

**Clinical trial results:****A Phase 2, Randomized, Double-Blind Trial to Evaluate the Safety and Immunogenicity of a Multivalent Pneumococcal Conjugate Vaccine in Healthy Infants****Summary**

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2020-003373-21   |
| Trial protocol           | Outside EU/EEA   |
| Global end of trial date | 11 February 2020 |

**Results information**

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 26 August 2020 |
| First version publication date | 26 August 2020 |

**Trial information****Trial identification**

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | B7471003 |
|-----------------------|----------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03512288 |
| 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., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact           | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

**Paediatric regulatory details**

|  |                      |
|--|----------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                  |
| EMA paediatric investigation plan number(s)                          | EMEA-002330-PIP01-18 |
| 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                       | 09 July 2020     |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 11 February 2020 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 11 February 2020 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To describe the safety profile of 20-valent pneumococcal conjugate vaccine (20vPnC) in healthy infants.

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 Council for Harmonisation (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                          | 16 April 2018 |
| Long term follow-up planned                               | Yes           |
| Long term follow-up rationale                             | Safety        |
| Long term follow-up duration                              | 6 Months      |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 460 |
| Worldwide total number of subjects   | 460                |
| 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)  | 460 |
| 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:

Subjects were enrolled from 16 April 2018 to 11 February 2020 in the United States.

### Pre-assignment

Screening details:

A total of 460 subjects of age greater than or equal to ( $\geq$ ) 42 to less than or equal to ( $\leq$ ) 98 days at baseline, were enrolled into the study. Out of these 460 subjects, 458 subjects received study treatment.

### Period 1

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

### Arms

|                              |        |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes    |
| <b>Arm title</b>             | 20vPnC |

Arm description:

Subjects were randomised to receive a single 0.5 millilitre (mL) intramuscular injection of 20-valent pneumococcal conjugate vaccine (20vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4 respectively).

|  |  |
|--|--|
| Arm type                               | Experimental                             |
| Investigational medicinal product name | 20-valent pneumococcal conjugate vaccine |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Injection                                |
| Routes of administration               | Intramuscular use                        |

Dosage and administration details:

Subjects received a single dose (0.5 mL) of 20vPnC vaccine intramuscularly into the anterolateral thigh muscle of the left leg at 2, 4, 6, and 12 months of age.

|                  |        |
|------------------|--------|
| <b>Arm title</b> | 13vPnC |
|------------------|--------|

Arm description:

Subjects were randomised to receive a single 0.5 mL intramuscular injection of 13-valent pneumococcal conjugate vaccine (13vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4, respectively).

|  |  |
|--|--|
| Arm type                               | Active comparator                        |
| Investigational medicinal product name | 13-valent pneumococcal conjugate vaccine |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Injection                                |
| Routes of administration               | Intramuscular use                        |

Dosage and administration details:

Subjects received a single dose (0.5 mL) of 13vPnC vaccine intramuscularly into the anterolateral thigh muscle of the left leg at 2, 4, 6, and 12 months of age.

| <b>Number of subjects in period 1</b>             | 20vPnC | 13vPnC |
|---|--------|--------|
| Started   | 232    | 228    |
| Vaccination 1                                     | 231    | 227    |
| Vaccination 2                                     | 222    | 213    |
| Vaccination 3                                     | 210    | 206    |
| Vaccination 4                                     | 197    | 194    |
| Completed   | 191    | 185    |
| Not completed                                     | 41     | 43     |
| Physician decision                                | -      | 2      |
| No longer met eligibility criteria                | 5      | 2      |
| Medication error without associated adverse event | 1      | -      |
| Adverse event                                     | 1      | -      |
| Randomised but not treated                        | 1      | 1      |
| Unspecified                                       | 1      | 1      |
| Lost to follow-up                                 | 12     | 15     |
| Withdrawal by parent/guardian                     | 14     | 18     |
| Protocol deviation                                | 6      | 4      |

## Baseline characteristics

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | 20vPnC |
|-----------------------|--------|

Reporting group description:

Subjects were randomised to receive a single 0.5 millilitre (mL) intramuscular injection of 20-valent pneumococcal conjugate vaccine (20vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4 respectively).

|                       |        |
|-----------------------|--------|
| Reporting group title | 13vPnC |
|-----------------------|--------|

Reporting group description:

Subjects were randomised to receive a single 0.5 mL intramuscular injection of 13-valent pneumococcal conjugate vaccine (13vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4, respectively).

| Reporting group values                                | 20vPnC | 13vPnC | Total |
|---|--------|--------|-------|
| Number of subjects                                    | 232    | 228    | 460   |
| Age Categorical<br>Units: Subjects                    |        |        |       |
| In utero  | 0      | 0      | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0      | 0      | 0     |
| Newborns (0-27 days)                                  | 0      | 0      | 0     |
| Infants and toddlers (28 days-23<br>months)           | 232    | 228    | 460   |
| 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<br>Units: days                         |        |        |       |
| arithmetic mean                                       | 64.5   | 64.5   | -     |
| standard deviation                                    | ± 8.07 | ± 6.68 | -     |
| Gender Categorical<br>Units: Subjects                 |        |        |       |
| Female  | 112    | 115    | 227   |
| Male  | 120    | 113    | 233   |
| Race<br>Units: Subjects                               |        |        |       |
| American Indian or Alaska Native                      | 4      | 3      | 7     |
| Asian   | 9      | 5      | 14    |
| Native Hawaiian or Other Pacific<br>Islander          | 1      | 3      | 4     |
| Black or African American                             | 35     | 29     | 64    |
| White   | 161    | 171    | 332   |
| More than one race                                    | 22     | 15     | 37    |
| Unknown or Not Reported                               | 0      | 2      | 2     |
| Ethnicity<br>Units: Subjects                          |        |        |       |
| Hispanic/Latino                                       | 41     | 40     | 81    |
| Non-Hispanic/non-Latino                               | 191    | 188    | 379   |



## End points

### End points reporting groups

|  |        |
|--|--------|
| Reporting group title  | 20vPnC |
| Reporting group description:   |        |
| Subjects were randomised to receive a single 0.5 millilitre (mL) intramuscular injection of 20-valent pneumococcal conjugate vaccine (20vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4 respectively). |        |
| Reporting group title  | 13vPnC |
| Reporting group description:   |        |
| Subjects were randomised to receive a single 0.5 mL intramuscular injection of 13-valent pneumococcal conjugate vaccine (13vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4, respectively).             |        |

### 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 <sup>[1]</sup> |
| End point description:   |  |
| Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 centimeter (cm). Redness and swelling were graded as mild (0.5 to 2.0 centimetre [cm]), moderate (greater than [ $>$ ] 2.0 to 7.0 cm) and severe ( $>$ 7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed " signifies subjects evaluable for this endpoint. |  |
| 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 planned to be analyzed for this endpoint.

| End point values                 | 20vPnC              | 13vPnC              |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 229                 | 224                 |  |  |
| Units: percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) |                     |                     |  |  |
| Redness: Any                     | 24.9 (19.4 to 31.0) | 25.4 (19.9 to 31.7) |  |  |
| Redness: Mild                    | 22.3 (17.1 to 28.2) | 23.7 (18.3 to 29.8) |  |  |
| Redness: Moderate                | 2.6 (1.0 to 5.6)    | 1.8 (0.5 to 4.5)    |  |  |
| Redness: Severe                  | 0 (0.0 to 1.6)      | 0 (0.0 to 1.6)      |  |  |
| Swelling: Any                    | 12.7 (8.6 to 17.7)  | 14.3 (10.0 to 19.6) |  |  |
| Swelling: Mild                   | 10.0 (6.5 to 14.7)  | 12.9 (8.8 to 18.1)  |  |  |
| Swelling: Moderate               | 2.2 (0.7 to 5.0)    | 1.3 (0.3 to 3.9)    |  |  |
| Swelling: Severe                 | 0.4 (0.0 to 2.4)    | 0 (0.0 to 1.6)      |  |  |

|                                      |                     |                     |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| Pain at the injection site: Any      | 51.1 (44.4 to 57.7) | 53.6 (46.8 to 60.2) |  |  |
| Pain at the injection site: Mild     | 32.3 (26.3 to 38.8) | 35.7 (29.4 to 42.4) |  |  |
| Pain at the injection site: Moderate | 18.3 (13.5 to 24.0) | 17.9 (13.1 to 23.5) |  |  |
| Pain at the injection site: Severe   | 0.4 (0.0 to 2.4)    | 0 (0.0 to 1.6)      |  |  |

## Statistical analyses

No statistical analyses for this end point

### 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 <sup>[2]</sup> |
|-----------------|--|

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit = 0.5 cm. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

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

End point timeframe:

Within 7 days after Vaccination 2

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 planned to be analyzed for this endpoint.

| End point values                 | 20vPnC              | 13vPnC              |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 215                 | 204                 |  |  |
| Units: percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) |                     |                     |  |  |
| Redness: Any                     | 24.7 (19.0 to 31.0) | 28.4 (22.4 to 35.2) |  |  |
| Redness: Mild                    | 21.9 (16.5 to 28.0) | 24.0 (18.3 to 30.5) |  |  |
| Redness: Moderate                | 2.8 (1.0 to 6.0)    | 4.4 (2.0 to 8.2)    |  |  |
| Redness: Severe                  | 0 (0.0 to 1.7)      | 0 (0.0 to 1.8)      |  |  |
| Swelling: Any                    | 16.3 (11.6 to 21.9) | 18.6 (13.5 to 24.7) |  |  |
| Swelling: Mild                   | 12.6 (8.4 to 17.7)  | 13.2 (8.9 to 18.7)  |  |  |
| Swelling: Moderate               | 3.7 (1.6 to 7.2)    | 5.4 (2.7 to 9.4)    |  |  |
| Swelling: Severe                 | 0 (0.0 to 1.7)      | 0 (0.0 to 1.8)      |  |  |
| Pain at the injection site: Any  | 42.8 (36.1 to 49.7) | 48.5 (41.5 to 55.6) |  |  |
| Pain at the injection site: Mild | 26.0 (20.3 to 32.5) | 28.9 (22.8 to 35.7) |  |  |

|                                      |                     |                     |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| Pain at the injection site: Moderate | 15.8 (11.2 to 21.4) | 19.6 (14.4 to 25.7) |  |  |
| Pain at the injection site: Severe   | 0.9 (0.1 to 3.3)    | 0 (0.0 to 1.8)      |  |  |

## 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 <sup>[3]</sup> |
|-----------------|--|

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit = 0.5 cm. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

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

End point timeframe:

Within 7 days after Vaccination 3

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 planned to be analyzed for this endpoint.

| End point values                     | 20vPnC              | 13vPnC              |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type                   | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed          | 201                 | 204                 |  |  |
| Units: percentage of subjects        |                     |                     |  |  |
| number (confidence interval 95%)     |                     |                     |  |  |
| Redness: Any                         | 26.9 (20.9 to 33.6) | 26.5 (20.6 to 33.1) |  |  |
| Redness: Mild                        | 26.4 (20.4 to 33.0) | 23.0 (17.4 to 29.4) |  |  |
| Redness: Moderate                    | 0.5 (0.0 to 2.7)    | 3.4 (1.4 to 6.9)    |  |  |
| Redness: Severe                      | 0 (0.0 to 1.8)      | 0 (0.0 to 1.8)      |  |  |
| Swelling: Any                        | 17.9 (12.9 to 23.9) | 19.6 (14.4 to 25.7) |  |  |
| Swelling: Mild                       | 16.9 (12.0 to 22.8) | 15.7 (11.0 to 21.4) |  |  |
| Swelling: Moderate                   | 1.0 (0.1 to 3.5)    | 3.4 (1.4 to 6.9)    |  |  |
| Swelling: Severe                     | 0 (0.0 to 1.8)      | 0.5 (0.0 to 2.7)    |  |  |
| Pain at the injection site: Any      | 44.3 (37.3 to 51.4) | 40.7 (33.9 to 47.8) |  |  |
| Pain at the injection site: Mild     | 28.9 (22.7 to 35.6) | 27.9 (21.9 to 34.6) |  |  |
| Pain at the injection site: Moderate | 14.9 (10.3 to 20.6) | 12.7 (8.5 to 18.1)  |  |  |
| Pain at the injection site: Severe   | 0.5 (0.0 to 2.7)    | 0 (0.0 to 1.8)      |  |  |

## 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 <sup>[4]</sup> |
|-----------------|--|

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit = 0.5 cm. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Dose 4 safety population included subjects who received Dose 4 and had safety follow up between Dose 4 and 6 months after Dose 4. Here, "number of subjects analyzed" signifies subjects evaluable for this endpoint.

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

End point timeframe:

Within 7 days after Vaccination 4

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 planned to be analyzed for this endpoint.

| End point values                     | 20vPnC              | 13vPnC              |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type                   | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed          | 186                 | 185                 |  |  |
| Units: percentage of subjects        |                     |                     |  |  |
| number (confidence interval 95%)     |                     |                     |  |  |
| Redness: Any                         | 25.8 (19.7 to 32.7) | 30.3 (23.7 to 37.4) |  |  |
| Redness: Mild                        | 24.2 (18.2 to 31.0) | 25.4 (19.3 to 32.3) |  |  |
| Redness: Moderate                    | 1.6 (0.3 to 4.6)    | 4.9 (2.2 to 9.0)    |  |  |
| Redness: Severe                      | 0 (0.0 to 2.0)      | 0 (0.0 to 2.0)      |  |  |
| Swelling: Any                        | 17.2 (12.1 to 23.4) | 14.1 (9.4 to 19.9)  |  |  |
| Swelling: Mild                       | 15.1 (10.2 to 21.0) | 12.4 (8.0 to 18.1)  |  |  |
| Swelling: Moderate                   | 2.2 (0.6 to 5.4)    | 1.6 (0.3 to 4.7)    |  |  |
| Swelling: Severe                     | 0 (0.0 to 2.0)      | 0 (0.0 to 2.0)      |  |  |
| Pain at the injection site: Any      | 35.5 (28.6 to 42.8) | 35.7 (28.8 to 43.0) |  |  |
| Pain at the injection site: Mild     | 26.9 (20.7 to 33.9) | 28.6 (22.3 to 35.7) |  |  |
| Pain at the injection site: Moderate | 8.6 (5.0 to 13.6)   | 7.0 (3.8 to 11.7)   |  |  |
| Pain at the injection site: Severe   | 0 (0.0 to 2.0)      | 0 (0.0 to 2.0)      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 1

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 1 <sup>[5]</sup> |
|-----------------|--|

End point description:

Systemic events included fever, decreased appetite, drowsiness, irritability and were recorded by using an electronic diary. Fever was categorised as  $\geq 38.0$  degree Celsius (C),  $\geq 38.0$  to 38.4 degree C,  $>38.4$  to 38.9 degree C,  $>38.9$  to 40.0 degree C and  $>40.0$  degree C. Decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabled, not interested in usual daily activity). Irritability was graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable; crying could not be comforted). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

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

End point timeframe:

Within 7 days after Vaccination 1

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 planned to be analyzed for this endpoint.

| End point values                             | 20vPnC              | 13vPnC              |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                           | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                  | 229                 | 224                 |  |  |
| Units: percentage of subjects                |                     |                     |  |  |
| number (confidence interval 95%)             |                     |                     |  |  |
| Fever: $\geq 38.0$ degree C                  | 14.4 (10.1 to 19.6) | 9.8 (6.3 to 14.5)   |  |  |
| Fever: $\geq 38.0$ degree C to 38.4 degree C | 10.0 (6.5 to 14.7)  | 6.3 (3.5 to 10.3)   |  |  |
| Fever: $>38.4$ degree C to 38.9 degree C     | 3.9 (1.8 to 7.3)    | 2.2 (0.7 to 5.1)    |  |  |
| Fever: $>38.9$ degree C to 40.0 degree C     | 0.4 (0.0 to 2.4)    | 1.3 (0.3 to 3.9)    |  |  |
| Fever: $>40.0$ degree C                      | 0 (0.0 to 1.6)      | 0 (0.0 to 1.6)      |  |  |
| Decreased appetite: Any                      | 25.3 (19.8 to 31.5) | 30.4 (24.4 to 36.8) |  |  |
| Decreased appetite: Mild                     | 16.2 (11.6 to 21.6) | 19.2 (14.3 to 25.0) |  |  |
| Decreased appetite: Moderate                 | 9.2 (5.8 to 13.7)   | 10.7 (7.0 to 15.5)  |  |  |
| Decreased appetite: Severe                   | 0 (0.0 to 1.6)      | 0.4 (0.0 to 2.5)    |  |  |
| Drowsiness: Any                              | 68.1 (61.7 to 74.1) | 71.0 (64.6 to 76.8) |  |  |
| Drowsiness: Mild                             | 51.1 (44.4 to 57.7) | 54.9 (48.1 to 61.5) |  |  |

|                                       |                     |                     |  |  |
|---------------------------------------|---------------------|---------------------|--|--|
| Drowsiness: Moderate                  | 16.6 (12.0 to 22.1) | 14.3 (10.0 to 19.6) |  |  |
| Drowsiness: Severe                    | 0.4 (0.0 to 2.4)    | 1.8 (0.5 to 4.5)    |  |  |
| Irritability: Any                     | 79.5 (73.7 to 84.5) | 77.7 (71.7 to 83.0) |  |  |
| Irritability: Mild                    | 23.6 (18.2 to 29.6) | 25.9 (20.3 to 32.1) |  |  |
| Irritability: Moderate                | 50.7 (44.0 to 57.3) | 47.3 (40.6 to 54.1) |  |  |
| Irritability: Severe                  | 5.2 (2.7 to 9.0)    | 4.5 (2.2 to 8.1)    |  |  |
| Use of antipyretic or pain medication | 38.0 (31.7 to 44.6) | 44.2 (37.6 to 51.0) |  |  |

## 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 <sup>[6]</sup> |
|-----------------|--|

End point description:

Systemic events included fever, decreased appetite, drowsiness, irritability and were recorded by using an electronic diary. Fever was categorised as  $\geq 38.0$  degree C,  $\geq 38.0$  to  $38.4$  degree C,  $>38.4$  to  $38.9$  degree C,  $>38.9$  to  $40.0$  degree C and  $>40.0$  degree C. Decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed).

Drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabled, not interested in usual daily activity). Irritability was graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable; crying could not be comforted). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

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

End point timeframe:

Within 7 days after Vaccination 2

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 planned to be analyzed for this endpoint.

| End point values                               | 20vPnC              | 13vPnC              |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                             | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                    | 215                 | 204                 |  |  |
| Units: percentage of subjects                  |                     |                     |  |  |
| number (confidence interval 95%)               |                     |                     |  |  |
| Fever: $\geq 38.0$ degree C                    | 17.2 (12.4 to 22.9) | 23.0 (17.4 to 29.4) |  |  |
| Fever: $\geq 38.0$ degree C to $38.4$ degree C | 10.2 (6.5 to 15.1)  | 12.7 (8.5 to 18.1)  |  |  |
| Fever: $>38.4$ degree C to $38.9$ degree C     | 4.2 (1.9 to 7.8)    | 7.8 (4.5 to 12.4)   |  |  |
| Fever: $>38.9$ degree C to $40.0$ degree C     | 2.8 (1.0 to 6.0)    | 2.5 (0.8 to 5.6)    |  |  |
| Fever: $>40.0$ degree C                        | 0 (0.0 to 1.7)      | 0 (0.0 to 1.8)      |  |  |
| Decreased appetite: Any                        | 23.3 (17.8 to 29.5) | 27.0 (21.0 to 33.6) |  |  |

|                                    |                     |                     |  |  |
|------------------------------------|---------------------|---------------------|--|--|
| Decreased appetite: Mild           | 14.4 (10.0 to 19.8) | 14.7 (10.1 to 20.3) |  |  |
| Decreased appetite: Moderate       | 7.9 (4.7 to 12.4)   | 11.8 (7.7 to 17.0)  |  |  |
| Decreased appetite: Severe         | 0.9 (0.1 to 3.3)    | 0.5 (0.0 to 2.7)    |  |  |
| Drowsiness: Any                    | 57.2 (50.3 to 63.9) | 56.4 (49.3 to 63.3) |  |  |
| Drowsiness: Mild                   | 37.2 (30.7 to 44.0) | 37.7 (31.1 to 44.8) |  |  |
| Drowsiness: Moderate               | 17.7 (12.8 to 23.4) | 16.7 (11.8 to 22.5) |  |  |
| Drowsiness: Severe                 | 2.3 (0.8 to 5.3)    | 2.0 (0.5 to 4.9)    |  |  |
| Irritability: Any                  | 71.2 (64.6 to 77.1) | 79.9 (73.7 to 85.2) |  |  |
| Irritability: Mild                 | 20.0 (14.9 to 26.0) | 22.5 (17.0 to 28.9) |  |  |
| Irritability: Moderate             | 48.8 (42.0 to 55.7) | 52.5 (45.4 to 59.5) |  |  |
| Irritability: Severe               | 2.3 (0.8 to 5.3)    | 4.9 (2.4 to 8.8)    |  |  |
| Use of antipyretic/pain medication | 39.5 (33.0 to 46.4) | 48.5 (41.5 to 55.6) |  |  |

## 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 <sup>[7]</sup> |
|-----------------|--|

End point description:

Systemic events included fever, decreased appetite, drowsiness, irritability and were recorded by using an electronic diary. Fever was categorised as  $\geq 38.0$  degree C,  $\geq 38.0$  to 38.4 degree C,  $>38.4$  to 38.9 degree C,  $>38.9$  to 40.0 degree C and  $>40.0$  degree C. Decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabled, not interested in usual daily activity). Irritability was graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable; crying could not be comforted). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

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

End point timeframe:

Within 7 days after Vaccination 3

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 planned to be analyzed for this endpoint.

| End point values                 | 20vPnC          | 13vPnC          |  |  |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type               | Reporting group | Reporting group |  |  |
| Number of subjects analysed      | 201             | 204             |  |  |
| Units: Percentage of subjects    |                 |                 |  |  |
| number (confidence interval 95%) |                 |                 |  |  |

|  |                     |                     |  |  |
|--|---------------------|---------------------|--|--|
| Fever: $\geq 38.0$ degree C                  | 17.9 (12.9 to 23.9) | 18.1 (13.1 to 24.1) |  |  |
| Fever: $\geq 38.0$ degree C to 38.4 degree C | 10.0 (6.2 to 14.9)  | 9.8 (6.1 to 14.7)   |  |  |
| Fever: $> 38.4$ degree C to 38.9 degree C    | 4.5 (2.1 to 8.3)    | 4.9 (2.4 to 8.8)    |  |  |
| Fever: $> 38.9$ degree C to 40.0 degree C    | 3.5 (1.4 to 7.0)    | 3.4 (1.4 to 6.9)    |  |  |
| Fever: $> 40.0$ degree C                     | 0 (0.0 to 1.8)      | 0 (0.0 to 1.8)      |  |  |
| Decreased appetite: Any                      | 30.8 (24.5 to 37.7) | 33.3 (26.9 to 40.3) |  |  |
| Decreased appetite: Mild                     | 20.9 (15.5 to 27.2) | 19.1 (14.0 to 25.2) |  |  |
| Decreased appetite: Moderate                 | 9.5 (5.8 to 14.4)   | 13.7 (9.3 to 19.2)  |  |  |
| Decreased appetite: Severe                   | 0.5 (0.0 to 2.7)    | 0.5 (0.0 to 2.7)    |  |  |
| Drowsiness: Any                              | 41.3 (34.4 to 48.4) | 45.6 (38.6 to 52.7) |  |  |
| Drowsiness: Mild                             | 28.9 (22.7 to 35.6) | 29.9 (23.7 to 36.7) |  |  |
| Drowsiness: Moderate                         | 11.4 (7.4 to 16.7)  | 15.7 (11.0 to 21.4) |  |  |
| Drowsiness: Severe                           | 1.0 (0.1 to 3.5)    | 0 (0.0 to 1.8)      |  |  |
| Irritability: Any                            | 72.6 (65.9 to 78.7) | 69.6 (62.8 to 75.8) |  |  |
| Irritability: Mild                           | 28.9 (22.7 to 35.6) | 27.5 (21.5 to 34.1) |  |  |
| Irritability: Moderate                       | 40.8 (33.9 to 47.9) | 37.7 (31.1 to 44.8) |  |  |
| Irritability: Severe                         | 3.0 (1.1 to 6.4)    | 4.4 (2.0 to 8.2)    |  |  |
| Use of antipyretic/pain medication           | 42.8 (35.8 to 49.9) | 47.1 (40.1 to 54.2) |  |  |

## 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 <sup>[8]</sup> |
| End point description:   |  |
| <p>Systemic events included fever, decreased appetite, drowsiness, irritability and were recorded by using an electronic diary. Fever was categorised as <math>\geq 38.0</math> degree C, <math>\geq 38.0</math> to 38.4 degree C, <math>&gt; 38.4</math> to 38.9 degree C, <math>&gt; 38.9</math> to 40.0 degree C and <math>&gt; 40.0</math> degree C. Decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabled, not interested in usual daily activity). Irritability was graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable; crying could not be comforted). Dose 4 safety population included subjects who received Dose 4 and had safety follow up between Dose 4 and 6 months after Dose 4. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.</p> |  |
| 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 planned to be analyzed for this endpoint.

| <b>End point values</b>            | 20vPnC              | 13vPnC              |  |  |
|------------------------------------|---------------------|---------------------|--|--|
| Subject group type                 | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed        | 186                 | 185                 |  |  |
| Units: Percentage of subjects      |                     |                     |  |  |
| number (confidence interval 95%)   |                     |                     |  |  |
| Fever: >=38.0°C                    | 12.4 (8.0 to 18.0)  | 14.6 (9.8 to 20.5)  |  |  |
| Fever: >=38.0°C to 38.4°C          | 5.9 (3.0 to 10.3)   | 4.3 (1.9 to 8.3)    |  |  |
| Fever: >38.4°C to 38.9°C           | 3.2 (1.2 to 6.9)    | 7.0 (3.8 to 11.7)   |  |  |
| Fever: >38.9°C to 40.0°C           | 3.2 (1.2 to 6.9)    | 3.2 (1.2 to 6.9)    |  |  |
| Fever: >40.0°C                     | 0 (0.0 to 2.0)      | 0 (0.0 to 2.0)      |  |  |
| Decreased appetite: Any            | 23.7 (17.7 to 30.4) | 29.2 (22.8 to 36.3) |  |  |
| Decreased appetite: Mild           | 13.4 (8.9 to 19.2)  | 15.7 (10.8 to 21.7) |  |  |
| Decreased appetite: Moderate       | 10.2 (6.3 to 15.5)  | 13.5 (8.9 to 19.3)  |  |  |
| Decreased appetite: Severe         | 0 (0.0 to 2.0)      | 0 (0.0 to 2.0)      |  |  |
| Drowsiness: Any                    | 32.8 (26.1 to 40.0) | 37.3 (30.3 to 44.7) |  |  |
| Drowsiness: Mild                   | 26.9 (20.7 to 33.9) | 25.4 (19.3 to 32.3) |  |  |
| Drowsiness: Moderate               | 4.8 (2.2 to 9.0)    | 11.9 (7.6 to 17.4)  |  |  |
| Drowsiness: Severe                 | 1.1 (0.1 to 3.8)    | 0 (0.0 to 2.0)      |  |  |
| Irritability: Any                  | 62.4 (55.0 to 69.3) | 62.7 (55.3 to 69.7) |  |  |
| Irritability: Mild                 | 23.7 (17.7 to 30.4) | 19.5 (14.0 to 25.9) |  |  |
| Irritability: Moderate             | 36.0 (29.1 to 43.4) | 40.0 (32.9 to 47.4) |  |  |
| Irritability: Severe               | 2.7 (0.9 to 6.2)    | 3.2 (1.2 to 6.9)    |  |  |
| Use of antipyretic/pain medication | 37.1 (30.1 to 44.5) | 44.3 (37.0 to 51.8) |  |  |

## Statistical analyses

No statistical analyses for this end point

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

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Adverse Events (AEs) From Vaccination 1 to 1 Month After Vaccination 3 <sup>[9]</sup> |
|-----------------|---|

End point description:

An AE was any untoward medical occurrence in study subjects who received study vaccine without regard to possibility of causal relationship. Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3.

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

End point timeframe:

From Vaccination 1 to 1 month after Vaccination 3

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 planned to be analyzed for this endpoint.

| End point values                 | 20vPnC              | 13vPnC              |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 231                 | 227                 |  |  |
| Units: percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) | 61.0 (54.4 to 67.4) | 56.4 (49.7 to 62.9) |  |  |

### Statistical analyses

No statistical analyses for this end point

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

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Adverse Events (AEs) 1 Month After Vaccination 4 <sup>[10]</sup> |
|-----------------|--|

End point description:

An AE was any untoward medical occurrence in study subjects who received study vaccine without regard to possibility of causal relationship. Dose 4 safety population included subjects who received Dose 4 and had safety follow up between Dose 4 and 6 months after Dose 4.

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

End point timeframe:

1 month after Vaccination 4

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 planned to be analyzed for this endpoint.

| End point values                 | 20vPnC              | 13vPnC              |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 197                 | 194                 |  |  |
| Units: percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) | 18.3 (13.1 to 24.4) | 25.3 (19.3 to 32.0) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Subjects With Serious Adverse Events (SAEs) From Vaccination 1 to 6 Months Following Vaccination 4

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Serious Adverse Events (SAEs) |
|-----------------|---|

## End point description:

An SAE is any untoward medical occurrence at any dose that results in death; is life-threatening (immediate risk of death); requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); results in congenital anomaly/birth defect. Overall safety analysis set included all subjects who received at least 1 dose of study vaccine (20vPnC or 13vPnC) and had safety follow up in the study.

End point type Primary

## End point timeframe:

Vaccination 1 to 6 months after Vaccination 4

## 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 planned to be analyzed for this endpoint.

| End point values                 | 20vPnC           | 13vPnC           |  |  |
|----------------------------------|------------------|------------------|--|--|
| Subject group type               | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed      | 231              | 227              |  |  |
| Units: percentage of subjects    |                  |                  |  |  |
| number (confidence interval 95%) | 5.2 (2.7 to 8.9) | 2.2 (0.7 to 5.1) |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Vaccination 1 to 6 Months Following Vaccination 4**End point title Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Vaccination 1 to 6 Months Following Vaccination 4<sup>[12]</sup>

## End point description:

An NDCMC is defined as a disease or medical condition, not previously identified, that is expected to be persistent or is otherwise long-lasting in its effects. Overall safety analysis set included all subjects who received at least 1 dose of study vaccine (20vPnC or 13vPnC) and had safety follow up in the study.

End point type Primary

## End point timeframe:

Vaccination 1 to 6 months after Vaccination 4

## 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 planned to be analyzed for this endpoint.

| End point values                 | 20vPnC           | 13vPnC           |  |  |
|----------------------------------|------------------|------------------|--|--|
| Subject group type               | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed      | 231              | 227              |  |  |
| Units: percentage of subjects    |                  |                  |  |  |
| number (confidence interval 95%) | 5.2 (2.7 to 8.9) | 3.5 (1.5 to 6.8) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at 1 Month After Vaccination 3

|                 |  |
|-----------------|--|
| End point title | Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at 1 Month After Vaccination 3 |
|-----------------|--|

End point description:

Pneumococcal IgG antibody against each of the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F) was measured centrally using direct binding Luminex assay. Results were expressed as IgG concentrations. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding confidence intervals (CIs) based on the Student t distribution. Dose 3 evaluable immunogenicity population: eligible subjects aged 42-98 days on dose 1, received assigned vaccine, had valid determinate IgG concentration for at least 1 serotype 1 month post dose 3, had blood collection within 27-56 days post dose 3, had not received prohibited vaccines before the blood draw at 1 month post dose 3, had no major protocol deviations.

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

End point timeframe:

1 month after Vaccination 3

| End point values                         | 20vPnC              | 13vPnC              |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 189                 | 187                 |  |  |
| Units: microgram per millilitre          |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| Serotype 1                               | 0.92 (0.81 to 1.05) | 1.16 (1.00 to 1.33) |  |  |
| Serotype 3                               | 0.43 (0.38 to 0.48) | 0.56 (0.49 to 0.64) |  |  |
| Serotype 4                               | 1.36 (1.16 to 1.61) | 1.64 (1.39 to 1.93) |  |  |
| Serotype 5                               | 0.93 (0.79 to 1.11) | 1.13 (0.96 to 1.34) |  |  |
| Serotype 6A                              | 2.28 (1.94 to 2.67) | 2.57 (2.16 to 3.05) |  |  |
| Serotype 6B                              | 0.63 (0.49 to 0.80) | 0.99 (0.77 to 1.27) |  |  |
| Serotype 7F                              | 2.15 (1.92 to 2.40) | 2.59 (2.28 to 2.93) |  |  |
| Serotype 9V                              | 1.22 (1.05 to 1.42) | 1.45 (1.24 to 1.70) |  |  |
| Serotype 14                              | 3.15 (2.69 to 3.70) | 3.60 (3.07 to 4.21) |  |  |
| Serotype 18C                             | 1.59 (1.37 to 1.84) | 2.05 (1.76 to 2.38) |  |  |
| Serotype 19A                             | 0.85 (0.74 to 0.96) | 1.02 (0.89 to 1.17) |  |  |
| Serotype 19F                             | 1.98 (1.76 to 2.22) | 2.28 (1.99 to 2.61) |  |  |
| Serotype 23F                             | 0.94 (0.78 to 1.14) | 1.26 (1.03 to 1.55) |  |  |
| Serotype 8                               | 2.09 (1.90 to 2.30) | 0.04 (0.03 to 0.04) |  |  |

|              |                     |                     |  |  |
|--------------|---------------------|---------------------|--|--|
| Serotype 10A | 1.67 (1.35 to 2.08) | 0.03 (0.03 to 0.03) |  |  |
| Serotype 11A | 1.94 (1.70 to 2.21) | 0.01 (0.01 to 0.01) |  |  |
| Serotype 12F | 0.86 (0.72 to 1.01) | 0.02 (0.02 to 0.02) |  |  |
| Serotype 15B | 5.86 (5.11 to 6.72) | 0.04 (0.04 to 0.05) |  |  |
| Serotype 22F | 4.62 (3.99 to 5.35) | 0.01 (0.01 to 0.01) |  |  |
| Serotype 33F | 2.21 (1.87 to 2.61) | 0.05 (0.04 to 0.05) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at 1 Month After Vaccination 4

|                 |  |
|-----------------|--|
| End point title | Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at 1 Month After Vaccination 4 |
|-----------------|--|

End point description:

Pneumococcal IgG antibody against each of the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F) was measured centrally using direct binding Luminex assay. Results were expressed as IgG concentrations. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student t distribution. Dose 4 evaluable immunogenicity population: eligible subjects aged 42-98 days on dose 1, received assigned vaccine as randomized for all 4 doses, with Dose 4 received in the defined window (365-386 days of age), had valid determinate IgG concentration for at least 1 serotype 1 month post dose 4, had blood collection within 27-56 days post dose 4, had not received prohibited vaccines before the blood draw at 1 month post dose 4, had no major protocol deviations.

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

End point timeframe:

1 Month after Vaccination 4

| End point values                         | 20vPnC                 | 13vPnC                 |  |  |
|--|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed              | 168                    | 166                    |  |  |
| Units: microgram per millilitre          |                        |                        |  |  |
| geometric mean (confidence interval 95%) |                        |                        |  |  |
| Serotype 1                               | 2.65 (2.33 to 3.02)    | 3.63 (3.20 to 4.11)    |  |  |
| Serotype 3                               | 1.15 (0.97 to 1.35)    | 1.49 (1.28 to 1.74)    |  |  |
| Serotype 4                               | 7.16 (6.22 to 8.24)    | 9.45 (8.16 to 10.95)   |  |  |
| Serotype 5                               | 3.41 (2.95 to 3.93)    | 4.95 (4.29 to 5.71)    |  |  |
| Serotype 6A                              | 13.77 (12.16 to 15.59) | 18.83 (16.39 to 21.63) |  |  |
| Serotype 6B                              | 6.37 (5.42 to 7.50)    | 9.73 (8.13 to 11.65)   |  |  |

|              |                        |                       |  |  |
|--------------|------------------------|-----------------------|--|--|
| Serotype 7F  | 6.14 (5.51 to 6.83)    | 9.32 (8.26 to 10.52)  |  |  |
| Serotype 9V  | 5.52 (4.82 to 6.31)    | 7.78 (6.77 to 8.95)   |  |  |
| Serotype 14  | 8.61 (7.32 to 10.12)   | 11.04 (9.44 to 12.90) |  |  |
| Serotype 18C | 5.58 (4.89 to 6.36)    | 8.46 (7.25 to 9.88)   |  |  |
| Serotype 19A | 5.71 (4.91 to 6.64)    | 7.05 (6.04 to 8.24)   |  |  |
| Serotype 19F | 7.79 (6.73 to 9.01)    | 9.30 (7.99 to 10.83)  |  |  |
| Serotype 23F | 6.06 (5.16 to 7.12)    | 9.81 (8.10 to 11.88)  |  |  |
| Serotype 8   | 3.12 (2.78 to 3.49)    | 0.05 (0.04 to 0.06)   |  |  |
| Serotype 10A | 9.93 (8.58 to 11.50)   | 0.03 (0.03 to 0.04)   |  |  |
| Serotype 11A | 5.70 (4.96 to 6.54)    | 0.01 (0.01 to 0.02)   |  |  |
| Serotype 12F | 1.92 (1.68 to 2.20)    | 0.02 (0.02 to 0.03)   |  |  |
| Serotype 15B | 18.45 (16.43 to 20.72) | 0.04 (0.04 to 0.05)   |  |  |
| Serotype 22F | 14.68 (12.62 to 17.08) | 0.01 (0.01 to 0.01)   |  |  |
| Serotype 33F | 4.70 (4.20 to 5.27)    | 0.05 (0.04 to 0.05)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects who Achieved Pre-specified Level of Pneumococcal IgG Concentrations Within 1 Month after Vaccination 3

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects who Achieved Pre-specified Level of Pneumococcal IgG Concentrations Within 1 Month after Vaccination 3 |
|-----------------|---|

End point description:

Subjects who achieved pre-specified level of serotypes were reported. Pre-specified levels of serotypes were- for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F:  $\geq 0.35$  microgram per millilitre, for serotype 5:  $\geq 0.23$  microgram per millilitre, for serotype 6B:  $\geq 0.10$  microgram per millilitre and for serotype 19A:  $\geq 0.12$  microgram per millilitre. Dose 3 evaluable immunogenicity population: eligible subjects aged 42-98 days on dose 1, received assigned vaccine, had valid determinate IgG concentration for at least 1 serotype 1 month post dose 3, had blood collection within 27-56 days post dose 3, had not received prohibited vaccines before the blood draw at 1 month post dose 3, had no major protocol deviations.

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

End point timeframe:

1 Month after Vaccination 3

| <b>End point values</b>          | 20vPnC               | 13vPnC              |  |  |
|----------------------------------|----------------------|---------------------|--|--|
| Subject group type               | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed      | 189                  | 187                 |  |  |
| Units: percentage of subjects    |                      |                     |  |  |
| number (confidence interval 95%) |                      |                     |  |  |
| Serotype 1                       | 87.8 (82.3 to 92.1)  | 87.7 (82.1 to 92.0) |  |  |
| Serotype 3                       | 65.1 (57.8 to 71.9)  | 75.4 (68.6 to 81.4) |  |  |
| Serotype 4                       | 87.8 (82.3 to 92.1)  | 91.4 (86.5 to 95.0) |  |  |
| Serotype 5                       | 87.8 (82.3 to 92.1)  | 89.8 (84.6 to 93.8) |  |  |
| Serotype 6A                      | 93.7 (89.2 to 96.7)  | 92.5 (87.8 to 95.8) |  |  |
| Serotype 6B                      | 86.8 (81.1 to 91.3)  | 90.4 (85.2 to 94.2) |  |  |
| Serotype 7F                      | 98.9 (96.2 to 99.9)  | 97.9 (94.6 to 99.4) |  |  |
| Serotype 9V                      | 89.4 (84.1 to 93.4)  | 89.3 (84.0 to 93.3) |  |  |
| Serotype 14                      | 94.2 (89.8 to 97.1)  | 95.7 (91.7 to 98.1) |  |  |
| Serotype 18C                     | 92.6 (87.9 to 95.9)  | 95.2 (91.1 to 97.8) |  |  |
| Serotype 19A                     | 98.4 (95.4 to 99.7)  | 97.9 (94.6 to 99.4) |  |  |
| Serotype 19F                     | 98.4 (95.4 to 99.7)  | 96.8 (93.1 to 98.8) |  |  |
| Serotype 23F                     | 79.9 (73.5 to 85.4)  | 81.8 (75.5 to 87.1) |  |  |
| Serotype 8                       | 99.5 (97.1 to 100.0) | 3.7 (1.5 to 7.6)    |  |  |
| Serotype 10A                     | 87.8 (82.3 to 92.1)  | 1.1 (0.1 to 3.8)    |  |  |
| Serotype 11A                     | 97.4 (93.9 to 99.1)  | 1.6 (0.3 to 4.6)    |  |  |
| Serotype 12F                     | 82.5 (76.4 to 87.7)  | 0.5 (0.0 to 2.9)    |  |  |
| Serotype 15B                     | 98.9 (96.2 to 99.9)  | 4.3 (1.9 to 8.3)    |  |  |
| Serotype 22F                     | 98.9 (96.2 to 99.9)  | 1.1 (0.1 to 3.8)    |  |  |
| Serotype 33F                     | 92.1 (87.2 to 95.5)  | 1.6 (0.3 to 4.6)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Local reactions and Systemic events: within 7 days after each vaccination (systematic assessment), Non serious AEs: Vaccination 1 to 1 month after Vaccination 3 and Vaccination 4 to 1 month after Vaccination 4, SAEs: up to 16 months after Vaccination 1

Adverse event reporting additional description:

Same event may appear as AE and SAE, what is presented are distinct events. Event may be categorized as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Overall safety analysis set was analysed.

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | 20vPnC |
|-----------------------|--------|

Reporting group description:

Subjects were randomised to receive a single 0.5 mL intramuscular injection of 20-valent pneumococcal conjugate vaccine (20vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4 respectively).

|                       |        |
|-----------------------|--------|
| Reporting group title | 13vPnC |
|-----------------------|--------|

Reporting group description:

Subjects were randomised to receive a single 0.5 mL intramuscular injection of 13-valent pneumococcal conjugate vaccine (13vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4, respectively).

| <b>Serious adverse events</b>                     | 20vPnC           | 13vPnC          |  |
|---|------------------|-----------------|--|
| Total subjects affected by serious adverse events |                  |                 |  |
| subjects affected / exposed                       | 12 / 231 (5.19%) | 5 / 227 (2.20%) |  |
| number of deaths (all causes)                     | 0                | 0               |  |
| number of deaths resulting from adverse events    | 0                | 0               |  |
| Nervous system disorders                          |                  |                 |  |
| Seizure like phenomena                            |                  |                 |  |
| subjects affected / exposed                       | 0 / 231 (0.00%)  | 1 / 227 (0.44%) |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1           |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0           |  |
| Blood and lymphatic system disorders              |                  |                 |  |
| Anaemia   |                  |                 |  |
| subjects affected / exposed                       | 1 / 231 (0.43%)  | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders   |                  |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Respiratory distress                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Oliguria  |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Bronchiolitis                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchitis viral                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Croup infectious                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 1 / 227 (0.44%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Parainfluenzae virus infection                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 231 (0.00%) | 1 / 227 (0.44%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 231 (0.00%) | 1 / 227 (0.44%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Meningitis viral                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory syncytial virus bronchiolitis       |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory syncytial virus infection           |                 |                 |  |
| subjects affected / exposed                     | 0 / 231 (0.00%) | 1 / 227 (0.44%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sepsis  |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Viral upper respiratory tract infection         |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Failure to thrive                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Malnutrition                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 231 (0.43%) | 0 / 227 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 1 %

| <b>Non-serious adverse events</b>                     | 20vPnC             | 13vPnC             |  |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                    |                    |  |
| subjects affected / exposed                           | 225 / 231 (97.40%) | 224 / 227 (98.68%) |  |
| General disorders and administration site conditions  |                    |                    |  |
| Injection site erythema (REDNESS)                     |                    |                    |  |
| alternative assessment type: Systematic               |                    |                    |  |
| subjects affected / exposed                           | 112 / 231 (48.48%) | 120 / 227 (52.86%) |  |
| occurrences (all)                                     | 212                | 225                |  |
| Injection site pain                                   |                    |                    |  |
| alternative assessment type: Systematic               |                    |                    |  |
| subjects affected / exposed                           | 163 / 231 (70.56%) | 167 / 227 (73.57%) |  |
| occurrences (all)                                     | 364                | 368                |  |
| Injection site swelling (SWELLING)                    |                    |                    |  |
| alternative assessment type: Systematic               |                    |                    |  |
| subjects affected / exposed                           | 76 / 231 (32.90%)  | 81 / 227 (35.68%)  |  |
| occurrences (all)                                     | 132                | 137                |  |
| Pyrexia   |                    |                    |  |
| subjects affected / exposed                           | 12 / 231 (5.19%)   | 10 / 227 (4.41%)   |  |
| occurrences (all)                                     | 13                 | 12                 |  |
| Pyrexia (FEVER)                                       |                    |                    |  |
| alternative assessment type: Systematic               |                    |                    |  |
| subjects affected / exposed                           | 90 / 231 (38.96%)  | 90 / 227 (39.65%)  |  |
| occurrences (all)                                     | 129                | 133                |  |
| Immune system disorders                               |                    |                    |  |
| Food allergy  |                    |                    |  |
| subjects affected / exposed                           | 0 / 231 (0.00%)    | 3 / 227 (1.32%)    |  |
| occurrences (all)                                     | 0                  | 3                  |  |
| Respiratory, thoracic and mediastinal disorders       |                    |                    |  |

|   |   |   |  |
|---|---|---|--|
| Cough<br>subjects affected / exposed<br>occurrences (all)   | 9 / 231 (3.90%)<br>10                                 | 8 / 227 (3.52%)<br>9                                  |  |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)  | 12 / 231 (5.19%)<br>12                                | 7 / 227 (3.08%)<br>7                                  |  |
| Psychiatric disorders<br>Irritability<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)   | 214 / 231 (92.64%)<br>597                             | 206 / 227 (90.75%)<br>595                             |  |
| Injury, poisoning and procedural complications<br>Fall<br>subjects affected / exposed<br>occurrences (all)  | 6 / 231 (2.60%)<br>6                                  | 2 / 227 (0.88%)<br>2                                  |  |
| Congenital, familial and genetic disorders<br>Plagiocephaly<br>subjects affected / exposed<br>occurrences (all)   | 2 / 231 (0.87%)<br>2                                  | 4 / 227 (1.76%)<br>4                                  |  |
| Nervous system disorders<br>Agitation neonatal<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypersomnia (INCREASED SLEEP)<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all) | 2 / 231 (0.87%)<br>3<br><br>188 / 231 (81.39%)<br>423 | 4 / 227 (1.76%)<br>5<br><br>189 / 227 (83.26%)<br>436 |  |
| Ear and labyrinth disorders<br>Ear pain<br>subjects affected / exposed<br>occurrences (all)   | 3 / 231 (1.30%)<br>3                                  | 2 / 227 (0.88%)<br>2                                  |  |
| Gastrointestinal disorders<br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea   | 10 / 231 (4.33%)<br>10                                | 6 / 227 (2.64%)<br>6                                  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed            | 10 / 231 (4.33%) | 10 / 227 (4.41%) |  |
| occurrences (all)                      | 11               | 11               |  |
| Gastrooesophageal reflux disease       |                  |                  |  |
| subjects affected / exposed            | 6 / 231 (2.60%)  | 10 / 227 (4.41%) |  |
| occurrences (all)                      | 6                | 10               |  |
| Haematochezia                          |                  |                  |  |
| subjects affected / exposed            | 0 / 231 (0.00%)  | 3 / 227 (1.32%)  |  |
| occurrences (all)                      | 0                | 3                |  |
| Teething                               |                  |                  |  |
| subjects affected / exposed            | 10 / 231 (4.33%) | 16 / 227 (7.05%) |  |
| occurrences (all)                      | 11               | 17               |  |
| Vomiting                               |                  |                  |  |
| subjects affected / exposed            | 8 / 231 (3.46%)  | 9 / 227 (3.96%)  |  |
| occurrences (all)                      | 10               | 9                |  |
| Skin and subcutaneous tissue disorders |                  |                  |  |
| Dermatitis atopic                      |                  |                  |  |
| subjects affected / exposed            | 6 / 231 (2.60%)  | 5 / 227 (2.20%)  |  |
| occurrences (all)                      | 6                | 5                |  |
| Dermatitis contact                     |                  |                  |  |
| subjects affected / exposed            | 3 / 231 (1.30%)  | 0 / 227 (0.00%)  |  |
| occurrences (all)                      | 3                | 0                |  |
| Dermatitis diaper                      |                  |                  |  |
| subjects affected / exposed            | 11 / 231 (4.76%) | 8 / 227 (3.52%)  |  |
| occurrences (all)                      | 12               | 8                |  |
| Drug eruption                          |                  |                  |  |
| subjects affected / exposed            | 1 / 231 (0.43%)  | 3 / 227 (1.32%)  |  |
| occurrences (all)                      | 1                | 3                |  |
| Eczema                                 |                  |                  |  |
| subjects affected / exposed            | 5 / 231 (2.16%)  | 3 / 227 (1.32%)  |  |
| occurrences (all)                      | 5                | 3                |  |
| Eczema infantile                       |                  |                  |  |
| subjects affected / exposed            | 1 / 231 (0.43%)  | 3 / 227 (1.32%)  |  |
| occurrences (all)                      | 1                | 3                |  |
| Rash                                   |                  |                  |  |
| subjects affected / exposed            | 5 / 231 (2.16%)  | 5 / 227 (2.20%)  |  |
| occurrences (all)                      | 5                | 5                |  |

|  |                        |                        |  |
|--|------------------------|------------------------|--|
| Urticaria<br>subjects affected / exposed<br>occurrences (all)                | 0 / 231 (0.00%)<br>0   | 4 / 227 (1.76%)<br>4   |  |
| Musculoskeletal and connective tissue disorders                              |                        |                        |  |
| Acquired plagiocephaly<br>subjects affected / exposed<br>occurrences (all)   | 1 / 231 (0.43%)<br>1   | 4 / 227 (1.76%)<br>4   |  |
| Torticollis<br>subjects affected / exposed<br>occurrences (all)              | 3 / 231 (1.30%)<br>3   | 2 / 227 (0.88%)<br>2   |  |
| Infections and infestations  |                        |                        |  |
| Bronchiolitis<br>subjects affected / exposed<br>occurrences (all)            | 11 / 231 (4.76%)<br>11 | 11 / 227 (4.85%)<br>11 |  |
| Candida infection<br>subjects affected / exposed<br>occurrences (all)        | 4 / 231 (1.73%)<br>4   | 5 / 227 (2.20%)<br>6   |  |
| Candida nappy rash<br>subjects affected / exposed<br>occurrences (all)       | 0 / 231 (0.00%)<br>0   | 5 / 227 (2.20%)<br>5   |  |
| Cellulitis<br>subjects affected / exposed<br>occurrences (all)               | 3 / 231 (1.30%)<br>3   | 1 / 227 (0.44%)<br>1   |  |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)           | 12 / 231 (5.19%)<br>12 | 11 / 227 (4.85%)<br>11 |  |
| Conjunctivitis bacterial<br>subjects affected / exposed<br>occurrences (all) | 3 / 231 (1.30%)<br>3   | 0 / 227 (0.00%)<br>0   |  |
| Croup infectious<br>subjects affected / exposed<br>occurrences (all)         | 4 / 231 (1.73%)<br>4   | 3 / 227 (1.32%)<br>3   |  |
| Ear infection<br>subjects affected / exposed<br>occurrences (all)            | 2 / 231 (0.87%)<br>2   | 4 / 227 (1.76%)<br>4   |  |
| Gastroenteritis  |                        |                        |  |

|  |                         |                         |
|--|-------------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)   | 2 / 231 (0.87%)<br>2    | 8 / 227 (3.52%)<br>9    |
| Gastroenteritis viral<br>subjects affected / exposed<br>occurrences (all)                        | 6 / 231 (2.60%)<br>7    | 1 / 227 (0.44%)<br>1    |
| Hand-foot-and-mouth disease<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 231 (0.43%)<br>1    | 3 / 227 (1.32%)<br>3    |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                              | 15 / 231 (6.49%)<br>17  | 16 / 227 (7.05%)<br>18  |
| Oral candidiasis<br>subjects affected / exposed<br>occurrences (all)                             | 3 / 231 (1.30%)<br>3    | 3 / 227 (1.32%)<br>4    |
| Otitis media<br>subjects affected / exposed<br>occurrences (all)                                 | 25 / 231 (10.82%)<br>35 | 21 / 227 (9.25%)<br>27  |
| Otitis media acute<br>subjects affected / exposed<br>occurrences (all)                           | 8 / 231 (3.46%)<br>8    | 15 / 227 (6.61%)<br>19  |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all)                                    | 3 / 231 (1.30%)<br>3    | 0 / 227 (0.00%)<br>0    |
| Respiratory syncytial virus<br>bronchiolitis<br>subjects affected / exposed<br>occurrences (all) | 2 / 231 (0.87%)<br>2    | 3 / 227 (1.32%)<br>3    |
| Respiratory tract infection viral<br>subjects affected / exposed<br>occurrences (all)            | 6 / 231 (2.60%)<br>7    | 4 / 227 (1.76%)<br>5    |
| Skin candida<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 231 (0.00%)<br>0    | 5 / 227 (2.20%)<br>5    |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)            | 40 / 231 (17.32%)<br>51 | 44 / 227 (19.38%)<br>55 |

|  |                           |                           |  |
|--|---------------------------|---------------------------|--|
| Viral infection<br>subjects affected / exposed<br>occurrences (all)  | 10 / 231 (4.33%)<br>11    | 10 / 227 (4.41%)<br>11    |  |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)  | 15 / 231 (6.49%)<br>18    | 11 / 227 (4.85%)<br>11    |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all) | 134 / 231 (58.01%)<br>214 | 136 / 227 (59.91%)<br>245 |  |
| Failure to thrive<br>subjects affected / exposed<br>occurrences (all)  | 2 / 231 (0.87%)<br>2      | 3 / 227 (1.32%)<br>3      |  |
| Feeding disorder<br>subjects affected / exposed<br>occurrences (all)   | 2 / 231 (0.87%)<br>2      | 3 / 227 (1.32%)<br>3      |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 05 June 2018     | <ol style="list-style-type: none"><li>1. Revised exclusion criteria to &lt;30 days to ensure subjects received the hepatitis B vaccine at less than 30 days of age.</li><li>2. Clarified that Pfizer will provide the diphtheria, tetanus, and acellular pertussis (DTaP)-containing vaccine, as antibody levels are assessed in the study.</li><li>3. Revised the lower range for moderate severity of injection site redness and swelling from 2.5 cm to &gt;2 .0 cm</li></ol> |
| 11 February 2020 | <ol style="list-style-type: none"><li>1. Exclusion criterion 5 was updated to "Prior receipt of hepatitis B vaccine at age <math>\geq</math>30 days" to clarify the age of administration and to enable the criterion to be answered with a "yes/no" response.</li></ol>   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported