 1.4 (0.2 to 5.0) | 1.4 (0.2 to 5.1) | | |
| Drowsiness: Any | 50.4 (41.8 to 58.9) | 52.1 (43.5 to 60.7) | | |
| Drowsiness: Mild | 23.4 (16.7 to 31.3) | 22.1 (15.6 to 29.9) | | |
| Drowsiness: Moderate | 25.5 (18.6 to 33.6) | 26.4 (19.3 to 34.5) | | |
| Drowsiness: Severe | 1.4 (0.2 to 5.0) | 3.6 (1.2 to 8.1) | | |

| | | | | |
|------------------------|---------------------|---------------------|--|--|
| Irritability: Any | 56.7 (48.1 to 65.0) | 60.0 (51.4 to 68.2) | | |
| Irritability: Mild | 29.1 (21.7 to 37.3) | 37.9 (29.8 to 46.4) | | |
| Irritability: Moderate | 24.8 (17.9 to 32.8) | 17.9 (11.9 to 25.2) | | |
| Irritability: Severe | 2.8 (0.8 to 7.1) | 4.3 (1.6 to 9.1) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 3

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 3 ^[5] |
|-----------------|--|

End point description:

Local reactions were recorded daily using an electronic diary. Local reactions included redness, swelling and pain at injection site. Redness and swelling were graded as mild (0.5 to 2.5 cm), moderate (2.5 to 7.0 cm) and, severe (> 7 cm). Pain at injection site was graded as mild (hurts if gently touched (example, whimpers, winces, protests, or withdraws), moderate (hurts if gently touched [with crying]), and severe (causes limitation of limb movement). Subjects may be represented in more than 1 row. Here, "Any" for each of 3 local reactions represents any grade of local reaction among mild, moderate or severe. Safety population for infant series included all subjects who received at least 1 dose of study vaccine during infant series. Here, "N": number subjects who were evaluable for this outcome measure.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Within 7 days after Vaccination 3

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 139 | 140 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Any | 20.1 (13.8 to 27.8) | 22.9 (16.2 to 30.7) | | |
| Redness: Mild | 20.1 (13.8 to 27.8) | 20.0 (13.7 to 27.6) | | |
| Redness: Moderate | 0 (0.0 to 2.6) | 2.9 (0.8 to 7.2) | | |
| Redness: Severe | 0 (0.0 to 2.6) | 0 (0.0 to 2.6) | | |
| Swelling: Any | 23.0 (16.3 to 30.9) | 27.1 (20.0 to 35.3) | | |
| Swelling: Mild | 20.9 (14.4 to 28.6) | 23.6 (16.8 to 31.5) | | |
| Swelling: Moderate | 2.2 (0.4 to 6.2) | 2.9 (0.8 to 7.2) | | |
| Swelling: Severe | 0 (0.0 to 2.6) | 0.7 (0.0 to 3.9) | | |

| | | | | |
|----------------------------------|---------------------|---------------------|--|--|
| Pain at injection site: Any | 55.4 (46.7 to 63.8) | 54.3 (45.7 to 62.7) | | |
| Pain at injection site: Mild | 30.2 (22.7 to 38.6) | 27.9 (20.6 to 36.1) | | |
| Pain at injection site: Moderate | 23.0 (16.3 to 30.9) | 21.4 (14.9 to 29.2) | | |
| Pain at injection site: Severe | 2.2 (0.4 to 6.2) | 5.0 (2.0 to 10.0) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 3

| | |
|---|--|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 3 ^[6] |
| End point description: | |
| Systemic Events:recorded daily using an daily e-diary. Systemic events:Fever graded 1)< 38.0 degrees C,2) >= 38.0 degree C to 38.4 degree C,3)38.5 degree C to 38.9 degree C,4)39.0 degree C to 40.0 degree C,5)>40.0 degree C; Decreased appetite graded: mild(decreased interest in eating),moderate(decreased oral intake), severe(refusal to feed);Drowsiness graded: mild(increased or prolonged sleeping bouts),moderate(lightly subdued; interfering with daily activity),severe (disabling;not interested in usual daily activity); Irritability graded: mild(easily consolable),moderate(required increased attention),severe(inconsolable;crying could not be comforted). Subjects may be represented in >1 row. "Any" for decreased appetite,increased sleep,irritability:any grade of these systemic events. Safety population for infant series:all subjects who received at least 1 dose of study vaccine during infant series. "N":subjects who were evaluable for this measure. | |
| End point type | Primary |
| End point timeframe: | |
| Within 7 days after Vaccination 3 | |

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 139 | 140 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: <38.0 degree C | 7.2 (3.5 to 12.8) | 9.3 (5.0 to 15.4) | | |
| Fever: >=38.0 degree C to 38.4 degree C | 4.3 (1.6 to 9.2) | 6.4 (3.0 to 11.9) | | |
| Fever: 38.5 degree C to 38.9 degree C | 2.2 (0.4 to 6.2) | 1.4 (0.2 to 5.1) | | |
| Fever: 39.0 degree C to 40.0 degree C | 0 (0.0 to 2.6) | 1.4 (0.2 to 5.1) | | |
| Fever: >40.0 degree C | 0.7 (0.0 to 3.9) | 0 (0.0 to 2.6) | | |
| Decreased appetite: Any | 34.5 (26.7 to 43.1) | 36.4 (28.5 to 45.0) | | |

| | | | | |
|------------------------------|---------------------|---------------------|--|--|
| Decreased appetite: Mild | 20.0 (13.8 to 27.8) | 23.6 (16.8 to 31.5) | | |
| Decreased appetite: Moderate | 11.5 (6.7 to 18.0) | 10.0 (5.6 to 16.2) | | |
| Decreased appetite: Severe | 2.9 (0.8 to 7.2) | 2.9 (0.8 to 7.2) | | |
| Drowsiness: Any | 36.0 (28.0 to 44.5) | 39.3 (31.1 to 47.9) | | |
| Drowsiness: Mild | 20.9 (14.4 to 28.6) | 19.3 (13.1 to 26.8) | | |
| Drowsiness: Moderate | 13.7 (8.4 to 20.5) | 17.9 (11.9 to 25.2) | | |
| Drowsiness: Severe | 1.4 (0.2 to 5.1) | 2.1 (0.4 to 6.1) | | |
| Irritability: Any | 54.7 (46.0 to 63.1) | 60.0 (51.4 to 68.2) | | |
| Irritability: Mild | 31.7 (24.0 to 40.1) | 37.9 (29.8 to 46.4) | | |
| Irritability: Moderate | 19.4 (13.2 to 27.0) | 15.7 (10.1 to 22.8) | | |
| Irritability: Severe | 3.6 (1.2 to 8.2) | 6.4 (3.0 to 11.9) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 4

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 4 ^[7] |
|-----------------|--|

End point description:

Local reactions were recorded daily using an electronic diary. Local reactions included redness, swelling and pain at injection site. Redness and swelling were graded as mild (0.5 to 2.5 cm), moderate (2.5 to 7.0 cm) and, severe (> 7 cm). Pain at injection site was graded as mild (hurts if gently touched (example, whimpers, winces, protests, or withdraws), moderate (hurts if gently touched [with crying]), and severe (causes limitation of limb movement). Subjects may be represented in more than 1 row. Here, "Any" for each of 3 local reactions represents any grade of local reaction among mild, moderate or severe. Safety population for infant series included all subjects who received at least 1 dose of study vaccine during infant series. Here, "N": number subjects who were evaluable for this outcome measure.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Within 7 days after Vaccination 4

Notes:

[7] - 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: Only descriptive data was analyzed for this endpoint.

| | | | | |
|----------------------------------|---|--|--|--|
| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 132 | 132 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |

| | | | | |
|----------------------------------|---------------------|---------------------|--|--|
| Redness: Any | 8.3 (4.2 to 14.4) | 11.4 (6.5 to 18.0) | | |
| Redness: Mild | 8.3 (4.2 to 14.4) | 10.6 (5.9 to 17.2) | | |
| Redness: Moderate | 0 (0.0 to 2.8) | 0.8 (0.0 to 4.1) | | |
| Redness: Severe | 0 (0.0 to 2.8) | 0 (0.0 to 2.8) | | |
| Swelling: Any | 9.1 (4.8 to 15.3) | 12.1 (7.1 to 18.9) | | |
| Swelling: Mild | 6.8 (3.2 to 12.5) | 11.4 (6.5 to 18.0) | | |
| Swelling: Moderate | 2.3 (0.5 to 6.5) | 0.8 (0.0 to 4.1) | | |
| Swelling: Severe | 0 (0.0 to 2.8) | 0 (0.0 to 2.8) | | |
| Pain at injection site: Any | 25.0 (17.9 to 33.3) | 19.7 (13.3 to 27.5) | | |
| Pain at injection site: Mild | 18.9 (12.6 to 26.7) | 13.6 (8.3 to 20.7) | | |
| Pain at injection site: Moderate | 6.1 (2.7 to 11.6) | 5.3 (2.2 to 10.6) | | |
| Pain at injection site: Severe | 0 (0.0 to 2.8) | 0.8 (0.0 to 4.1) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 4

| | |
|---|--|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 4 ^[8] |
| End point description: | |
| Systemic Events:recorded daily using an daily e-diary. Systemic events:Fever graded 1)< 38.0 degrees C,2) >= 38.0 degree C to 38.4 degree C,3)38.5 degree C to 38.9 degree C,4)39.0 degree C to 40.0 degree C,5)>40.0 degree C; Decreased appetite graded: mild(decreased interest in eating),moderate(decreased oral intake), severe(refusal to feed);Drowsiness graded: mild(increased or prolonged sleeping bouts),moderate(lightly subdued; interfering with daily activity),severe (disabling;not interested in usual daily activity); Irritability graded: mild(easily consolable),moderate(required increased attention),severe(inconsolable;crying could not be comforted). Subjects may be represented in >1 row. "Any" for decreased appetite,increased sleep,irritability:any grade of these systemic events. Safety population for infant series:all subjects who received at least 1 dose of study vaccine during infant series. "N":subjects who were evaluable for this measure. | |
| End point type | Primary |
| End point timeframe: | |
| Within 7 days after Vaccination 4 | |

Notes:

[8] - 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: Only descriptive data was analyzed for this endpoint.

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 132 | 132 | | |
| Units: percentage of subjects | | | | |

| number (confidence interval 95%) | | | | |
|---|---------------------|---------------------|--|--|
| Fever: <38.0 degree C | 3.0 (0.8 to 7.6) | 4.5 (1.7 to 9.6) | | |
| Fever: >=38.0 degree C to 38.4 degree C | 1.5 (0.2 to 5.4) | 3.8 (1.2 to 8.6) | | |
| Fever: 38.5 degree C to 38.9 degree C | 0 (0.0 to 2.8) | 0 (0.0 to 2.8) | | |
| Fever: 39.0 degree C to 40.0 degree C | 0 (0.0 to 2.8) | 0.8 (0.0 to 4.1) | | |
| Fever: >40.0 degree C | 1.5 (0.2 to 5.4) | 0 (0.0 to 2.8) | | |
| Decreased appetite: Any | 15.2 (9.5 to 22.4) | 16.7 (10.7 to 24.1) | | |
| Decreased appetite: Mild | 10.6 (5.9 to 17.2) | 6.8 (3.2 to 12.5) | | |
| Decreased appetite: Moderate | 4.5 (1.7 to 9.6) | 9.8 (5.3 to 16.3) | | |
| Decreased appetite: Severe | 0 (0.0 to 2.8) | 0 (0.0 to 2.8) | | |
| Drowsiness: Any | 7.6 (3.7 to 13.5) | 18.9 (12.6 to 26.7) | | |
| Drowsiness: Mild | 3.8 (1.2 to 8.6) | 12.9 (7.7 to 19.8) | | |
| Drowsiness: Moderate | 3.8 (1.2 to 8.6) | 6.1 (2.7 to 11.6) | | |
| Drowsiness: Severe | 0 (0.0 to 2.8) | 0 (0.0 to 2.8) | | |
| Irritability: Any | 24.2 (17.2 to 32.5) | 23.5 (16.5 to 31.6) | | |
| Irritability: Mild | 15.9 (10.1 to 23.3) | 16.7 (10.7 to 24.1) | | |
| Irritability: Moderate | 7.6 (3.7 to 13.5) | 5.3 (2.2 to 10.6) | | |
| Irritability: Severe | 0.8 (0.0 to 4.1) | 1.5 (0.2 to 5.4) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) After Vaccination 1 up to 1 Month After Vaccination 3

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Adverse Events (AEs) After Vaccination 1 up to 1 Month After Vaccination 3 ^[9] |
|-----------------|---|

End point description:

An AE was any untoward medical occurrence in a subjects who received study vaccine without regard to possibility of causal relationship. Safety population for infant series included all subjects who received at least 1 dose of study vaccine during infant series.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

First Vaccination 1 up to 1 Month after Vaccination 3 (for a maximum study duration of 3 months)

Notes:

[9] - 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: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 150 | 150 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 47.3 (39.1 to 55.6) | 49.3 (41.1 to 57.6) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) From Vaccination 4 up to 1 Month After Vaccination 4

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Adverse Events (AEs) From Vaccination 4 up to 1 Month After Vaccination 4 ^[10] |
|-----------------|---|

End point description:

An AE was any untoward medical occurrence in a subjects who received study vaccine without regard to possibility of causal relationship. Safety population for toddler dose included all subjects who received at least 1 dose of study vaccine during toddler dosing.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Vaccination 4 up to 1 month after Vaccination 4 (for a maximum study duration of 1 month)

Notes:

[10] - 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: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 139 | 139 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 7.9 (4.0 to 13.7) | 8.6 (4.5 to 14.6) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) After Vaccination 1 up to 1 Month After Vaccination 4

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Serious Adverse Events (SAEs) After Vaccination 1 up to 1 Month After Vaccination 4 ^[11] |
|-----------------|---|

End point description:

An AE was any untoward medical occurrence in a subject who received study vaccine without regard to possibility of causal relationship. A SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Safety population for study included all subjects who received at least 1 dose of study vaccine in study.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Vaccination 1 up to 1 month after Vaccination 4 (for a maximum study duration of 11.5 months)

Notes:

[11] - 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: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 150 | 150 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 8.0 (4.2 to 13.6) | 4.7 (1.9 to 9.4) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With New Diagnosed Chronic Medical Condition (NDCMC) From 1 Month After Vaccination 3 up to Vaccination 4

| | |
|-----------------|--|
| End point title | Number of Subjects With New Diagnosed Chronic Medical Condition (NDCMC) From 1 Month After Vaccination 3 up to Vaccination 4 ^[12] |
|-----------------|--|

End point description:

A newly diagnosed chronic medical condition was defined as a disease or medical condition, not previously identified, that was expected to be persistent or otherwise long-lasting in its effects. Safety population for study included all subjects who received at least 1 dose of study vaccine in study.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From 1 month after Vaccination 3 up to Vaccination 4 (for a maximum study duration of 7.5 months)

Notes:

[12] - 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: Only descriptive data was analyzed for this endpoint.

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 150 | 150 | | |

| | | | | |
|-----------------|---|---|--|--|
| Units: subjects | 0 | 0 | | |
|-----------------|---|---|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Immunoglobulin G (IgG) Concentrations Greater Than or Equal to (\geq) Pre-defined Thresholds for Each of the Pneumococcal Serotypes Measured 1 Month After Vaccination 3

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Immunoglobulin G (IgG) Concentrations Greater Than or Equal to (\geq) Pre-defined Thresholds for Each of the Pneumococcal Serotypes Measured 1 Month After Vaccination 3 |
|-----------------|--|

End point description:

Percentage of subjects achieving predefined antibody threshold: ≥ 0.35 microgram per milliliter (mcg/mL) for the 10 pneumococcal serotypes 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F and 23F; threshold ≥ 0.23 mcg/mL for serotype 5, threshold ≥ 0.10 mcg/mL for serotype 6B, threshold ≥ 0.12 mcg/mL for serotype 19A, along with the corresponding 95 percent (%) confidence interval (CI) are reported. Evaluable immunogenicity population for infant series: all eligible subjects aged 6 weeks at time of Dose 1, who received 3 doses of infant series vaccine, had blood drawn post-Dose 3 within 27 to 56 days (inclusive) post Dose 3, had at least 1 valid and determinate assay result post Dose 3, and had no major protocol violations.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month after Vaccination 3

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 136 | 133 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype: 1 | 91.2 (85.1 to 95.4) | 85.0 (77.7 to 90.6) | | |
| Serotype: 3 | 91.9 (86.0 to 95.9) | 85.7 (78.6 to 91.2) | | |
| Serotype: 4 | 91.2 (85.1 to 95.4) | 91.0 (84.8 to 95.3) | | |
| Serotype: 5 | 84.6 (77.4 to 90.2) | 82.0 (74.4 to 88.1) | | |
| Serotype: 6A | 83.8 (76.5 to 89.6) | 71.4 (63.0 to 78.9) | | |
| Serotype: 6B | 77.2 (69.2 to 84.0) | 75.2 (67.0 to 82.3) | | |
| Serotype: 7F | 96.3 (91.6 to 98.8) | 93.2 (87.5 to 96.9) | | |

| | | | | |
|---------------|-----------------------|---------------------|--|--|
| Serotype: 9V | 85.3 (78.2 to 90.8) | 83.5 (76.0 to 89.3) | | |
| Serotype: 14 | 88.2 (81.6 to 93.1) | 82.7 (75.2 to 88.7) | | |
| Serotype: 18C | 92.6 (86.9 to 96.4) | 84.2 (76.9 to 90.0) | | |
| Serotype: 19A | 100.0 (97.3 to 100.0) | 98.5 (94.7 to 99.8) | | |
| Serotype: 19F | 97.8 (93.7 to 99.5) | 95.5 (90.4 to 98.3) | | |
| Serotype: 23F | 84.6 (77.4 to 90.2) | 76.7 (68.6 to 83.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Immunoglobulin G (IgG) Concentrations Greater Than or Equal to (\geq) Pre-defined Thresholds for Each of the Pneumococcal Serotypes Measured 1 Month After Vaccination 4

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Immunoglobulin G (IgG) Concentrations Greater Than or Equal to (\geq) Pre-defined Thresholds for Each of the Pneumococcal Serotypes Measured 1 Month After Vaccination 4 |
|-----------------|--|

End point description:

Percentage of subjects achieving predefined antibody threshold ≥ 0.35 mcg/mL for the 10 pneumococcal serotypes 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F and 23F, threshold ≥ 0.23 mcg/mL for serotype 5, threshold ≥ 0.10 mcg/mL for serotype 6B, threshold ≥ 0.12 mcg/mL for serotype 19A, along with the corresponding 95% CI are reported. Evaluable immunogenicity population for toddler dose: all eligible subjects who received 3 doses in infant series and 1 toddler dose of vaccine, had blood drawn post Dose 4 within 27 to 56 days, inclusive, post Dose 4, had at least 1 valid and determinate assay result post Dose 4, and had no major protocol violations. "Overall number of Subjects Analyzed": signifies number of subjects evaluable for this measure.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month after Vaccination 4

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 132 | 129 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype: 1 | 99.2 (95.9 to 100.0) | 100.0 (97.2 to 100.0) | | |
| Serotype: 3 | 97.0 (92.4 to 99.2) | 98.4 (94.5 to 99.8) | | |
| Serotype: 4 | 99.2 (95.9 to 100.0) | 100.0 (97.2 to 100.0) | | |

| | | | | |
|---------------|----------------------|-----------------------|--|--|
| Serotype: 5 | 99.2 (95.9 to 100.0) | 100.0 (97.2 to 100.0) | | |
| Serotype: 6A | 96.2 (91.4 to 98.8) | 96.9 (92.3 to 99.1) | | |
| Serotype: 6B | 98.5 (94.6 to 99.8) | 96.9 (92.3 to 99.1) | | |
| Serotype: 7F | 99.2 (95.9 to 100.0) | 99.2 (95.8 to 100.0) | | |
| Serotype: 9V | 98.5 (94.6 to 99.8) | 99.2 (95.8 to 100.0) | | |
| Serotype: 14 | 97.7 (93.5 to 99.5) | 96.1 (91.2 to 98.7) | | |
| Serotype: 18C | 97.0 (92.4 to 99.2) | 99.2 (95.8 to 100.0) | | |
| Serotype: 19A | 99.2 (95.9 to 100.0) | 99.2 (95.8 to 100.0) | | |
| Serotype: 19F | 98.5 (94.6 to 99.8) | 100.0 (97.2 to 100.0) | | |
| Serotype: 23F | 99.2 (95.9 to 100.0) | 96.9 (92.3 to 99.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 3

| | |
|-----------------|---|
| End point title | Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 3 |
|-----------------|---|

End point description:

Antibody (IgG) GMC for the 13 pneumococcal serotypes (serotypes 1, 3, 4, 5, 6A, 6B, 7F 9V, 14, 18C, 19A, 19F and 23F) and corresponding 2-sided 95% CI are reported. Evaluable immunogenicity population for infant series: all eligible subjects aged 6 weeks at time of Dose 1, who received 3 doses of infant series vaccine, had blood drawn post-Dose 3 within 27 to 56 days (inclusive) post Dose 3, had at least 1 valid and determinate assay result post Dose 3, and had no major protocol violations.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month after Vaccination 3

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|--|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 136 | 133 | | |
| Units: mcg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype: 1 | 1.36 (1.15 to 1.60) | 1.13 (0.94 to 1.36) | | |

| | | | | |
|---------------|---------------------|---------------------|--|--|
| Serotype: 3 | 1.01 (0.88 to 1.16) | 0.93 (0.80 to 1.07) | | |
| Serotype: 4 | 1.67 (1.40 to 1.98) | 1.75 (1.45 to 2.11) | | |
| Serotype: 5 | 0.83 (0.67 to 1.02) | 0.86 (0.67 to 1.11) | | |
| Serotype: 6A | 1.45 (1.13 to 1.87) | 0.86 (0.66 to 1.12) | | |
| Serotype: 6B | 0.41 (0.31 to 0.55) | 0.33 (0.24 to 0.46) | | |
| Serotype: 7F | 2.01 (1.74 to 2.33) | 1.85 (1.52 to 2.26) | | |
| Serotype: 9V | 1.42 (1.17 to 1.73) | 1.28 (1.02 to 1.62) | | |
| Serotype: 14 | 1.66 (1.33 to 2.06) | 1.39 (1.09 to 1.76) | | |
| Serotype: 18C | 1.81 (1.50 to 2.18) | 1.37 (1.10 to 1.71) | | |
| Serotype: 19A | 2.33 (1.96 to 2.78) | 1.86 (1.51 to 2.28) | | |
| Serotype: 19F | 2.89 (2.52 to 3.31) | 2.43 (2.04 to 2.89) | | |
| Serotype: 23F | 1.48 (1.20 to 1.81) | 0.94 (0.73 to 1.21) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 4

| | |
|-----------------|---|
| End point title | Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 4 |
|-----------------|---|

End point description:

Antibody (IgG) GMC for the 13 pneumococcal serotypes (serotypes 1, 3, 4, 5, 6A, 6B, 7F 9V, 14, 18C, 19A, 19F and 23F) and corresponding 2-sided 95% CI are reported. Evaluable immunogenicity population for toddler dose: all eligible subjects who received 3 doses in infant series and 1 toddler dose of vaccine, had blood drawn post-Dose 4 within 27 to 56 days (inclusive) post Dose 4, had at least 1 valid and determinate assay result post Dose 4, and had no major protocol violations.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month after Vaccination 4

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 132 | 130 | | |
| Units: mcg/mL | | | | |
| geometric mean (confidence interval) | | | | |

| | | | | |
|---------------|------------------------|------------------------|--|--|
| 95%) | | | | |
| Serotype: 1 | 4.35 (3.71 to 5.10) | 4.27 (3.65 to 4.99) | | |
| Serotype: 3 | 1.58 (1.36 to 1.83) | 1.63 (1.43 to 1.86) | | |
| Serotype: 4 | 10.58 (8.89 to 12.60) | 11.91 (10.19 to 13.93) | | |
| Serotype: 5 | 5.16 (4.37 to 6.10) | 5.68 (4.81 to 6.70) | | |
| Serotype: 6A | 18.55 (14.32 to 24.02) | 20.51 (16.32 to 25.78) | | |
| Serotype: 6B | 11.76 (9.24 to 14.98) | 10.87 (8.14 to 14.53) | | |
| Serotype: 7F | 7.92 (6.88 to 9.13) | 8.29 (7.17 to 9.57) | | |
| Serotype: 9V | 8.78 (7.19 to 10.73) | 9.57 (8.00 to 11.44) | | |
| Serotype: 14 | 13.20 (10.69 to 16.30) | 11.78 (9.31 to 14.90) | | |
| Serotype: 18C | 6.21 (5.19 to 7.44) | 6.27 (5.25 to 7.48) | | |
| Serotype: 19A | 12.26 (10.26 to 14.65) | 12.02 (9.75 to 14.82) | | |
| Serotype: 19F | 13.65 (11.16 to 16.69) | 14.09 (11.71 to 16.96) | | |
| Serotype: 23F | 10.89 (8.78 to 13.50) | 9.90 (7.75 to 12.66) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Activity (OPA) Geometric Mean Titers (GMTs) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 3

| | |
|-----------------|--|
| End point title | Opsonophagocytic Activity (OPA) Geometric Mean Titers (GMTs) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 3 |
|-----------------|--|

End point description:

Antibody-mediated serum OPA against the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) was measured centrally using a pneumococcal OPA assay. Initial results were measured as OPA titers, which were then logarithmically transformed for analysis; geometric means calculated and expressed as GMTs. Evaluable immunogenicity population for infant series: all eligible subjects aged 6 weeks at time of Dose 1, who received 3 doses of infant series vaccine, had blood drawn post Dose 3 within 27 to 56 days (inclusive) post Dose 3, had at least 1 valid and determinate assay result post Dose 3, and had no major protocol violations.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month after Vaccination 3

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|--|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 136 | 133 | | |
| Units: titer (1/dilution) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype: 1 | 21.8 (18.1 to 26.2) | 22.5 (18.1 to 27.9) | | |
| Serotype: 3 | 79.7 (68.8 to 92.3) | 72.8 (62.7 to 84.6) | | |
| Serotype: 4 | 1158.8 (938.3 to 1431.1) | 1159.2 (948.3 to 1417.0) | | |
| Serotype: 5 | 37.0 (31.4 to 43.5) | 40.9 (34.0 to 49.3) | | |
| Serotype: 6A | 1211.7 (896.4 to 1638.0) | 1321.9 (1026.7 to 1701.9) | | |
| Serotype: 6B | 1145.8 (870.4 to 1508.3) | 957.6 (708.2 to 1294.8) | | |
| Serotype: 7F | 1743.3 (1436.6 to 2115.5) | 1178.8 (952.6 to 1458.6) | | |
| Serotype: 9V | 643.9 (498.6 to 831.7) | 683.3 (522.6 to 893.3) | | |
| Serotype: 14 | 496.9 (344.2 to 717.3) | 341.8 (236.0 to 495.0) | | |
| Serotype: 18C | 3055.8 (2378.5 to 3926.0) | 2183.9 (1686.9 to 2827.3) | | |
| Serotype: 19A | 219.3 (169.4 to 283.9) | 275.7 (212.0 to 358.6) | | |
| Serotype: 19F | 236.1 (191.6 to 291.1) | 272.7 (219.1 to 339.4) | | |
| Serotype: 23F | 1036.4 (746.9 to 1438.0) | 926.8 (673.9 to 1274.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Activity (OPA) Geometric Mean Titers (GMT) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 4

| | |
|-----------------|---|
| End point title | Opsonophagocytic Activity (OPA) Geometric Mean Titers (GMT) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 4 |
|-----------------|---|

End point description:

Antibody-mediated serum OPA against the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) was measured centrally using a pneumococcal OPA assay. Initial results were measured as OPA titers, which were then logarithmically transformed for analysis; geometric means calculated and expressed as GMTs. Evaluable immunogenicity population for toddler dose: all eligible subjects who received 3 doses in infant series and 1 toddler dose of vaccine, had blood drawn post Dose 4 within 27 to 56 days (inclusive) post Dose 4, had at least 1 valid and determinate assay result post Dose 4, and had no major protocol violations.

| | |
|-----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 1 month after Vaccination 4 | |

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|--|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 132 | 130 | | |
| Units: titer (1/dilution) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype: 1 | 204.2 (164.7 to 253.3) | 217.0 (176.4 to 266.9) | | |
| Serotype: 3 | 121.0 (104.4 to 140.3) | 129.8 (111.7 to 150.8) | | |
| Serotype: 4 | 2991.4 (2437.5 to 3671.3) | 2519.0 (2098.7 to 3023.6) | | |
| Serotype: 5 | 157.6 (131.9 to 188.3) | 153.4 (126.6 to 185.8) | | |
| Serotype: 6A | 2945.7 (2376.0 to 3652.1) | 3092.5 (2493.5 to 3835.4) | | |
| Serotype: 6B | 1948.9 (1521.4 to 2496.7) | 1750.1 (1360.9 to 2250.8) | | |
| Serotype: 7F | 4161.5 (3498.0 to 4950.9) | 4353.8 (3706.5 to 5114.0) | | |
| Serotype: 9V | 6927.5 (5765.9 to 8323.2) | 6460.4 (5277.3 to 7908.7) | | |
| Serotype: 14 | 1505.8 (1246.5 to 1819.0) | 1302.2 (1106.1 to 1533.2) | | |
| Serotype: 18C | 8028.3 (6233.7 to 10339.7) | 7830.0 (5998.5 to 10220.7) | | |
| Serotype: 19A | 1848.9 (1472.0 to 2322.2) | 1832.5 (1454.9 to 2308.1) | | |
| Serotype: 19F | 808.0 (633.0 to 1033.5) | 766.0 (609.2 to 963.2) | | |
| Serotype: 23F | 3125.0 (2450.8 to 3984.7) | 3348.8 (2639.5 to 4248.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Opsonophagocytic Activity (OPA) Titers \geq Lower Limit of Quantitation (LLOQ) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 3

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Opsonophagocytic Activity (OPA) Titers \geq Lower Limit of Quantitation (LLOQ) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 3 |
|-----------------|--|

End point description:

Percentage of subjects achieving OPA titer \geq LLOQ along with 95% CI for the 13 pneumococcal serotypes (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F) determined in blood samples of subjects was presented. LLOQ (measured in mcg/mL) for each serotype is as follows: Serotype 1=18; Serotype 3=12; Serotype 4=21; Serotype 5=29; Serotype 6A=37; Serotype 6B=43; Serotype 7F=113; Serotype 9V=141; Serotype 14=35; Serotype 18C=31; Serotype 19A=18; Serotype 19F=48; Serotype 23F=13. Evaluable immunogenicity population for infant series: all eligible subjects aged 6 weeks at time of Dose 1, who received 3 doses of vaccine, had blood drawn post-Dose 3 within 27 to 56 days (inclusive) post Dose 3, had at least 1 valid and determinate assay result post Dose 3, and had no major protocol violations. "Overall Number of Subjects Analyzed": signifies number of subjects evaluable for this measure. "Number Analyzed, n": signifies subjects evaluable for specific serotype.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month after Vaccination 3

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 114 | 108 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype: 1 (n=111, 106) | 51.4 (41.7 to 61.0) | 46.2 (36.5 to 56.2) | | |
| Serotype: 3 (n=109, 107) | 98.2 (93.5 to 99.8) | 98.1 (93.4 to 99.8) | | |
| Serotype: 4 (n=105, 101) | 98.1 (93.3 to 99.8) | 99.0 (94.6 to 100.0) | | |
| Serotype: 5 (n=114, 107) | 62.3 (52.7 to 71.2) | 62.6 (52.7 to 71.8) | | |
| Serotype: 6A (n= 113, 107) | 91.2 (84.3 to 95.7) | 94.4 (88.2 to 97.9) | | |
| Serotype: 6B (n=109, 104) | 94.5 (88.4 to 98.0) | 92.3 (85.4 to 96.6) | | |
| Serotype: 7F (n=96, 93) | 99.0 (94.3 to 100.0) | 96.8 (90.9 to 99.3) | | |
| Serotype: 9V (n=103, 100) | 88.3 (80.5 to 93.8) | 88.0 (80.0 to 93.6) | | |
| Serotype: 14 (n= 111, 108) | 82.9 (74.6 to 89.4) | 76.9 (67.8 to 84.4) | | |
| Serotype: 18C (n=103, 99) | 98.1 (93.2 to 99.8) | 98.0 (92.9 to 99.8) | | |
| Serotype: 19A (n= 101, 92) | 92.1 (85.0 to 96.5) | 95.7 (89.2 to 98.8) | | |
| Serotype: 19F (n=107, 105) | 89.7 (82.3 to 94.8) | 91.4 (84.4 to 96.0) | | |
| Serotype: 23F (n= 99, 98) | 94.9 (88.6 to 98.3) | 94.9 (88.5 to 98.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Opsonophagocytic Activity (OPA) Titers \geq Lower Limit of Quantitation (LLOQ) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 4

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Opsonophagocytic Activity (OPA) Titers \geq Lower Limit of Quantitation (LLOQ) for Each of Pneumococcal Serotypes Measured 1 Month After Vaccination 4 |
|-----------------|--|

End point description:

Percentage of subjects achieving OPA titer \geq LLOQ along with 95% CI for the 13 pneumococcal serotypes (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F) determined in blood samples of subjects was presented. LLOQ (measured in mcg/mL) for each serotype is as follows: Serotype 1=18; Serotype 3=12; Serotype 4=21; Serotype 5=29; Serotype 6A=37; Serotype 6B=43; Serotype 7F=113; Serotype 9V=141; Serotype 14=35; Serotype 18C=31; Serotype 19A=18; Serotype 19F=48; Serotype 23F=13. Evaluable immunogenicity population for toddler dose: all eligible subjects who received 3 doses in infant series and 1 toddler dose of vaccine, had blood drawn post Dose 4 within 27 to 56 days (inclusive) post Dose 4, had at least 1 valid and determinate assay result post Dose 4, and had no major protocol violations. "Overall Number of Subjects Analyzed": signifies number of subjects evaluable for this measure. "Number Analyzed, n": signifies subjects evaluable for specific serotype.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month after Vaccination 4

| End point values | 13vPnC: Multi-dose Vial (With Preservative) | 13vPnC: Single-dose Prefilled Syringe (Without Preservative) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 106 | 102 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype: 1 (n=105, 102) | 97.1 (91.9 to 99.4) | 97.1 (91.6 to 99.4) | | |
| Serotype: 3 (n=106, 101) | 98.1 (93.4 to 99.8) | 100.0 (96.4 to 100.0) | | |
| Serotype: 4 (n=102, 99) | 100.0 (96.4 to 100.0) | 100.0 (96.3 to 100.0) | | |
| Serotype: 5 (n=105, 102) | 95.2 (89.2 to 98.4) | 97.1 (91.6 to 99.4) | | |
| Serotype: 6A (n=104, 101) | 100.0 (96.5 to 100.0) | 99.0 (94.6 to 100.0) | | |
| Serotype: 6B (n=101, 101) | 97.0 (91.6 to 99.4) | 95.0 (88.8 to 98.4) | | |
| Serotype: 7F (n=97, 90) | 100.0 (96.3 to 100.0) | 100.0 (96.0 to 100.0) | | |

| | | | | |
|----------------------------|-----------------------|-----------------------|--|--|
| Serotype: 9V (n=100, 98) | 100.0 (96.4 to 100.0) | 99.0 (94.4 to 100.0) | | |
| Serotype: 14 (n=106, 101) | 100.0 (96.6 to 100.0) | 100.0 (96.4 to 100.0) | | |
| Serotype: 18C (n=100, 100) | 99.0 (94.6 to 100.0) | 99.0 (94.6 to 100.0) | | |
| Serotype: 19A (n=97, 96) | 100.0 (96.3 to 100.0) | 99.0 (94.3 to 100.0) | | |
| Serotype: 19F (n=102, 99) | 96.1 (90.3 to 98.9) | 97.0 (91.4 to 99.4) | | |
| Serotype: 23F (n=102, 96) | 99.0 (94.7 to 100.0) | 99.0 (94.3 to 100.0) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs= Infant series: 12 months post Vaccination 1; Toddler dose: 1 month post Vaccination 4, Non-SAEs=Infant series: 3 months post Vaccination 1; Toddler dose: 1 month post Vaccination 4, Local reactions and systemic events= 7 days post any vaccination

Adverse event reporting additional description:

An AE term may be reported as both a serious and non-serious AE, but are distinct events. An AE may be serious for 1 subject and non-serious for another subject or a subject may have experienced both a serious and non-serious episode of the same event. Safety population for infant series and toddler dose evaluated respectively.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 22.1 |

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | 13vPnC, MDV With Preservative: Infant Series |
|-----------------------|--|

Reporting group description:

Infant series: subjects were randomized to receive a single 0.5 mL dose of 13vPnC with preservative 2-PE from a MDV, intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) along with 2 routine vaccines: 1) DTP-Hib-HBV vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice).

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| Reporting group title | 13vPnC, PFS Without Preservative: Infant Series |
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Reporting group description:

Infant series: subjects were randomized to receive a single 0.5 mL dose of 13vPnC without preservative 2-PE from a single-dose PFS, intramuscularly at age of 6 weeks (Vaccination 1), 10 weeks (Vaccination 2) and 14 weeks (Vaccination 3) along with 2 routine vaccines: 1) DTP-Hib-HBV vaccine, 2) rotavirus vaccine. Subjects were followed-up to 1 month after Vaccination 3. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice).

| | |
|-----------------------|---|
| Reporting group title | 13vPnC, MDV With Preservative: Toddler Dose |
|-----------------------|---|

Reporting group description:

Toddler dose followed infant series. Toddler dose: subjects were administered with a single 0.5 mL dose of 13vPnC vaccine with preservative 2-PE from MDV, intramuscularly at age of 12 months (Vaccination 4) along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice).

| | |
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| Reporting group title | 13vPnC, PFS Without Preservative: Toddler Dose |
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Reporting group description:

Toddler dose followed infant series. Toddler dose: subjects were administered with a single 0.5 mL dose of 13vPnC vaccine without preservative 2-PE from single dose PFS, intramuscularly at age of 12 months (Vaccination 4) along with routine hepatitis A virus vaccine. Subjects were followed-up to 1 month after Vaccination 4. Different limbs were used to administer study vaccine and routine vaccines (according to local clinical practice).

| Serious adverse events | 13vPnC, MDV With Preservative: Infant Series | 13vPnC, PFS Without Preservative: Infant Series | 13vPnC, MDV With Preservative: Toddler Dose |
|---|--|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 150 (3.33%) | 4 / 150 (2.67%) | 1 / 139 (0.72%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |

| | | | | |
|---|---|-----------------|-----------------|-----------------|
| Nervous system disorders Seizure | subjects affected / exposed | 0 / 150 (0.00%) | 2 / 150 (1.33%) | 0 / 139 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | | | | |
| Febrile convulsion | subjects affected / exposed | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 1 / 139 (0.72%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | | | | |
| Blood and lymphatic system disorders Anaemia | subjects affected / exposed | 0 / 150 (0.00%) | 1 / 150 (0.67%) | 0 / 139 (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 Bronchiolitis | subjects affected / exposed | 4 / 150 (2.67%) | 2 / 150 (1.33%) | 0 / 139 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | 0 / 0 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | | | | |
| Lower respiratory tract infection | subjects affected / exposed | 1 / 150 (0.67%) | 0 / 150 (0.00%) | 0 / 139 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | | | | |
| Urinary tract infection | subjects affected / exposed | 0 / 150 (0.00%) | 1 / 150 (0.67%) | 0 / 139 (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 |
| | | | | |
| Escherichia urinary tract infection | subjects affected / exposed | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 1 / 139 (0.72%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | | | | |

| | | | |
|------------------------------------|---|--|--|
| Serious adverse events | 13vPnC, PFS Without Preservative: Toddler Dose | | |
| Total subjects affected by serious | | | |

| | | | |
|---|-----------------|--|--|
| adverse events | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Nervous system disorders | | | |
| Seizure | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | 13vPnC, MDV With Preservative: Infant Series | 13vPnC, PFS Without Preservative: Infant Series | 13vPnC, MDV With Preservative: Toddler Dose |
|---|--|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 145 / 150 (96.67%) | 141 / 150 (94.00%) | 58 / 139 (41.73%) |
| Nervous system disorders | | | |
| Hypersomnia (Increased sleep) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 105 / 150 (70.00%) | 116 / 150 (77.33%) | 10 / 139 (7.19%) |
| occurrences (all) | 228 | 274 | 10 |
| General disorders and administration site conditions | | | |
| Injection site pain-1 | | | |
| subjects affected / exposed | 44 / 150 (29.33%) | 46 / 150 (30.67%) | 0 / 139 (0.00%) |
| occurrences (all) | 103 | 111 | 0 |
| Injection site pain-2 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 117 / 150 (78.00%) | 125 / 150 (83.33%) | 33 / 139 (23.74%) |
| occurrences (all) | 261 | 291 | 33 |
| Injection site swelling | | | |
| subjects affected / exposed | 17 / 150 (11.33%) | 16 / 150 (10.67%) | 0 / 139 (0.00%) |
| occurrences (all) | 22 | 20 | 0 |
| Pyrexia-1 | | | |
| subjects affected / exposed | 12 / 150 (8.00%) | 7 / 150 (4.67%) | 0 / 139 (0.00%) |
| occurrences (all) | 15 | 12 | 0 |
| Pyrexia- 2 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 37 / 150 (24.67%) | 32 / 150 (21.33%) | 0 / 139 (0.00%) |
| occurrences (all) | 45 | 41 | 0 |
| Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 64 / 150 (42.67%) | 70 / 150 (46.67%) | 12 / 139 (8.63%) |
| occurrences (all) | 116 | 149 | 12 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|--|---------------------------|---------------------------|-------------------------|
| Erythema (Redness) alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 52 / 150 (34.67%) 92 | 49 / 150 (32.67%) 96 | 11 / 139 (7.91%) 11 |
| Psychiatric disorders Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 114 / 150 (76.00%) 293 | 117 / 150 (78.00%) 315 | 32 / 139 (23.02%) 36 |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 16 / 150 (10.67%) 16 | 10 / 150 (6.67%) 15 | 0 / 139 (0.00%) 0 |
| Metabolism and nutrition disorders Decreased appetite alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 92 / 150 (61.33%) 186 | 107 / 150 (71.33%) 213 | 20 / 139 (14.39%) 24 |

| | | | |
|--|---|--|--|
| Non-serious adverse events | 13vPnC, PFS Without Preservative: Toddler Dose | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 54 / 139 (38.85%) | | |
| Nervous system disorders Hypersomnia (Increased sleep) alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 25 / 139 (17.99%) 27 | | |
| General disorders and administration site conditions Injection site pain-1 subjects affected / exposed occurrences (all) Injection site pain-2 alternative assessment type: Systematic subjects affected / exposed occurrences (all) Injection site swelling | 0 / 139 (0.00%) 0 26 / 139 (18.71%) 27 | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia-1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia- 2</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Swelling</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 139 (0.00%)</p> <p>0</p> <p>0 / 139 (0.00%)</p> <p>0</p> <p>0 / 139 (0.00%)</p> <p>0</p> <p>16 / 139 (11.51%)</p> <p>18</p> | | |
| <p>Skin and subcutaneous tissue disorders</p> <p>Erythema (Redness)</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>15 / 139 (10.79%)</p> <p>17</p> | | |
| <p>Psychiatric disorders</p> <p>Irritability</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>31 / 139 (22.30%)</p> <p>35</p> | | |
| <p>Infections and infestations</p> <p>Upper respiratory tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 139 (0.00%)</p> <p>0</p> | | |
| <p>Metabolism and nutrition disorders</p> <p>Decreased appetite</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>22 / 139 (15.83%)</p> <p>28</p> | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported