



## Clinical trial results:

### Safety and Immunogenicity of GSK Meningococcal Group B Vaccine and 13-valent Pneumococcal Vaccine administered concomitantly with Routine Infant Vaccines to Healthy Infants

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2016-003268-37   |
| Trial protocol           | Outside EU/EEA   |
| Global end of trial date | 27 December 2024 |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 13 March 2026 |
| First version publication date | 13 March 2026 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 205239 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03621670 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline   |
| Sponsor organisation address | 79 New Oxford Street, London, WC1A1DG, United Kingdom, TW8 9GS                    |
| Public contact               | GSK Response Center, GlaxoSmithKline, 44 8664357343, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 44 8664357343, GSKClinicalSupportHD@gsk.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                       | 15 October 2025  |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 27 December 2024 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

- To assess the safety and tolerability of rMenB+OMV NZ, PCV13 and other RIV when administered concomitantly to healthy infants at 2, 4, 6 and 12 months of age, throughout the study duration.
- To demonstrate the sufficiency of the immune response to rMenB+OMV NZ when administered concomitantly with PCV13 and other RIV to healthy infants at 2, 4 and 6 months of age, at 1 month after the 3rd vaccination.
- To demonstrate the sufficiency of the immune response to rMenB+OMV NZ when administered concomitantly with PCV13 and other RIV to healthy infants at 2, 4, 6 and 12 months of age, at 1 month after the 4th vaccination.
- To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV to healthy infants 2, 4 and 6 months of age, compared to PCV13 without rMenB+OMV NZ, at 1 month after the 3rd vaccination.

Protection of trial subjects:

All subjects were observed closely for at least 30 minutes in the clinic after vaccination, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines. Study vaccines were administered only by personnel qualified to perform that function according to the routine clinical practice and under applicable local laws and regulations for the specific study site. All subjects were followed up for safety for a period of 6 months to 1 year after the last vaccination.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 27 July 2018 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United States: 1196 |
| Worldwide total number of subjects   | 1196                |
| 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) | 1196 |
| 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:

Out of the 1196 participants enrolled, only 1184 participants were included in the Exposed Set and started the study.

### Period 1

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

### Arms

|                              |                |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes            |
| <b>Arm title</b>             | MenB+PCV Group |

Arm description:

Infant participants received rMenB+OMV NZ (Bexsero) along with PCV13 (Pevnar 13), Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by rMenB+OMV NZ, PCV13, Pediarix and Hiberix on Day 121 and rMenB+OMV NZ, PCV13/PCV20, M-M-R II and Varivax on Day 301.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Bexsero  |
| Investigational medicinal product code |  |
| Other name                             | GSK Biologicals' Meningococcal group-B vaccine/ rMenB+OMV NZ |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe                 |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

4 doses per participant

|  |  |
|--|--|
| Investigational medicinal product name | Pevnar13/20                                  |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Intramuscular use                            |

Dosage and administration details:

4 doses per participant

|  |  |
|--|--|
| Investigational medicinal product name | Pediarix                                     |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Intramuscular use                            |

Dosage and administration details:

3 doses per participant

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Varivax                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

|  |  |
|--|--|
| Dosage and administration details:   |  |
| 1 dose per participant   |  |
| Investigational medicinal product name   | Rotarix                                      |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Oral liquid                                  |
| Routes of administration   | Oral use                                     |
| Dosage and administration details:   |  |
| 2 doses per participant  |  |
| Investigational medicinal product name   | M-M-R II                                     |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection                       |
| Routes of administration   | Subcutaneous use                             |
| Dosage and administration details:   |  |
| 1 dose per participant   |  |
| Investigational medicinal product name   | Hiberix                                      |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection                       |
| Routes of administration   | Intramuscular use                            |
| Dosage and administration details:   |  |
| 3 doses per participant  |  |
| <b>Arm title</b>   | Placebo+PCV Group                            |
| Arm description:   |  |
| Infant participants received PCV13 along with placebo, Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by PCV13, Placebo, Pediarix and Hiberix on Day 121 and PCV13/PCV20, Placebo M-M-R II and Varivax on Day 301. |  |
| Arm type   | Placebo                                      |
| Investigational medicinal product name   | Placebo                                      |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection                       |
| Routes of administration   | Intramuscular use                            |
| Dosage and administration details:   |  |
| 4 doses per participant  |  |
| Investigational medicinal product name   | Pediarix                                     |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection in pre-filled syringe |
| Routes of administration   | Intramuscular use                            |
| Dosage and administration details:   |  |
| 3 doses per participant  |  |
| Investigational medicinal product name   | Varivax                                      |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection                       |
| Routes of administration   | Subcutaneous use                             |
| Dosage and administration details:   |  |
| 1 dose per participant   |  |

|   |  |
|---|--|
| Investigational medicinal product name                        | Rotarix                                      |
| Investigational medicinal product code                        |  |
| Other name  |  |
| Pharmaceutical forms  | Oral liquid                                  |
| Routes of administration                                      | Oral use                                     |
| Dosage and administration details:<br>2 doses per participant |  |
| Investigational medicinal product name                        | M-M-R II                                     |
| Investigational medicinal product code                        |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection                       |
| Routes of administration                                      | Subcutaneous use                             |
| Dosage and administration details:<br>1 dose per participant  |  |
| Investigational medicinal product name                        | Prevnar13/20                                 |
| Investigational medicinal product code                        |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration                                      | Intramuscular use                            |
| Dosage and administration details:<br>4 doses per participant |  |
| Investigational medicinal product name                        | Hiberix                                      |
| Investigational medicinal product code                        |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection                       |
| Routes of administration                                      | Intramuscular use                            |
| Dosage and administration details:<br>3 doses per participant |  |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | MenB+PCV Group | Placebo+PCV Group |
|---|----------------|-------------------|
| Started   | 781            | 403               |
| Completed   | 642            | 326               |
| Not completed                                       | 139            | 77                |
| Adverse event, non-fatal                            | 3              | 1                 |
| Not willing / Not able to be contacted              | 9              | 13                |
| Protocol Deviation                                  | 7              | 3                 |
| Not specified                                       | 13             | 5                 |
| Lost to follow-up                                   | 32             | 25                |
| Consent withdrawal not due to AEs                   | 54             | 18                |
| Migrated / Moved from the study area                | 21             | 12                |

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Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of the 1196 participants enrolled, only 1184 participants were included in the Exposed Set and started the study.

## Baseline characteristics

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | MenB+PCV Group |
|-----------------------|----------------|

Reporting group description:

Infant participants received rMenB+OMV NZ (Bexsero) along with PCV13 (Pevnar 13), Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by rMenB+OMV NZ, PCV13, Pediarix and Hiberix on Day 121 and rMenB+OMV NZ, PCV13/PCV20, M-M-R II and Varivax on Day 301.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Placebo+PCV Group |
|-----------------------|-------------------|

Reporting group description:

Infant participants received PCV13 along with placebo, Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by PCV13, Placebo, Pediarix and Hiberix on Day 121 and PCV13/PCV20, Placebo M-M-R II and Varivax on Day 301.

| Reporting group values                                | MenB+PCV Group | Placebo+PCV Group | Total |
|---|----------------|-------------------|-------|
| Number of subjects                                    | 781            | 403               | 1184  |
| Age categorial<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)           | 781            | 403               | 1184  |
| 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     |
| Sex: Female, Male<br>Units: Participants              |                |                   |       |
| Male  | 401            | 207               | 608   |
| Female  | 380            | 196               | 576   |
| Race/Ethnicity, Customized<br>Units: Subjects         |                |                   |       |
| Asian   | 39             | 21                | 60    |
| Black or African American                             | 84             | 33                | 117   |
| White   | 531            | 288               | 819   |
| Other (Not specified)                                 | 107            | 56                | 163   |
| American Indian or Alaska Native                      | 17             | 4                 | 21    |
| Native Hawaiian or Other Pacific<br>Islander          | 3              | 1                 | 4     |

## End points

### End points reporting groups

|  |                   |
|--|-------------------|
| Reporting group title  | MenB+PCV Group    |
| Reporting group description:   |                   |
| Infant participants received rMenB+OMV NZ (Bexsero) along with PCV13 (Pevnar 13), Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by rMenB+OMV NZ, PCV13, Pediarix and Hiberix on Day 121 and rMenB+OMV NZ, PCV13/PCV20, M-M-R II and Varivax on Day 301. |                   |
| Reporting group title  | Placebo+PCV Group |
| Reporting group description:   |                   |
| Infant participants received PCV13 along with placebo, Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by PCV13, Placebo, Pediarix and Hiberix on Day 121 and PCV13/PCV20, Placebo M-M-R II and Varivax on Day 301.                                       |                   |

### Primary: Number of participants reporting any solicited administration site events after the first vaccination administered at Day 1

|  |  |
|--|--|
| End point title  | Number of participants reporting any solicited administration site events after the first vaccination administered at Day 1 <sup>[1]</sup> |
| End point description:   |  |
| Assessed solicited administration site events include injection site tenderness (administration site pain), erythema (redness), swelling and induration. Any solicited administration site events = occurrence of the event regardless of intensity grade. Data for Rotarix is not presented as it was administered orally. Analysis was performed on the Solicited Safety Set, which included all participants who received a study vaccination and had solicited adverse event data available for the specified duration. Participants in the Placebo+PCV group did not receive Bexsero vaccine, hence they were not analyzed. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| Day 1 to Day 7   |  |

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| End point values            | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 768             | 394               |  |  |
| Units: Participants         |                 |                   |  |  |
| Erythema, Bexsero           | 156             | 0                 |  |  |
| Erythema, Pevnar 13         | 100             | 39                |  |  |
| Erythema, Placebo           | 0               | 25                |  |  |
| Erythema, Pediarix          | 72              | 32                |  |  |
| Erythema, Hiberix           | 74              | 17                |  |  |
| Induration, Bexsero         | 204             | 0                 |  |  |
| Induration, Pevnar 13       | 127             | 67                |  |  |
| Induration, Placebo         | 0               | 22                |  |  |
| Induration, Pediarix        | 70              | 34                |  |  |
| Induration, Hiberix         | 77              | 20                |  |  |
| Swelling, Bexsero           | 132             | 0                 |  |  |
| Swelling, Pevnar 13         | 77              | 34                |  |  |
| Swelling, Placebo           | 0               | 21                |  |  |
| Swelling, Pediarix          | 53              | 21                |  |  |

|                        |     |     |  |  |
|------------------------|-----|-----|--|--|
| Swelling, Hiberix      | 54  | 12  |  |  |
| Tenderness, Bexsero    | 352 | 0   |  |  |
| Tenderness, Prevnar 13 | 310 | 107 |  |  |
| Tenderness, Placebo    | 0   | 81  |  |  |
| Tenderness, Pediarix   | 270 | 92  |  |  |
| Tenderness, Hiberix    | 284 | 74  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any solicited systemic events after the first vaccination administered at Day 1

|                 |   |
|-----------------|---|
| End point title | Number of participants reporting any solicited systemic events after the first vaccination administered at Day 1 <sup>[2]</sup> |
|-----------------|---|

End point description:

Assessed systemic events include change in eating habits, sleepiness, vomiting, diarrhea, irritability, persistent crying, and fever, defined as body temperature greater than or equal to ( $\geq$ )38.0°C/100.4°F. Any solicited systemic events = occurrence of the event regardless of intensity grade. Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

Day 1 to Day 7

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| End point values            | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 768             | 394               |  |  |
| Units: Participants         |                 |                   |  |  |
| Change in eating habits     | 329             | 122               |  |  |
| Diarrhea                    | 173             | 84                |  |  |
| Irritability                | 601             | 242               |  |  |
| Persistent crying           | 248             | 89                |  |  |
| Sleepiness                  | 560             | 246               |  |  |
| Vomiting                    | 176             | 79                |  |  |
| Fever                       | 252             | 34                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any solicited administration site events after the second vaccination administered at Day 61

|                 |   |
|-----------------|---|
| End point title | Number of participants reporting any solicited administration |
|-----------------|---|

End point description:

Data for Rotarix is not presented as it was administered orally. Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type Primary

End point timeframe:

Day 61 to Day 67

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| End point values            | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 699             | 364               |  |  |
| Units: Participants         |                 |                   |  |  |
| Erythema, Bexsero           | 200             | 0                 |  |  |
| Erythema, Prevnar 13        | 129             | 62                |  |  |
| Erythema, Placebo           | 0               | 44                |  |  |
| Erythema, Pediarix          | 99              | 54                |  |  |
| Erythema, Hiberix           | 86              | 41                |  |  |
| Induration, Bexsero         | 213             | 0                 |  |  |
| Induration, Prevnar 13      | 142             | 63                |  |  |
| Induration, Placebo         | 0               | 32                |  |  |
| Induration, Pediarix        | 109             | 55                |  |  |
| Induration, Hiberix         | 80              | 32                |  |  |
| Swelling, Bexsero           | 112             | 0                 |  |  |
| Swelling, Prevnar 13        | 74              | 38                |  |  |
| Swelling, Placebo           | 0               | 19                |  |  |
| Swelling, Pediarix          | 52              | 33                |  |  |
| Tenderness, Bexsero         | 269             | 0                 |  |  |
| Swelling, Hiberix           | 49              | 17                |  |  |
| Tenderness, Prevnar 13      | 227             | 81                |  |  |
| Tenderness, Placebo         | 0               | 65                |  |  |
| Tenderness, Pediarix        | 201             | 67                |  |  |
| Tenderness, Hiberix         | 207             | 52                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any solicited systemic events after the second vaccination administered at Day 61

End point title Number of participants reporting any solicited systemic events after the second vaccination administered at Day 61<sup>[4]</sup>

End point description:

Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

Day 61 to Day 67

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| <b>End point values</b>     | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 699             | 364               |  |  |
| Units: Participants         |                 |                   |  |  |
| Change in eating habits     | 238             | 90                |  |  |
| Diarrhea                    | 119             | 66                |  |  |
| Irritability                | 514             | 215               |  |  |
| Persistent crying           | 209             | 73                |  |  |
| Sleepiness                  | 455             | 183               |  |  |
| Vomiting                    | 104             | 49                |  |  |
| Fever                       | 269             | 64                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any solicited administration site events after the third vaccination administered at Day 121

|                 |  |
|-----------------|--|
| End point title | Number of participants reporting any solicited administration site events after the third vaccination administered at Day 121 <sup>[5]</sup> |
|-----------------|--|

End point description:

Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis. Participants in the Placebo+PCV group did not receive Bexsero vaccine, hence they were not analyzed.

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

End point timeframe:

Day 121 to Day 127

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| <b>End point values</b>     | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 676             | 352               |  |  |
| Units: Participants         |                 |                   |  |  |
| Erythema, Bexsero           | 181             | 0                 |  |  |
| Erythema, Prevnar 13        | 127             | 71                |  |  |
| Erythema, Placebo           | 0               | 43                |  |  |
| Erythema, Pediarix          | 114             | 65                |  |  |

|                       |     |    |  |  |
|-----------------------|-----|----|--|--|
| Erythema, Hiberix     | 97  | 38 |  |  |
| Induration, Bexsero   | 187 | 0  |  |  |
| Induration, Pevnar 13 | 128 | 60 |  |  |
| Induration, Placebo   | 0   | 26 |  |  |
| Induration, Pediarix  | 124 | 70 |  |  |
| Induration, Hiberix   | 86  | 28 |  |  |
| Swelling, Bexsero     | 103 | 0  |  |  |
| Swelling, Pevnar 13   | 67  | 39 |  |  |
| Swelling, Placebo     | 0   | 13 |  |  |
| Swelling, Pediarix    | 55  | 28 |  |  |
| Swelling, Hiberix     | 36  | 8  |  |  |
| Tenderness, Bexsero   | 244 | 0  |  |  |
| Tenderness, Pevnar 13 | 210 | 66 |  |  |
| Tenderness, Placebo   | 0   | 52 |  |  |
| Tenderness, Pediarix  | 188 | 58 |  |  |
| Tenderness, Hiberix   | 194 | 45 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any solicited systemic events after the third vaccination administered at Day 121

|                 |   |
|-----------------|---|
| End point title | Number of participants reporting any solicited systemic events after the third vaccination administered at Day 121 <sup>[6]</sup> |
|-----------------|---|

End point description:

Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

Day 121 to Day 127

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| End point values            | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 676             | 352               |  |  |
| Units: Participants         |                 |                   |  |  |
| Change in eating habits     | 205             | 94                |  |  |
| Diarrhea                    | 87              | 44                |  |  |
| Irritability                | 454             | 179               |  |  |
| Persistent crying           | 151             | 59                |  |  |
| Sleepiness                  | 326             | 142               |  |  |
| Vomiting                    | 88              | 46                |  |  |
| Fever                       | 216             | 55                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any solicited administration site events after the fourth vaccination administered at Day 301

|                        |   |
|------------------------|---|
| End point title        | Number of participants reporting any solicited administration site events after the fourth vaccination administered at Day 301 <sup>[7]</sup>         |
| End point description: | Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis. |
| End point type         | Primary   |
| End point timeframe:   | Day 301 to Day 307  |

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| End point values            | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 579             | 299               |  |  |
| Units: Participants         |                 |                   |  |  |
| Erythema, Bexsero           | 180             | 0                 |  |  |
| Erythema, Prevnar 13/20     | 119             | 37                |  |  |
| Erythema, Placebo           | 0               | 25                |  |  |
| Erythema, MMR II            | 64              | 24                |  |  |
| Erythema, Varivax           | 62              | 20                |  |  |
| Induration, Bexsero         | 179             | 0                 |  |  |
| Induration, Prevnar 13/20   | 109             | 32                |  |  |
| Induration, Placebo         | 0               | 24                |  |  |
| Induration, MMR II          | 46              | 17                |  |  |
| Induration, Varivax         | 38              | 15                |  |  |
| Swelling, Bexsero           | 91              | 0                 |  |  |
| Swelling, Prevnar 13/20     | 52              | 18                |  |  |
| Swelling, Placebo           | 0               | 8                 |  |  |
| Swelling, MMR II            | 26              | 12                |  |  |
| Swelling, Varivax           | 23              | 9                 |  |  |
| Tenderness, Bexsero         | 223             | 0                 |  |  |
| Tenderness, Prevnar 13/20   | 181             | 35                |  |  |
| Tenderness, Placebo         | 0               | 31                |  |  |
| Tenderness, MMR II          | 130             | 28                |  |  |
| Tenderness, Varivax         | 119             | 27                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any solicited systemic events after the fourth vaccination administered at Day 301

|                 |  |
|-----------------|--|
| End point title | Number of participants reporting any solicited systemic events after the fourth vaccination administered at Day 301 <sup>[8]</sup> |
|-----------------|--|

End point description:

Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

Day 301 to Day 307

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| End point values            | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 614             | 314               |  |  |
| Units: Participants         |                 |                   |  |  |
| Change in eating habits     | 219             | 75                |  |  |
| Diarrhea                    | 85              | 40                |  |  |
| Irritability                | 401             | 153               |  |  |
| Persistent crying           | 115             | 29                |  |  |
| Rash                        | 71              | 30                |  |  |
| Sleepiness                  | 273             | 96                |  |  |
| Vomiting                    | 60              | 32                |  |  |
| Fever                       | 118             | 22                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants with any solicited systemic AEs during the 30 days after the fourth vaccination at Day 301

|                 |  |
|-----------------|--|
| End point title | Number of participants with any solicited systemic AEs during the 30 days after the fourth vaccination at Day 301 <sup>[9]</sup> |
|-----------------|--|

End point description:

Systemic events assessed included rash, parotid/salivary gland swelling, and fever. These systemic adverse events were recorded for 30 days following MMR and VV vaccine administration. Any solicited systemic events = occurrence of the event regardless of intensity grade. Analysis was performed on the

Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

Day 301 to Day 330

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| <b>End point values</b>         | MenB+PCV Group  | Placebo+PCV Group |  |  |
|---------------------------------|-----------------|-------------------|--|--|
| Subject group type              | Reporting group | Reporting group   |  |  |
| Number of subjects analysed     | 627             | 321               |  |  |
| Units: Participants             |                 |                   |  |  |
| Parotid/Salivary gland swelling | 20              | 17                |  |  |
| Rash                            | 206             | 95                |  |  |
| Fever                           | 197             | 70                |  |  |

## Statistical analyses

No statistical analyses for this end point

### **Primary: Number of participants reporting any unsolicited adverse events (AEs) after the first vaccination administered at Day 1**

|                 |   |
|-----------------|---|
| End point title | Number of participants reporting any unsolicited adverse events (AEs) after the first vaccination administered at Day 1 <sup>[10]</sup> |
|-----------------|---|

End point description:

An unsolicited AEs is an AE that is not solicited using a subject diary and that is spontaneously communicated by the parent(s)/ Legally Authorized Representatives (LARs) who has signed the informed consent or a solicited local or systemic AE that continues beyond the solicited period after vaccination. Any = occurrence of the event regardless of the intensity grade. Analysis was performed on the Unsolicited Safety Set, which included all participants who received a study vaccination and had unsolicited adverse event data available for the specified duration.

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

End point timeframe:

Day 1 to Day 30

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| <b>End point values</b>     | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 775             | 401               |  |  |
| Units: Participants         | 214             | 103               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any SAEs, AEs leading to withdrawal, AESIs and MAAEs

|                 |   |
|-----------------|---|
| End point title | Number of participants reporting any SAEs, AEs leading to withdrawal, AESIs and MAAEs <sup>[11]</sup> |
|-----------------|---|

End point description:

An SAE is any untoward medical occurrence that results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization and that results in disability/incapacity. An AE leading to withdrawal includes any AEs/SAEs collected and recorded from the time of the 1st receipt of study vaccines until study end which are identified as reasons for withdrawal of the participant from the study. AESIs are pre-defined (serious or non-serious) AEs of scientific and medical concern specific to the product or program which might warrant further investigation in order to characterize and understand it. MAAEs includes any AEs that required hospitalization, or an otherwise unscheduled visit to or from medical personnel for any reason, including emergency room visits. Analysis was performed on the Unsolicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

Day 1 up to study end (Day 481 for participants who have not reached 6-month follow-up at the time of Protocol Amendment 7; Day 661 for all others)

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| End point values            | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 775             | 401               |  |  |
| Units: Participants         |                 |                   |  |  |
| AEs leading to withdrawal   | 3               | 1                 |  |  |
| SAEs                        | 35              | 19                |  |  |
| AESIs                       | 6               | 3                 |  |  |
| MAAEs                       | 375             | 177               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any unsolicited AEs after the fourth vaccination administered at day 301

|                 |   |
|-----------------|---|
| End point title | Number of participants reporting any unsolicited AEs after the fourth vaccination administered at day 301 <sup>[12]</sup> |
|-----------------|---|

End point description:

Analysis was performed on the Unsolicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

Day 301 to Day 330

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| <b>End point values</b>     | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 668             | 339               |  |  |
| Units: Participants         | 248             | 144               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any unsolicited AEs after the third vaccination administered at Day 121

|                 |  |
|-----------------|--|
| End point title | Number of participants reporting any unsolicited AEs after the third vaccination administered at Day 121 <sup>[13]</sup> |
|-----------------|--|

End point description:

Analysis was performed on the Unsolicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

Day 121 to Day 150

Notes:

[13] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| <b>End point values</b>     | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 725             | 374               |  |  |
| Units: Participants         | 230             | 120               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of participants reporting any unsolicited AEs after the second vaccination administered at Day 61

|                 |  |
|-----------------|--|
| End point title | Number of participants reporting any unsolicited AEs after the second vaccination administered at Day 61 <sup>[14]</sup> |
|-----------------|--|

End point description:

Analysis was performed on the Unsolicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

Day 61 to Day 90

Notes:

[14] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

| <b>End point values</b>     | MenB+PCV Group  | Placebo+PCV Group |  |  |
|-----------------------------|-----------------|-------------------|--|--|
| Subject group type          | Reporting group | Reporting group   |  |  |
| Number of subjects analysed | 745             | 388               |  |  |
| Units: Participants         | 225             | 119               |  |  |

## Statistical analyses

No statistical analyses for this end point

### **Primary: Percentage of participants with human serum bactericidal assay (hSBA) antibody titers $\geq$ Lower Limit of Quantitation (LLOQ) for each of the Serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4) and M13520 (NHBA)**

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with human serum bactericidal assay (hSBA) antibody titers $\geq$ Lower Limit of Quantitation (LLOQ) for each of the Serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4) and M13520 (NHBA) <sup>[15][16]</sup> |
|-----------------|--|

End point description:

Serum bactericidal activity is assessed using hSBA against Neisseria meningitidis serogroup B test strains: M14459 (fHbp); 96217 (NadA); NZ98/254 (PorA P1.4); M13520 (NHBA). The sufficiency of the immune response to rMenB+OMV NZ at one month after the third vaccination was to be demonstrated if the lower confidence limit for the percentage of participants achieving hSBA titers  $\geq$  LLOQ is  $\geq$  60% for each of the M14459, 96217, NZ98/254, M13520 test strain. This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the Per Protocol Set (PPS) for immunogenicity, which included all participants in the Full Analysis Set (FAS) who correctly received the vaccine, with no protocol deviation and are not excluded due to other reasons defined prior to unblinding or analysis. Only participants with data available for the specified analysis at the specified timepoint were included.

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

End point timeframe:

At Day 151 (1 month after the third vaccination)

Notes:

[15] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                   | MenB+PCV Group      |  |  |  |
|------------------------------------|---------------------|--|--|--|
| Subject group type                 | Reporting group     |  |  |  |
| Number of subjects analysed        | 553                 |  |  |  |
| Units: Percentage of participants  |                     |  |  |  |
| number (confidence interval 99.2%) |                     |  |  |  |
| M14459 (fHbp)                      | 92.2 (88.6 to 94.9) |  |  |  |
| 96217 (NadA)                       | 99.4 (97.9 to 99.9) |  |  |  |
| NZ98/254 (PorA)                    | 73.5 (68.2 to 78.3) |  |  |  |
| M13520 (NHBA)                      | 53.0 (47.3 to 58.6) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of participants with hSBA titers $\geq$ LLOQ against all serogroup B test strains combined (composite response)

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with hSBA titers $\geq$ LLOQ against all serogroup B test strains combined (composite response) <sup>[17][18]</sup> |
|-----------------|--|

End point description:

The immune response to the rMenB+OMV NZ vaccine is assessed by measuring serum bactericidal activity using hSBA against four Neisseria meningitidis serogroup B test strains: M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA). The composite response is defined as the percentage of participants with hSBA titers  $\geq$  Lower Limit of Quantitation (LLOQ) across all four strains combined. The sufficiency of the immune response to rMenB+OMV NZ at one month after the third vaccination was to be demonstrated if the lower confidence limit for the percentage of participants achieving hSBA titers  $\geq$  LLOQ is  $\geq$  50% for all strains combined. This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 151 (1 month after the third vaccination)

Notes:

[17] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                   | MenB+PCV Group      |  |  |  |
|------------------------------------|---------------------|--|--|--|
| Subject group type                 | Reporting group     |  |  |  |
| Number of subjects analysed        | 524                 |  |  |  |
| Units: Percentage of participants  |                     |  |  |  |
| number (confidence interval 99.2%) | 42.7 (37.0 to 48.6) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### **Primary: Percentage of Participants with hSBA Antibody Titers $\geq 8$ for Strains M14459 (fHbp), NZ98/254 (PorA P1.4), and M13520 (NHBA) and $\geq 16$ for Strain 96217 (NadA) (Composite response across all strains)**

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with hSBA Antibody Titers $\geq 8$ for Strains M14459 (fHbp), NZ98/254 (PorA P1.4), and M13520 (NHBA) and $\geq 16$ for Strain 96217 (NadA) (Composite response across all strains) <sup>[19][20]</sup> |
|-----------------|--|

#### End point description:

The immune response to the rMenB+OMV NZ vaccine is assessed by measuring serum bactericidal activity using hSBA against four Neisseria meningitidis serogroup B test strains: M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA). The composite response is defined as the percentage of participants with hSBA titers  $\geq$  Lower Limit of Quantitation (LLOQ) across all four strains combined. The sufficiency of the immune response to rMenB+OMV NZ at one month after the 4th vaccination was to be demonstrated if the lower confidence limit for the percentage of participants achieving hSBA titers  $\geq 8$  (for strains M14459, NZ98/254, M13520) and  $\geq 16$  (for strain 96217) is  $\geq 65\%$  for all strains combined. This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

#### End point timeframe:

At Day 331 (1 month after the fourth vaccination)

#### Notes:

[19] - 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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                   | MenB+PCV Group      |  |  |  |
|------------------------------------|---------------------|--|--|--|
| Subject group type                 | Reporting group     |  |  |  |
| Number of subjects analysed        | 478                 |  |  |  |
| Units: Percentage of participants  |                     |  |  |  |
| number (confidence interval 95.8%) | 63.2 (58.5 to 67.7) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

**Primary: Percentage of Participants with hSBA Antibody Titers  $\geq 8$  for Strains M14459 (fHbp); 96217 (NadA); NZ98/254 (PorA P1.4); M13520 (NHBA) and  $\geq 16$  for Strain 96217**

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with hSBA Antibody Titers $\geq 8$ for Strains M14459 (fHbp); 96217 (NadA); NZ98/254 (PorA P1.4); M13520 (NHBA) and $\geq 16$ for Strain 96217 <sup>[21][22]</sup> |
|-----------------|---|

End point description:

Serum bactericidal activity is assessed using human complement (hSBA) against Neisseria meningitidis serogroup B test strains: M14459 (fHbp); 96217 (NadA); NZ98/254 (PorA P1.4); M13520 (NHBA). The sufficiency of the immune response to rMenB+OMV NZ at one month after the 4th vaccination was to be demonstrated if the lower confidence limit for the percentage of participants achieving hSBA titers  $\geq 8$  (for strains M14459, NZ98/254, M13520) and  $\geq 16$  (for strain 96217) is  $\geq 75\%$  for each of the M14459, 96217, NZ98/254, M13520 test strains. This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 331 (1 month after the fourth vaccination)

Notes:

[21] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                   | MenB+PCV Group      |  |  |  |
|------------------------------------|---------------------|--|--|--|
| Subject group type                 | Reporting group     |  |  |  |
| Number of subjects analysed        | 505                 |  |  |  |
| Units: Percentage of participants  |                     |  |  |  |
| number (confidence interval 95.8%) |                     |  |  |  |
| M14459 (fHbp)                      | 89.0 (85.8 to 91.7) |  |  |  |
| 96217 (NadA)                       | 99.6 (98.5 to 100)  |  |  |  |
| NZ98/254 (PorA P1.4)               | 83.2 (79.4 to 86.5) |  |  |  |
| M13520 (NHBA)                      | 76.6 (72.5 to 80.4) |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Adjusted Geometric Mean Concentrations (GMCs) of Immunoglobulin (IgG) Antibodies Against 13 PCV13 Antigens at 1 Month After Third Vaccination**

|                 |   |
|-----------------|---|
| End point title | Adjusted Geometric Mean Concentrations (GMCs) of Immunoglobulin (IgG) Antibodies Against 13 PCV13 Antigens at 1 Month After Third Vaccination |
|-----------------|---|

End point description:

The immune response to PCV13 is evaluated by measuring IgG levels using electrochemiluminescence (ECL) assay. Adjusted GMCs are assessed for each of the 13 PCV13 antigens at 1 month after the third

vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 151 (1 month after the third vaccination)

| End point values   | MenB+PCV Group   | Placebo+PCV Group |  |  |
|--|------------------|-------------------|--|--|
| Subject group type   | Reporting group  | Reporting group   |  |  |
| Number of subjects analysed                                | 244              | 278               |  |  |
| Units: Microgram per milliliter( $\mu\text{g}/\text{mL}$ ) |                  |                   |  |  |
| geometric mean (confidence interval 98.3%)                 |                  |                   |  |  |
| Serotype 1   | 1.6 (1.4 to 1.9) | 1.5 (1.3 to 1.8)  |  |  |
| Serotype 3   | 0.5 (0.4 to 0.6) | 0.5 (0.4 to 0.6)  |  |  |
| Serotype 4   | 1.1 (0.9 to 1.3) | 1.1 (1.0 to 1.3)  |  |  |
| Serotype 5   | 1.0 (0.8 to 1.2) | 1.0 (0.8 to 1.2)  |  |  |
| Serotype 6   | 2.4 (2.0 to 2.8) | 2.5 (2.1 to 2.9)  |  |  |
| Serotype 6B  | 1.5 (1.1 to 1.9) | 1.8 (1.4 to 2.3)  |  |  |
| Serotype 7F  | 2.8 (2.4 to 3.3) | 2.9 (2.5 to 3.3)  |  |  |
| Serotype 9V  | 1.3 (1.1 to 1.6) | 1.4 (1.2 to 1.6)  |  |  |
| Serotype 14  | 5.9 (4.7 to 7.4) | 5.8 (4.8 to 7.2)  |  |  |
| Serotype 18C   | 1.5 (1.3 to 1.8) | 1.5 (1.3 to 1.8)  |  |  |
| Serotype 19A   | 1.7 (1.4 to 2.0) | 1.8 (1.6 to 2.2)  |  |  |
| Serotype 19F   | 2.5 (2.1 to 2.9) | 2.5 (2.2 to 2.9)  |  |  |
| Serotype 23F   | 0.9 (0.7 to 1.1) | 1.0 (0.8 to 1.2)  |  |  |

## Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Between-group analysis |
|----------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 1.05                               |
| Confidence interval                     |                                    |
| level                                   | Other: 98.3 %                      |
| sides                                   | 2-sided                            |
| lower limit                             | 0.9                                |
| upper limit                             | 1.23                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Group GMC Ratio                    |
| Point estimate   | 0.9                                |
| Confidence interval  |                                    |
| level  | Other: 98.3 %                      |
| sides  | 2-sided                            |
| lower limit  | 0.77                               |
| upper limit  | 1.06                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Group GMC Ratio                    |
| Point estimate   | 0.95                               |
| Confidence interval  |                                    |
| level  | Other: 98.3 %                      |
| sides  | 2-sided                            |
| lower limit  | 0.81                               |
| upper limit  | 1.11                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Group GMC Ratio                    |
| Point estimate   | 1.01                               |

|                     |               |
|---------------------|---------------|
| Confidence interval |               |
| level               | Other: 98.3 % |
| sides               | 2-sided       |
| lower limit         | 0.82          |
| upper limit         | 1.24          |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.8                                |
| Confidence interval                     |                                    |
| level                                   | Other: 98.3 %                      |
| sides                                   | 2-sided                            |
| lower limit                             | 0.63                               |
| upper limit                             | 1.02                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.98                               |
| Confidence interval                     |                                    |
| level                                   | Other: 98.3 %                      |
| sides                                   | 2-sided                            |
| lower limit                             | 0.85                               |
| upper limit                             | 1.12                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 1.03                               |
| Confidence interval                     |                                    |
| level                                   | Other: 98.3 %                      |
| sides                                   | 2-sided                            |
| lower limit                             | 0.86                               |
| upper limit                             | 1.22                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.98                               |
| Confidence interval                     |                                    |
| level                                   | Other: 98.3 %                      |
| sides                                   | 2-sided                            |
| lower limit                             | 0.84                               |
| upper limit                             | 1.15                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.94                               |
| Confidence interval                     |                                    |
| level                                   | Other: 98.3 %                      |
| sides                                   | 2-sided                            |
| lower limit                             | 0.8                                |
| upper limit                             | 1.12                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Group GMC Ratio                    |
| Point estimate   | 0.91                               |
| Confidence interval  |                                    |
| level  | Other: 98.3 %                      |
| sides  | 2-sided                            |
| lower limit  | 0.77                               |
| upper limit  | 1.06                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Group GMC Ratio                    |
| Point estimate   | 1                                  |
| Confidence interval  |                                    |
| level  | Other: 98.3 %                      |
| sides  | 2-sided                            |
| lower limit  | 0.85                               |
| upper limit  | 1.18                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 522             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |                 |
| Parameter estimate                      | Group GMC Ratio |
| Point estimate                          | 0.99            |
| Confidence interval                     |                 |
| level                                   | Other: 98.3 %   |
| sides                                   | 2-sided         |
| lower limit                             | 0.86            |
| upper limit                             | 1.14            |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.87                               |
| Confidence interval                     |                                    |
| level                                   | Other: 98.3 %                      |
| sides                                   | 2-sided                            |
| lower limit                             | 0.73                               |
| upper limit                             | 1.05                               |

**Secondary: Adjusted GMCs of IgG Antibodies Against 13 PCV13 Antigens at 1 Month after the fourth vaccination administered at Day 301**

|                 |   |
|-----------------|---|
| End point title | Adjusted GMCs of IgG Antibodies Against 13 PCV13 Antigens at 1 Month after the fourth vaccination administered at Day 301 |
|-----------------|---|

End point description:

The immune response to PCV13 is evaluated by measuring IgG levels using ECL assay. Adjusted GMCs are assessed for each of the 13 PCV13 antigens at 1 month after the fourth vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 331 (1 month after the fourth vaccination)

| <b>End point values</b>                  | MenB+PCV Group   | Placebo+PCV Group |  |  |
|--|------------------|-------------------|--|--|
| Subject group type                       | Reporting group  | Reporting group   |  |  |
| Number of subjects analysed              | 225              | 240               |  |  |
| Units: µg/mL                             |                  |                   |  |  |
| geometric mean (confidence interval 95%) |                  |                   |  |  |
| Serotype 1                               | 1.8 (1.5 to 2.1) | 1.8 (1.6 to 2.1)  |  |  |
| Serotype 3                               | 0.5 (0.4 to 0.6) | 0.5 (0.5 to 0.6)  |  |  |
| Serotype 4                               | 1.5 (1.2 to 1.8) | 1.7 (1.4 to 2.0)  |  |  |
| Serotype 5                               | 1.8 (1.5 to 2.1) | 1.8 (1.6 to 2.1)  |  |  |
| Serotype 6                               | 5.2 (4.4 to 6.1) | 6.0 (5.2 to 7.0)  |  |  |
| Serotype 6B                              | 4.7 (3.9 to 5.6) | 5.4 (4.6 to 6.4)  |  |  |
| Serotype 7F                              | 3.7 (3.2 to 4.4) | 4.6 (4.0 to 5.3)  |  |  |
| Serotype 9V                              | 2.3 (2.0 to 2.8) | 2.6 (2.2 to 3.1)  |  |  |
| Serotype 14                              | 7.0 (5.8 to 8.4) | 7.1 (6.0 to 8.4)  |  |  |
| Serotype 18C                             | 2.0 (1.7 to 2.4) | 2.2 (1.9 to 2.6)  |  |  |
| Serotype 19A                             | 4.5 (3.8 to 5.3) | 5.5 (4.7 to 6.4)  |  |  |
| Serotype 19F                             | 4.8 (4.1 to 5.7) | 5.0 (4.3 to 5.9)  |  |  |
| Serotype 23F                             | 1.9 (1.5 to 2.3) | 1.9 (1.6 to 2.3)  |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Between-group analysis             |
|--|------------------------------------|
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 465                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Group GMC Ratio                    |
| Point estimate   | 0.9                                |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | 0.77                               |
| upper limit  | 1.07                               |

| <b>Statistical analysis title</b>  | Between-group analysis             |
|--|------------------------------------|
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 465             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |                 |
| Parameter estimate                      | Group GMC Ratio |
| Point estimate                          | 0.9             |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | 0.79            |
| upper limit                             | 1.03            |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 465                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.95                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.82                               |
| upper limit                             | 1.11                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 465                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.97                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.82                               |
| upper limit                             | 1.16                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 465                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Group GMC Ratio                    |
| Point estimate   | 0.9                                |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | 0.77                               |
| upper limit  | 1.06                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 465                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Group GMC Ratio                    |
| Point estimate   | 0.99                               |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | 0.83                               |
| upper limit  | 1.17                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 465                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Group GMC Ratio                    |
| Point estimate   | 0.89                               |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.76    |
| upper limit         | 1.04    |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 465                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.82                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.71                               |
| upper limit                             | 0.95                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 465                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.96                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.83                               |
| upper limit                             | 1.12                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 465                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.86                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.73                               |
| upper limit                             | 1.02                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 465                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.86                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.74                               |
| upper limit                             | 0.99                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 465                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.97                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.83                               |
| upper limit                             | 1.12                               |

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Between-group analysis             |
| Statistical analysis description:<br>To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups   | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis   | 465                                |
| Analysis specification  | Pre-specified                      |
| Analysis type   |                                    |
| Parameter estimate  | Group GMC Ratio                    |
| Point estimate  | 0.81                               |
| Confidence interval   |                                    |
| level   | 95 %                               |
| sides   | 2-sided                            |
| lower limit   | 0.7                                |
| upper limit   | 0.93                               |

**Secondary: Percentage of participants with serum pneumococcal anti-capsular polysaccharide IgG  $\geq$  0.35  $\mu\text{g}/\text{mL}$**

|                 |   |
|-----------------|---|
| End point title | Percentage of participants with serum pneumococcal anti-capsular polysaccharide IgG $\geq$ 0.35 $\mu\text{g}/\text{mL}$ |
|-----------------|---|

End point description:

The immune response to PCV13 is evaluated by measuring the percentage of participants with serum IgG concentrations  $\geq$  0.35  $\mu\text{g}/\text{mL}$  for each of the 13 PCV13 antigens at 1 month after the third and fourth vaccinations. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 151 (1 month after the third vaccination) and Day 331 (1 month after the fourth vaccination)

| <b>End point values</b>           | MenB+PCV Group      | Placebo+PCV Group   |  |  |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type                | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed       | 244                 | 278                 |  |  |
| Units: Percentage of participants |                     |                     |  |  |
| number (confidence interval 95%)  |                     |                     |  |  |
| Serotype 1, At Day 151            | 99.2 (97.1 to 99.9) | 97.1 (94.4 to 98.7) |  |  |
| Serotype 1, At Day 331            | 98.7 (96.2 to 99.7) | 97.1 (94.1 to 98.8) |  |  |
| Serotype 3, At Day 151            | 59.8 (53.4 to 66.0) | 61.5 (55.5 to 67.3) |  |  |
| Serotype 3, At Day 331            | 63.6 (56.9 to 69.8) | 69.5 (63.2 to 75.2) |  |  |
| Serotype 4, At Day 151            | 94.3 (90.6 to 96.8) | 96.0 (93.0 to 98.0) |  |  |

|                          |                     |                     |  |
|--------------------------|---------------------|---------------------|--|
| Serotype 4, At Day 331   | 97.8 (94.9 to 99.3) | 96.7 (93.5 to 98.6) |  |
| Serotype 5, At Day 151   | 91.0 (86.7 to 94.3) | 87.4 (82.9 to 91.1) |  |
| Serotype 5, At Day 331   | 96.0 (92.5 to 98.2) | 98.8 (96.4 to 99.7) |  |
| Serotype 6, At Day 151   | 99.2 (97.1 to 99.9) | 99.6 (98.0 to 100)  |  |
| Serotype 6, At Day 331   | 100 (98.4 to 100)   | 99.6 (97.7 to 100)  |  |
| Serotype 6B, At Day 151  | 89.8 (85.2 to 93.3) | 92.4 (88.7 to 95.3) |  |
| Serotype 6B, At Day 331  | 100 (98.4 to 100)   | 99.6 (97.7 to 100)  |  |
| Serotype 7F, At Day 151  | 99.6 (97.7 to 100)  | 100 (98.7 to 100)   |  |
| Serotype 7F, At Day 331  | 99.6 (97.5 to 100)  | 100 (98.5 to 100)   |  |
| Serotype 9V, At Day 151  | 95.1 (91.6 to 97.4) | 93.2 (89.5 to 95.8) |  |
| Serotype 9V, At Day 331  | 98.7 (96.1 to 99.7) | 98.8 (96.4 to 99.7) |  |
| Serotype 14, At Day 151  | 98.0 (95.3 to 99.3) | 98.6 (96.4 to 99.6) |  |
| Serotype 14, At Day 331  | 100 (98.4 to 100)   | 100 (98.5 to 100)   |  |
| Serotype 18C, At Day 151 | 97.5 (94.7 to 99.1) | 96.8 (93.9 to 98.5) |  |
| Serotype 18C, At Day 331 | 99.1 (96.8 to 99.9) | 99.2 (97.0 to 99.9) |  |
| Serotype 19A, At Day 151 | 96.7 (93.6 to 98.6) | 98.6 (96.4 to 99.6) |  |
| Serotype 19A, At Day 331 | 100 (98.4 to 100)   | 99.6 (97.7 to 100)  |  |
| Serotype 19F, At Day 151 | 99.6 (97.7 to 100)  | 100 (98.7 to 100)   |  |
| Serotype 19F, At Day 331 | 100 (98.4 to 100)   | 100 (98.5 to 100)   |  |
| Serotype 23F, At Day 151 | 87.3 (82.5 to 91.2) | 87.0 (82.5 to 90.7) |  |
| Serotype 23F, At Day 331 | 97.3 (94.3 to 99.0) | 97.1 (94.1 to 98.8) |  |

## Statistical analyses

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Between-group analysis             |
| Statistical analysis description:   |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the third vaccination. |                                    |
| <b>Comparison groups</b>  | MenB+PCV Group v Placebo+PCV Group |

|   |                          |
|---|--------------------------|
| Number of subjects included in analysis | 522                      |
| Analysis specification                  | Pre-specified            |
| Analysis type                           |                          |
| Parameter estimate                      | Difference in percentage |
| Point estimate                          | 2.06                     |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | -0.38                    |
| upper limit                             | 4.87                     |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | 1.58                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -1.28                              |
| upper limit                             | 4.74                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | -0.41                              |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -2.29                              |
| upper limit                             | 0.96                               |

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Between-group analysis             |
| Statistical analysis description:   |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups   | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis   | 522                                |
| Analysis specification  | Pre-specified                      |
| Analysis type   |                                    |
| Parameter estimate  | Difference in percentage           |
| Point estimate  | 0.42                               |
| Confidence interval   |                                    |
| level   | 95 %                               |
| sides   | 2-sided                            |
| lower limit   | -1.27                              |
| upper limit   | 2.33                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Difference in percentage           |
| Point estimate   | -2.69                              |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | -7.86                              |
| upper limit  | 2.21                               |

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Between-group analysis             |
| Statistical analysis description:   |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups   | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis   | 522                                |
| Analysis specification  | Pre-specified                      |
| Analysis type   |                                    |
| Parameter estimate  | Difference in percentage           |
| Point estimate  | 0.42                               |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.27   |
| upper limit         | 2.33    |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | -0.46                              |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -2.62                              |
| upper limit                             | 1.27                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | -2.75                              |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -6.33                              |
| upper limit                             | 0.16                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | 3.57                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -1.86                              |
| upper limit                             | 8.96                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | 1.11                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -2.17                              |
| upper limit                             | 4.51                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | -1.78                              |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -5.87                              |
| upper limit                             | 1.97                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Difference in percentage           |
| Point estimate   | -5.9                               |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | -14.45                             |
| upper limit  | 2.69                               |

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Between-group analysis             |
| Statistical analysis description:   |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the third vaccination. |                                    |
| Comparison groups   | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis   | 522                                |
| Analysis specification  | Pre-specified                      |
| Analysis type   |                                    |
| Parameter estimate  | Difference in percentage           |
| Point estimate  | -1.67                              |
| Confidence interval   |                                    |
| level   | 95 %                               |
| sides   | 2-sided                            |
| lower limit   | -10.07                             |
| upper limit   | 6.7                                |

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Between-group analysis             |
| Statistical analysis description:   |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups   | MenB+PCV Group v Placebo+PCV Group |

|   |                          |
|---|--------------------------|
| Number of subjects included in analysis | 522                      |
| Analysis specification                  | Pre-specified            |
| Analysis type                           |                          |
| Parameter estimate                      | Difference in percentage |
| Point estimate                          | -0.44                    |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | -2.48                    |
| upper limit                             | 1.14                     |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | 0.29                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -5.62                              |
| upper limit                             | 6.07                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | 0                                  |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -1.68                              |
| upper limit                             | 1.58                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Difference in percentage           |
| Point estimate   | -0.41                              |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | -2.29                              |
| upper limit  | 0.96                               |

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Between-group analysis             |
| Statistical analysis description:   |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups   | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis   | 522                                |
| Analysis specification  | Pre-specified                      |
| Analysis type   |                                    |
| Parameter estimate  | Difference in percentage           |
| Point estimate  | 0.42                               |
| Confidence interval   |                                    |
| level   | 95 %                               |
| sides   | 2-sided                            |
| lower limit   | -1.27                              |
| upper limit   | 2.33                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Difference in percentage           |
| Point estimate   | -1.84                              |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -5.06   |
| upper limit         | 0.83    |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | 0.25                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -3.13                              |
| upper limit                             | 3.58                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | 0.78                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -2.4                               |
| upper limit                             | 3.91                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | 0                                  |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -1.68                              |
| upper limit                             | 1.58                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | -0.61                              |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -3.43                              |
| upper limit                             | 1.87                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 522                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | -0.09                              |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -2.76                              |
| upper limit                             | 2.44                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 522                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Difference in percentage           |
| Point estimate   | 1.92                               |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | -2.3                               |
| upper limit  | 6.12                               |

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Between-group analysis             |
| Statistical analysis description:   |                                    |
| To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination. |                                    |
| Comparison groups   | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis   | 522                                |
| Analysis specification  | Pre-specified                      |
| Analysis type   |                                    |
| Parameter estimate  | Difference in percentage           |
| Point estimate  | -0.06                              |
| Confidence interval   |                                    |
| level   | 95 %                               |
| sides   | 2-sided                            |
| lower limit   | -2.44                              |
| upper limit   | 2.2                                |

### **Secondary: Adjusted GMCs against 3 pertussis antigens (pertussis toxin [PT], pertactin [PRN], filamentous hemagglutinin [FHA])**

|  |   |
|--|---|
| End point title  | Adjusted GMCs against 3 pertussis antigens (pertussis toxin [PT], pertactin [PRN], filamentous hemagglutinin [FHA]) |
| End point description:   |   |
| The immune response to DTaP-HBV-IPV (Pediarix) vaccine is evaluated. IgG concentrations for pertussis antigens (PT, FHA, PRN) are measured at 1 month after the third vaccination and are expressed as international units per millilitre (IU/mL). Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis. |   |
| End point type   | Secondary   |

End point timeframe:

At Day 151 (1 month after the third vaccination)

| <b>End point values</b>                  | MenB+PCV Group        | Placebo+PCV Group      |  |  |
|--|-----------------------|------------------------|--|--|
| Subject group type                       | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed              | 470                   | 266                    |  |  |
| Units: IU/mL                             |                       |                        |  |  |
| geometric mean (confidence interval 95%) |                       |                        |  |  |
| PT                                       | 50.3 (45.1 to 56.0)   | 59.6 (53.2 to 66.8)    |  |  |
| FHA                                      | 106.7 (96.4 to 118.0) | 133.1 (119.5 to 148.2) |  |  |
| Pertactin                                | 41.7 (36.1 to 48.1)   | 65.7 (56.4 to 76.4)    |  |  |

### Statistical analyses

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of PT, FHA and PRN, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 736                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.84                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.76                               |
| upper limit                             | 0.94                               |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of PT, FHA and PRN, at one month after the third vaccination.

|                   |                                    |
|-------------------|------------------------------------|
| Comparison groups | MenB+PCV Group v Placebo+PCV Group |
|-------------------|------------------------------------|

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 736             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |                 |
| Parameter estimate                      | Group GMC Ratio |
| Point estimate                          | 0.63            |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | 0.55            |
| upper limit                             | 0.73            |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Between-group analysis |
|-----------------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of PT, FHA and PRN, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 736                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Group GMC Ratio                    |
| Point estimate                          | 0.8                                |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.73                               |
| upper limit                             | 0.88                               |

**Secondary: Percentage of participants with antibodies concentrations against hepatitis B surface antigen (AntiHBsAg)  $\geq$  10 mIU/mL**

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with antibodies concentrations against hepatitis B surface antigen (AntiHBsAg) $\geq$ 10 mIU/mL |
|-----------------|--|

End point description:

The immune response to DTaP-HBV-IPV vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for Hepatitis B (HepB) antigens are measured at 1 month after the third vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 151 (1 month after the third vaccination)

| <b>End point values</b>           | MenB+PCV Group    | Placebo+PCV Group  |  |  |
|-----------------------------------|-------------------|--------------------|--|--|
| Subject group type                | Reporting group   | Reporting group    |  |  |
| Number of subjects analysed       | 105               | 138                |  |  |
| Units: Percentage of participants |                   |                    |  |  |
| number (confidence interval 95%)  | 100 (96.5 to 100) | 99.3 (96.0 to 100) |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Between-group analysis             |
|--|------------------------------------|
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of Hep B, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 243                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Difference in percentage           |
| Point estimate   | 0.72                               |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | -2.83                              |
| upper limit  | 4                                  |

## Secondary: Percentage of participants with anti-diphtheria and anti-tetanus antibody concentrations $\geq 0.1$ IU/mL

|  |   |
|--|---|
| End point title  | Percentage of participants with anti-diphtheria and anti-tetanus antibody concentrations $\geq 0.1$ IU/mL |
| End point description:   |   |
| The immune response to DTaP-HBV-IPV vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for diphtheria (D) and tetanus (T) were measured at 1 month after the third vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| At Day 151 (1 month after the third vaccination)   |   |

| <b>End point values</b>           | MenB+PCV Group     | Placebo+PCV Group |  |  |
|-----------------------------------|--------------------|-------------------|--|--|
| Subject group type                | Reporting group    | Reporting group   |  |  |
| Number of subjects analysed       | 224                | 143               |  |  |
| Units: Percentage of participants |                    |                   |  |  |
| number (confidence interval 95%)  |                    |                   |  |  |
| Tetanus Toxoid                    | 100 (98.4 to 100)  | 100 (97.5 to 100) |  |  |
| Diphtheria Toxoid                 | 99.5 (97.5 to 100) | 100 (97.3 to 100) |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Between-group analysis             |
|--|------------------------------------|
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of T, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 367                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Difference in percentage           |
| Point estimate   | -0.45                              |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | -2.53                              |
| upper limit  | 2.3                                |

| <b>Statistical analysis title</b>  | Between-group analysis             |
|--|------------------------------------|
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of D, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 367                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Difference in percentage           |
| Point estimate   | 0                                  |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | -1.69                              |
| upper limit  | 2.62                               |

**Secondary: Percentage of participants with anti-polyribosyl-ribitol phosphate (PRP) concentration  $\geq 0.15 \mu\text{g/mL}$  and  $\geq 1 \mu\text{g/mL}$**

|                 |   |
|-----------------|---|
| End point title | Percentage of participants with anti-polyribosyl-ribitol phosphate (PRP) concentration $\geq 0.15 \mu\text{g/mL}$ and $\geq 1 \mu\text{g/mL}$ |
|-----------------|---|

End point description:

The immune response to Hib vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for Haemophilus influenzae type b (Hib) are measured at 1 month after the third vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 151 (1 month after the third vaccination)

| End point values                  | MenB+PCV Group      | Placebo+PCV Group   |  |  |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type                | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed       | 347                 | 264                 |  |  |
| Units: Percentage of participants |                     |                     |  |  |
| number (confidence interval 95%)  |                     |                     |  |  |
| $\geq 0.15 \mu\text{g/mL}$        | 98.3 (96.3 to 99.4) | 97.7 (95.1 to 99.2) |  |  |
| $\geq 1 \mu\text{g/mL}$           | 87.0 (83.0 to 90.4) | 84.1 (79.1 to 88.3) |  |  |

**Statistical analyses**

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Between-group analysis |
|----------------------------|------------------------|

Statistical analysis description:

To demonstrate the immunological non-inferiority of Hib vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to Hib vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of Hib, at one month after the third vaccination.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis | 611                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| Parameter estimate                      | Difference in percentage           |
| Point estimate                          | 2.94                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -2.63                              |
| upper limit                             | 8.78                               |

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Between-group analysis             |
| Statistical analysis description:  |                                    |
| To demonstrate the immunological non-inferiority of Hib vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to Hib vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of Hib, at one month after the third vaccination. |                                    |
| Comparison groups  | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis  | 611                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  |                                    |
| Parameter estimate   | Difference in percentage           |
| Point estimate   | 0.54                               |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | -1.79                              |
| upper limit  | 3.32                               |

### Secondary: Adjusted GMCs for anti-measles antibodies

|  |   |
|--|---|
| End point title  | Adjusted GMCs for anti-measles antibodies |
| End point description:   |   |
| The immune response to MMR vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for measles antigens are measured using adjusted GMCs at 1 month after fourth vaccination and are expressed as milli-International Units per milliliter (mIU/mL). Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis. |   |
| End point type   | Secondary                                 |
| End point timeframe:   |   |
| At Day 331 (1 month after the fourth vaccination)  |   |

| End point values                         | MenB+PCV Group          | Placebo+PCV Group       |  |  |
|--|-------------------------|-------------------------|--|--|
| Subject group type                       | Reporting group         | Reporting group         |  |  |
| Number of subjects analysed              | 435                     | 235                     |  |  |
| Units: mIU/mL                            |                         |                         |  |  |
| geometric mean (confidence interval 95%) | 877.3 (743.7 to 1035.0) | 873.5 (732.2 to 1042.0) |  |  |

### Statistical analyses

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Between-group analysis             |
| Statistical analysis description:   |                                    |
| To demonstrate the immunological non-inferiority of MMR vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to MMR vaccine concomitantly administered with PCV13, without rMenB+OMV NZ, at one month after fourth vaccination. |                                    |
| Comparison groups   | MenB+PCV Group v Placebo+PCV Group |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 670             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |                 |
| Parameter estimate                      | Group GMC Ratio |
| Point estimate                          | 1               |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | 0.86            |
| upper limit                             | 1.17            |

### Secondary: Adjusted GMCs for anti-mumps antibodies

|                        |   |
|------------------------|---|
| End point title        | Adjusted GMCs for anti-mumps antibodies   |
| End point description: | The immune response to MMR vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for mumps antigens are measured using adjusted GMCs at 1 month after fourth vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis. |
| End point type         | Secondary   |
| End point timeframe:   | At Day 331 (1 month after the fourth vaccination)   |

| End point values                              | MenB+PCV Group         | Placebo+PCV Group       |  |  |
|---|------------------------|-------------------------|--|--|
| Subject group type                            | Reporting group        | Reporting group         |  |  |
| Number of subjects analysed                   | 435                    | 235                     |  |  |
| Units: Arbitrary Units per milliliter (AU/mL) |                        |                         |  |  |
| geometric mean (confidence interval 95%)      | 744.5 (628.5 to 882.0) | 856.8 (715.0 to 1026.7) |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | Between-group analysis  |
| Statistical analysis description:       | To demonstrate the immunological non-inferiority of MMR vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to MMR vaccine concomitantly administered with PCV13, without rMenB+OMV NZ, at one month after fourth vaccination. |
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group  |
| Number of subjects included in analysis | 670   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| Parameter estimate                      | Group GMC Ratio   |
| Point estimate                          | 0.87  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.74    |
| upper limit         | 1.02    |

### Secondary: Adjusted GMCs for anti-rubella antibodies

|   |   |
|---|---|
| End point title   | Adjusted GMCs for anti-rubella antibodies |
| End point description:  |   |
| The immune response to MMR vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for rubella antigens are measured using adjusted GMCs at 1 month after fourth vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis. |   |
| End point type  | Secondary                                 |
| End point timeframe:  |   |
| At Day 331 (1 month after the fourth vaccination)   |   |

| End point values                         | MenB+PCV Group      | Placebo+PCV Group   |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 432                 | 235                 |  |  |
| Units: IU/mL                             |                     |                     |  |  |
| geometric mean (confidence interval 95%) | 57.7 (50.0 to 66.6) | 54.0 (46.3 to 63.0) |  |  |

### Statistical analyses

|   |                                    |
|---|------------------------------------|
| Statistical analysis title  | Between-group analysis             |
| Statistical analysis description:   |                                    |
| To demonstrate the immunological non-inferiority of MMR vaccine when administered concomitantly with rMenB+OMV NZ, VV and PCV13 compared to MMR vaccine concomitantly administered with PCV13, without rMenB+OMV NZ, at one month after fourth vaccination. |                                    |
| Comparison groups   | MenB+PCV Group v Placebo+PCV Group |
| Number of subjects included in analysis   | 667                                |
| Analysis specification  | Pre-specified                      |
| Analysis type   |                                    |
| Parameter estimate  | Group GMC Ratio                    |
| Point estimate  | 1.07                               |
| Confidence interval   |                                    |
| level   | 95 %                               |
| sides   | 2-sided                            |
| lower limit   | 0.93                               |
| upper limit   | 1.22                               |

## Secondary: Adjusted GMCs for anti-Varicella (VV) antibodies

|                        |   |
|------------------------|---|
| End point title        | Adjusted GMCs for anti-Varicella (VV) antibodies  |
| End point description: | The immune response to varicella (VV) vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for varicella antigens are measured using GMCs at 1 month after fourth vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis. |
| End point type         | Secondary   |
| End point timeframe:   | At Day 331 (1 month after the fourth vaccination)   |

| End point values                         | MenB+PCV Group            | Placebo+PCV Group         |  |  |
|--|---------------------------|---------------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed              | 437                       | 231                       |  |  |
| Units: mIU/mL                            |                           |                           |  |  |
| geometric mean (confidence interval 95%) | 1283.8 (1137.4 to 1449.2) | 1208.9 (1060.5 to 1378.2) |  |  |

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Between-group analysis   |
| Statistical analysis description:       | To demonstrate the immunological non-inferiority of VV vaccine when administered concomitantly with rMenB+OMV NZ, MMR and PCV13 compared to VV vaccine concomitantly administered with PCV13, without rMenB+OMV NZ, at one month after fourth vaccination. |
| Comparison groups                       | MenB+PCV Group v Placebo+PCV Group   |
| Number of subjects included in analysis | 668  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           |  |
| Parameter estimate                      | Group GMC Ratio  |
| Point estimate                          | 1.06   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.95   |
| upper limit                             | 1.19   |

## Secondary: Percentage of participants with hSBA antibody titers $\geq 5$ , $\geq 8$ and $\geq 16$ for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with hSBA antibody titers $\geq 5$ , $\geq 8$ and $\geq 16$ for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) <sup>[23]</sup> |
|-----------------|--|

End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type Secondary

End point timeframe:

At Day 151 (1 month after the third vaccination)

Notes:

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                  | MenB+PCV Group      |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 553                 |  |  |  |
| Units: Percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| M14459 (fHbp), $\geq 5$           | 92.2 (89.6 to 94.3) |  |  |  |
| M14459 (fHbp), $\geq 8$           | 82.9 (79.4 to 86.0) |  |  |  |
| M14459 (fHbp), $\geq 16$          | 50.5 (46.2 to 54.8) |  |  |  |
| 96217 (NadA), $\geq 5$            | 99.6 (98.6 to 100)  |  |  |  |
| 96217 (NadA), $\geq 8$            | 99.6 (98.6 to 100)  |  |  |  |
| 96217 (NadA), $\geq 16$           | 99.4 (98.3 to 99.9) |  |  |  |
| NZ98/254 (PorA P1.4), $\geq 5$    | 77.7 (74.0 to 81.1) |  |  |  |
| NZ98/254 (PorA P1.4), $\geq 8$    | 61.8 (57.6 to 65.9) |  |  |  |
| NZ98/254 (PorA P1.4), $\geq 16$   | 31.1 (27.2 to 35.1) |  |  |  |
| M13520 (NHBA), $\geq 5$           | 60.4 (56.2 to 64.5) |  |  |  |
| M13520 (NHBA), $\geq 8$           | 32.4 (28.5 to 36.4) |  |  |  |
| M13520 (NHBA), $\geq 16$          | 9.4 (7.1 to 12.1)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### **Secondary: Percentage of participants with hSBA antibody titers $\geq 5$ and $\geq 8$ for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)**

End point title Percentage of participants with hSBA antibody titers  $\geq 5$  and  $\geq 8$  for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)<sup>[24]</sup>

End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type Secondary

End point timeframe:

At Day 301 (6 months after third vaccination)

Notes:

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                  | MenB+PCV Group      |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 540                 |  |  |  |
| Units: Percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| M14459 (fHbp), $\geq 5$           | 14.5 (11.6 to 17.9) |  |  |  |
| M14459 (fHbp), $\geq 8$           | 4.8 (3.2 to 7.1)    |  |  |  |
| 96217 (NadA) $\geq 5$             | 97.8 (96.1 to 98.9) |  |  |  |
| 96217 (NadA), $\geq 8$            | 96.4 (94.4 to 97.9) |  |  |  |
| NZ98/254 (PorA P1.4), $\geq 5$    | 20.2 (16.8 to 23.8) |  |  |  |
| NZ98/254 (PorA P1.4), $\geq 8$    | 12.2 (9.6 to 15.3)  |  |  |  |
| M13520 (NHBA), $\geq 5$           | 10.2 (7.8 to 13.1)  |  |  |  |
| M13520 (NHBA) $\geq 8$            | 5.9 (4.1 to 8.3)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with hSBA antibody titers $\geq 5$ for each of the Serogroup B Test Strain M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

End point title Percentage of participants with hSBA antibody titers  $\geq 5$  for each of the Serogroup B Test Strain M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)<sup>[25]</sup>

End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type Secondary

End point timeframe:

At Day 331 (1 month after the fourth vaccination)

Notes:

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                  | MenB+PCV Group      |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 505                 |  |  |  |
| Units: Percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| M14459 (fHbp), >= 5               | 94.5 (92.1 to 96.4) |  |  |  |
| 96217 (NadA), >= 5                | 99.6 (98.5 to 99.9) |  |  |  |
| NZ98/254 (PorA P1.4), >= 5        | 89.6 (86.6 to 92.1) |  |  |  |
| M13520 (NHBA), >= 5               | 91.5 (88.7 to 93.8) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: hSBA Geometric Mean Titers (GMTs) against each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

|                 |   |
|-----------------|---|
| End point title | hSBA Geometric Mean Titers (GMTs) against each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) <sup>[26]</sup> |
|-----------------|---|

End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 151 (1 month after the third vaccination), Day 301 (6 months after the third vaccination), and Day 331 (1 month after the fourth vaccination)

Notes:

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                         | MenB+PCV Group      |  |  |  |
|--|---------------------|--|--|--|
| Subject group type                       | Reporting group     |  |  |  |
| Number of subjects analysed              | 553                 |  |  |  |
| Units: Titer                             |                     |  |  |  |
| geometric mean (confidence interval 95%) |                     |  |  |  |
| M14459 (fHbp), Day 151                   | 15.1 (13.7 to 16.7) |  |  |  |

|                               |                           |  |  |  |
|-------------------------------|---------------------------|--|--|--|
| M14459 (fHbp), Day 301        | 3.0 (2.8 to 3.2)          |  |  |  |
| M14459 (fHbp), Day 331        | 24.3 (21.3 to 27.8)       |  |  |  |
| 96217 (NadA), Day 151         | 488.2 (437.3 to 545.0)    |  |  |  |
| 96217 (NadA), Day 301         | 89.1 (77.3 to 102.7)      |  |  |  |
| 96217 (NadA), Day 331         | 1349.0 (1195.3 to 1522.5) |  |  |  |
| NZ98/254 (PorA P1.4), Day 151 | 10.1 (8.9 to 11.4)        |  |  |  |
| NZ98/254 (PorA P1.4), Day 301 | 3.8 (3.5 to 4.0)          |  |  |  |
| NZ98/254 (PorA P1.4), Day 331 | 20.3 (17.3 to 23.7)       |  |  |  |
| M13520 (NHBA), Day 151        | 5.5 (5.0 to 6.0)          |  |  |  |
| M13520 (NHBA), Day 301        | 3.5 (3.3 to 3.7)          |  |  |  |
| M13520 (NHBA), Day 331        | 12.7 (11.2 to 14.4)       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: hSBA Geometric Mean Ratios (GMRs) over pre fourth vaccination against each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

|                 |   |
|-----------------|---|
| End point title | hSBA Geometric Mean Ratios (GMRs) over pre fourth vaccination against each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) <sup>[27]</sup> |
|-----------------|---|

End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 331 (1 month after the fourth vaccination) compared to Day 301 (pre-fourth vaccination)

Notes:

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                         | MenB+PCV Group      |  |  |  |
|--|---------------------|--|--|--|
| Subject group type                       | Reporting group     |  |  |  |
| Number of subjects analysed              | 465                 |  |  |  |
| Units: Ratio                             |                     |  |  |  |
| geometric mean (confidence interval 95%) |                     |  |  |  |
| M14459 (fHbp)                            | 8.7 (7.6 to 10.0)   |  |  |  |
| 96217 (NadA)                             | 17.4 (15.1 to 20.1) |  |  |  |

|                      |                  |  |  |  |
|----------------------|------------------|--|--|--|
| NZ98/254 (PorA P1.4) | 5.5 (4.7 to 6.5) |  |  |  |
| M13520 (NHBA)        | 3.9 (3.4 to 4.4) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with hSBA antibody titers $\geq$ LLOQ for each of the Serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with hSBA antibody titers $\geq$ LLOQ for each of the Serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) <sup>[28]</sup> |
|-----------------|--|

End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 301 (6 months after the third vaccination) and Day 331 (1 month after the fourth vaccination)

Notes:

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                  | MenB+PCV Group      |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 540                 |  |  |  |
| Units: Percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| M14459 (fHbp), Day 301            | 14.5 (11.6 to 17.9) |  |  |  |
| M14459 (fHbp), Day 331            | 94.5 (92.1 to 96.4) |  |  |  |
| 96217 (NadA), Day 301             | 94.1 (91.6 to 96.0) |  |  |  |
| 96217 (NadA), Day 331             | 99.6 (98.5 to 99.9) |  |  |  |
| M13520 (NHBA), Day 301            | 8.5 (6.3 to 11.2)   |  |  |  |
| M13520 (NHBA), Day 331            | 86.1 (82.8 to 89.0) |  |  |  |
| NZ98/254 (PorA P1.4), Day 301     | 17.5 (14.4 to 21.0) |  |  |  |
| NZ98/254 (PorA P1.4), Day 331     | 87.6 (84.4 to 90.3) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Percentage of participants with 4-fold rise in hSBA titers for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)**

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|                 |  |
|-----------------|--|
| End point title | Percentage of participants with 4-fold rise in hSBA titers for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) <sup>[29]</sup> |
|-----------------|--|

End point description:

A 4-fold rise in hSBA titers is defined as - if pre-vaccination titer <Limit of Detection (LOD), then a post-vaccination titer  $\geq 4$  times the LOD or  $\geq$  LLOQ, whichever is greater; - if pre-vaccination titer is  $\geq$  LOD but <LLOQ, then a post-vaccination titer  $\geq 4$  times the LLOQ; - if pre-vaccination titer is  $\geq$  LLOQ, then a post-vaccination titer  $\geq 4$  times the pre-vaccination titer, where pre-vaccination titer=pre-4th dose titers (Day 301). This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 331 (1 month after the fourth vaccination) relative to Day 301 (pre-fourth vaccination)

Notes:

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

Justification: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

| End point values                  | MenB+PCV Group      |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 465                 |  |  |  |
| Units: Percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| M14459 (fHbp), Day 331            | 72.0 (67.5 to 76.1) |  |  |  |
| 96217 (NadA), Day 331             | 94.8 (92.2 to 96.7) |  |  |  |
| M13520 (NHBA), Day 331            | 36.1 (31.8 to 40.7) |  |  |  |
| NZ98/254 (PorA P1.4), Day 331     | 54.2 (49.5 to 58.9) |  |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Percentage of participants with anti-HBs antibody concentrations  $\geq 100$  mIU/mL**

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|                 |  |
|-----------------|--|
| End point title | Percentage of participants with anti-HBs antibody concentrations $\geq 100$ mIU/mL |
|-----------------|--|

End point description:

Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 151 (1 month after the third vaccination)

| <b>End point values</b>           | MenB+PCV Group      | Placebo+PCV Group   |  |  |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type                | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed       | 105                 | 138                 |  |  |
| Units: Percentage of participants |                     |                     |  |  |
| number (confidence interval 95%)  | 98.1 (93.3 to 99.8) | 96.4 (91.7 to 98.8) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: GMCs for Anti-HBsAg antibodies

End point title | GMCs for Anti-HBsAg antibodies

End point description:

Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type | Secondary

End point timeframe:

At Day 151 (1 month after the third vaccination)

| <b>End point values</b>                  | MenB+PCV Group            | Placebo+PCV Group         |  |  |
|--|---------------------------|---------------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed              | 105                       | 138                       |  |  |
| Units: mIU/mL                            |                           |                           |  |  |
| geometric mean (confidence interval 95%) | 2201.0 (1554.7 to 3116.0) | 2404.8 (1803.1 to 3207.3) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with anti-diphtheria and anti-tetanus antibody concentrations $\geq 1$ IU/mL

End point title | Percentage of participants with anti-diphtheria and anti-tetanus antibody concentrations  $\geq 1$  IU/mL

End point description:

Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

|  |           |
|--|-----------|
| End point type                                   | Secondary |
| End point timeframe:                             |           |
| At Day 151 (1 month after the third vaccination) |           |

| <b>End point values</b>           | MenB+PCV Group      | Placebo+PCV Group   |  |  |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type                | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed       | 224                 | 143                 |  |  |
| Units: Percentage of participants |                     |                     |  |  |
| number (confidence interval 95%)  |                     |                     |  |  |
| Tetanus Toxoid                    | 67.0 (60.4 to 73.1) | 69.2 (61.0 to 76.7) |  |  |
| Diphtheria Toxoid                 | 40.0 (33.5 to 46.8) | 55.1 (46.4 to 63.7) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: GMCs for anti-diphtheria and anti-tetanus antibodies

|   |  |
|---|--|
| End point title   | GMCs for anti-diphtheria and anti-tetanus antibodies |
| End point description:  |  |
| Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| At Day 151 (1 month after the third vaccination)  |  |

| <b>End point values</b>                  | MenB+PCV Group   | Placebo+PCV Group |  |  |
|--|------------------|-------------------|--|--|
| Subject group type                       | Reporting group  | Reporting group   |  |  |
| Number of subjects analysed              | 224              | 143               |  |  |
| Units: IU/mL                             |                  |                   |  |  |
| geometric mean (confidence interval 95%) |                  |                   |  |  |
| Tetanus Toxoid                           | 1.5 (1.3 to 1.8) | 1.6 (1.3 to 1.9)  |  |  |
| Diphtheria Toxoid                        | 0.9 (0.8 to 1.1) | 1.2 (1.0 to 1.5)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with anti-polio type 1, 2 and 3 neutralization

**antibody titers  $\geq$  8**

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with anti-polio type 1, 2 and 3 neutralization antibody titers $\geq$ 8 |
|-----------------|--|

End point description:

Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 151 (1 month after the third vaccination)

| <b>End point values</b>           | MenB+PCV Group     | Placebo+PCV Group  |  |  |
|-----------------------------------|--------------------|--------------------|--|--|
| Subject group type                | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed       | 106                | 120                |  |  |
| Units: Percentage of participants |                    |                    |  |  |
| number (confidence interval 95%)  |                    |                    |  |  |
| Polio 1                           | 100 (96.4 to 100)  | 100 (97.0 to 100)  |  |  |
| Polio 2                           | 99.1 (94.9 to 100) | 100 (96.9 to 100)  |  |  |
| Polio 3                           | 100 (96.3 to 100)  | 99.1 (95.1 to 100) |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of participants with seroresponse for anti-Varicella (VV), anti-measles virus, anti-mumps virus and anti-rubella virus antibodies**

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with seroresponse for anti-Varicella (VV), anti-measles virus, anti-mumps virus and anti-rubella virus antibodies |
|-----------------|--|

End point description:

Seroresponse is defined as post-vaccination anti-VZV virus, anti-measles virus, anti-mumps virus and anti-rubella virus antibody concentration  $\geq$  a protective threshold among participants who were seronegative (antibody concentration  $<$  assay cut-off) before vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

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

End point timeframe:

At Day 331 (1 month after the fourth vaccination)

| <b>End point values</b>           | MenB+PCV Group      | Placebo+PCV Group   |  |  |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type                | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed       | 364                 | 201                 |  |  |
| Units: Percentage of participants |                     |                     |  |  |
| number (confidence interval 95%)  |                     |                     |  |  |
| Mumps                             | 81.6 (77.2 to 85.5) | 85.9 (80.2 to 90.4) |  |  |
| Measles                           | 94.8 (91.9 to 96.9) | 97.9 (94.7 to 99.4) |  |  |
| Rubella                           | 86.4 (82.3 to 89.8) | 83.9 (78.1 to 88.7) |  |  |
| VZV gE                            | 97.3 (95.0 to 98.7) | 97.5 (94.3 to 99.2) |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: Day 1 to Day 7 post each vaccination, Solicited systemic AEs of salivary gland swelling, fever and rash: Day 1 to Day 30 post fourth vaccination; Unsolicited AEs: Day 1 to Day 30 post each vaccination.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 27.1   |

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Placebo+PCV Group |
|-----------------------|-------------------|

Reporting group description:

Infant participants received PCV13 along with placebo, Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by PCV13, Placebo, Pediarix and Hiberix on Day 121 and PCV13/PCV20, Placebo M-M-R II and Varivax on Day 301.

|                       |                |
|-----------------------|----------------|
| Reporting group title | MenB+PCV Group |
|-----------------------|----------------|

Reporting group description:

Infant participants received rMenB+OMV NZ (Bexsero) along with PCV13 (Prevnar 13), Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by rMenB+OMV NZ, PCV13, Pediarix and Hiberix on Day 121 and rMenB+OMV NZ, PCV13/PCV20, M-M-R II and Varivax on Day 301.

| <b>Serious adverse events</b>                                       | Placebo+PCV Group | MenB+PCV Group   |  |
|---|-------------------|------------------|--|
| Total subjects affected by serious adverse events                   |                   |                  |  |
| subjects affected / exposed   | 19 / 403 (4.71%)  | 35 / 781 (4.48%) |  |
| number of deaths (all causes)                                       | 0                 | 0                |  |
| number of deaths resulting from adverse events                      | 0                 | 0                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                  |  |
| Neuroblastoma   |                   |                  |  |
| subjects affected / exposed   | 0 / 403 (0.00%)   | 1 / 781 (0.13%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0            |  |
| Injury, poisoning and procedural complications                      |                   |                  |  |
| Near drowning   |                   |                  |  |
| subjects affected / exposed   | 0 / 403 (0.00%)   | 1 / 781 (0.13%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0            |  |
| Skull fracture  |                   |                  |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                                 | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all             | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           |  |
| <b>Congenital, familial and genetic disorders</b>           |                 |                 |  |
| Bronchogenic cyst   |                 |                 |  |
| subjects affected / exposed                                 | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all             | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           |  |
| <b>Nervous system disorders</b>                             |                 |                 |  |
| Subarachnoid haemorrhage                                    |                 |                 |  |
| subjects affected / exposed                                 | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all             | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           |  |
| Seizure   |                 |                 |  |
| subjects affected / exposed                                 | 0 / 403 (0.00%) | 2 / 781 (0.26%) |  |
| occurrences causally related to treatment / all             | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           |  |
| Febrile convulsion  |                 |                 |  |
| subjects affected / exposed                                 | 1 / 403 (0.25%) | 3 / 781 (0.38%) |  |
| occurrences causally related to treatment / all             | 0 / 1           | 0 / 3           |  |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           |  |
| <b>General disorders and administration site conditions</b> |                 |                 |  |
| Influenza like illness                                      |                 |                 |  |
| subjects affected / exposed                                 | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all             | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           |  |
| PFAPA syndrome  |                 |                 |  |
| subjects affected / exposed                                 | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all             | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           |  |
| Pyrexia   |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                            | 0 / 403 (0.00%) | 2 / 781 (0.26%) |  |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           |  |
| <b>Blood and lymphatic system disorders</b>            |                 |                 |  |
| Lymphadenitis  |                 |                 |  |
| subjects affected / exposed                            | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           |  |
| <b>Immune system disorders</b>                         |                 |                 |  |
| Anaphylactic reaction                                  |                 |                 |  |
| subjects affected / exposed                            | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           |  |
| Serum sickness   |                 |                 |  |
| subjects affected / exposed                            | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           |  |
| <b>Gastrointestinal disorders</b>                      |                 |                 |  |
| Vomiting   |                 |                 |  |
| subjects affected / exposed                            | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           |  |
| Abdominal pain   |                 |                 |  |
| subjects affected / exposed                            | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           |  |
| <b>Respiratory, thoracic and mediastinal disorders</b> |                 |                 |  |
| Acute respiratory failure                              |                 |                 |  |
| subjects affected / exposed                            | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           |  |
| Asthma   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Adenoidal hypertrophy</b>                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Respiratory failure</b>                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Obstructive sleep apnoea syndrome</b>        |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Bronchial hyperreactivity</b>                |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Tonsillar hypertrophy</b>                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Infections and infestations</b>              |                 |                 |  |
| <b>Gastroenteritis</b>                          |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 3 / 781 (0.38%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Gastroenteritis viral</b>                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Influenza</b>                                |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 403 (0.25%) | 2 / 781 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lower respiratory tract infection               |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Picornavirus infection                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 2 / 781 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Coxsackie viral infection                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Complicated appendicitis                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Clostridium difficile colitis                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cellulitis                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia bacterial                             |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchiolitis                                   |                 |                 |  |
| subjects affected / exposed                     | 2 / 403 (0.50%) | 4 / 781 (0.51%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 4           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Adenovirus infection                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| COVID-19  |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory syncytial virus bronchiolitis       |                 |                 |  |
| subjects affected / exposed                     | 2 / 403 (0.50%) | 3 / 781 (0.38%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory syncytial virus bronchitis          |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory syncytial virus infection           |                 |                 |  |
| subjects affected / exposed                     | 2 / 403 (0.50%) | 2 / 781 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory tract infection viral               |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Rhinovirus infection                            |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tonsillitis                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper respiratory tract infection               |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 0 / 781 (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 / 403 (0.25%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Viral infection                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Dehydration                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 403 (0.25%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diabetic ketoacidosis                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Type 1 diabetes mellitus                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>  | Placebo+PCV Group  | MenB+PCV Group   |  |
|--|--|--|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 389 / 403 (96.53%)   | 771 / 781 (98.72%)   |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Haemangioma of skin<br>subjects affected / exposed<br>occurrences (all)   | 1 / 403 (0.25%)<br>1   | 1 / 781 (0.13%)<br>1   |  |
| Vascular disorders<br>Scalp haematoma<br>subjects affected / exposed<br>occurrences (all)<br><br>Cyanosis<br>subjects affected / exposed<br>occurrences (all)<br><br>Flushing<br>subjects affected / exposed<br>occurrences (all)<br><br>Lymphoedema<br>subjects affected / exposed<br>occurrences (all)<br><br>Pallor<br>subjects affected / exposed<br>occurrences (all) | 1 / 403 (0.25%)<br>1<br><br>1 / 403 (0.25%)<br>1<br><br>0 / 403 (0.00%)<br>0<br><br>0 / 403 (0.00%)<br>0<br><br>1 / 403 (0.25%)<br>1 | 1 / 781 (0.13%)<br>1<br><br>1 / 781 (0.13%)<br>1<br><br>1 / 781 (0.13%)<br>1<br><br>1 / 781 (0.13%)<br>1<br><br>3 / 781 (0.38%)<br>3 |  |
| General disorders and administration site conditions<br>Injection site dryness<br>subjects affected / exposed<br>occurrences (all)<br><br>Administration site erythema<br>subjects affected / exposed<br>occurrences (all)<br><br>Administration site induration<br>subjects affected / exposed<br>occurrences (all)<br><br>Administration site pain                       | 1 / 403 (0.25%)<br>1<br><br>170 / 403 (42.18%)<br>170<br><br>180 / 403 (44.67%)<br>180   | 0 / 781 (0.00%)<br>0<br><br>460 / 781 (58.90%)<br>460<br><br>480 / 781 (61.46%)<br>480   |  |

|  |                           |                           |
|--|---------------------------|---------------------------|
| subjects affected / exposed<br>occurrences (all)                                 | 201 / 403 (49.88%)<br>201 | 582 / 781 (74.52%)<br>582 |
| Administration site swelling<br>subjects affected / exposed<br>occurrences (all) | 122 / 403 (30.27%)<br>122 | 322 / 781 (41.23%)<br>322 |
| Adverse drug reaction<br>subjects affected / exposed<br>occurrences (all)        | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |
| Adverse food reaction<br>subjects affected / exposed<br>occurrences (all)        | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |
| Chills<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 403 (0.25%)<br>1      | 1 / 781 (0.13%)<br>1      |
| Crying<br>subjects affected / exposed<br>occurrences (all)                       | 163 / 403 (40.45%)<br>163 | 432 / 781 (55.31%)<br>433 |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 403 (0.50%)<br>2      | 2 / 781 (0.26%)<br>2      |
| Hypothermia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |
| Induration<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |
| Inflammation<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |
| Influenza like illness<br>subjects affected / exposed<br>occurrences (all)       | 0 / 403 (0.00%)<br>0      | 3 / 781 (0.38%)<br>3      |
| Injection site bruising<br>subjects affected / exposed<br>occurrences (all)      | 6 / 403 (1.49%)<br>6      | 6 / 781 (0.77%)<br>6      |
| Injection site discolouration  |                           |                           |

|                               |                 |                 |
|-------------------------------|-----------------|-----------------|
| subjects affected / exposed   | 0 / 403 (0.00%) | 1 / 781 (0.13%) |
| occurrences (all)             | 0               | 1               |
| Injection site erythema       |                 |                 |
| subjects affected / exposed   | 0 / 403 (0.00%) | 2 / 781 (0.26%) |
| occurrences (all)             | 0               | 2               |
| Injection site laceration     |                 |                 |
| subjects affected / exposed   | 1 / 403 (0.25%) | 0 / 781 (0.00%) |
| occurrences (all)             | 1               | 0               |
| Injection site nodule         |                 |                 |
| subjects affected / exposed   | 1 / 403 (0.25%) | 0 / 781 (0.00%) |
| occurrences (all)             | 1               | 0               |
| Injection site rash           |                 |                 |
| subjects affected / exposed   | 2 / 403 (0.50%) | 2 / 781 (0.26%) |
| occurrences (all)             | 6               | 2               |
| Injection site reaction       |                 |                 |
| subjects affected / exposed   | 1 / 403 (0.25%) | 1 / 781 (0.13%) |
| occurrences (all)             | 1               | 2               |
| Injection site swelling       |                 |                 |
| subjects affected / exposed   | 0 / 403 (0.00%) | 1 / 781 (0.13%) |
| occurrences (all)             | 0               | 1               |
| Injection site urticaria      |                 |                 |
| subjects affected / exposed   | 0 / 403 (0.00%) | 1 / 781 (0.13%) |
| occurrences (all)             | 0               | 2               |
| Injury associated with device |                 |                 |
| subjects affected / exposed   | 0 / 403 (0.00%) | 1 / 781 (0.13%) |
| occurrences (all)             | 0               | 1               |
| Irritability postvaccinal     |                 |                 |
| subjects affected / exposed   | 0 / 403 (0.00%) | 1 / 781 (0.13%) |
| occurrences (all)             | 0               | 1               |
| Pain                          |                 |                 |
| subjects affected / exposed   | 1 / 403 (0.25%) | 1 / 781 (0.13%) |
| occurrences (all)             | 1               | 1               |
| Peripheral swelling           |                 |                 |
| subjects affected / exposed   | 0 / 403 (0.00%) | 1 / 781 (0.13%) |
| occurrences (all)             | 0               | 1               |
| Pyrexia                       |                 |                 |

|  |                           |                           |  |
|--|---------------------------|---------------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 172 / 403 (42.68%)<br>184 | 521 / 781 (66.71%)<br>543 |  |
| Swelling<br>subjects affected / exposed<br>occurrences (all)   | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Swelling face<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Tenderness<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Vaccination site bruising<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Vaccination site irritation<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Injection site induration<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Immune system disorders<br>Drug hypersensitivity<br>subjects affected / exposed<br>occurrences (all) | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Food allergy<br>subjects affected / exposed<br>occurrences (all)                                     | 2 / 403 (0.50%)<br>2      | 5 / 781 (0.64%)<br>5      |  |
| Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Social circumstances<br>Child abuse<br>subjects affected / exposed<br>occurrences (all)              | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Reproductive system and breast<br>disorders  |                           |                           |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Epididymal cyst                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |  |
| occurrences (all)                               | 0                | 1                |  |
| Genital labial adhesions                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |  |
| occurrences (all)                               | 0                | 1                |  |
| Genital rash                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |  |
| occurrences (all)                               | 0                | 1                |  |
| Penile adhesion                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 403 (0.00%)  | 3 / 781 (0.38%)  |  |
| occurrences (all)                               | 0                | 4                |  |
| Penile cyst                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |  |
| occurrences (all)                               | 0                | 1                |  |
| Penile dermatitis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |  |
| occurrences (all)                               | 0                | 1                |  |
| Vaginal discharge                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |  |
| occurrences (all)                               | 1                | 0                |  |
| Respiratory, thoracic and mediastinal disorders |                  |                  |  |
| Nasal congestion                                |                  |                  |  |
| subjects affected / exposed                     | 17 / 403 (4.22%) | 39 / 781 (4.99%) |  |
| occurrences (all)                               | 19               | 44               |  |
| Asthma  |                  |                  |  |
| subjects affected / exposed                     | 0 / 403 (0.00%)  | 2 / 781 (0.26%)  |  |
| occurrences (all)                               | 0                | 2                |  |
| Brief resolved unexplained event                |                  |                  |  |
| subjects affected / exposed                     | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |  |
| occurrences (all)                               | 0                | 1                |  |
| Bronchial hyperreactivity                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 403 (0.25%)  | 1 / 781 (0.13%)  |  |
| occurrences (all)                               | 1                | 1                |  |
| Choking   |                  |                  |  |

|                                    |                  |                  |
|------------------------------------|------------------|------------------|
| subjects affected / exposed        | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)                  | 1                | 0                |
| Cough                              |                  |                  |
| subjects affected / exposed        | 20 / 403 (4.96%) | 51 / 781 (6.53%) |
| occurrences (all)                  | 25               | 58               |
| Dysphonia                          |                  |                  |
| subjects affected / exposed        | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)                  | 1                | 0                |
| Epistaxis                          |                  |                  |
| subjects affected / exposed        | 1 / 403 (0.25%)  | 1 / 781 (0.13%)  |
| occurrences (all)                  | 1                | 1                |
| Hiccups                            |                  |                  |
| subjects affected / exposed        | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)                  | 1                | 0                |
| Oropharyngeal pain                 |                  |                  |
| subjects affected / exposed        | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                  | 0                | 1                |
| Respiratory disorder               |                  |                  |
| subjects affected / exposed        | 3 / 403 (0.74%)  | 4 / 781 (0.51%)  |
| occurrences (all)                  | 5                | 4                |
| Respiratory symptom                |                  |                  |
| subjects affected / exposed        | 17 / 403 (4.22%) | 31 / 781 (3.97%) |
| occurrences (all)                  | 20               | 39               |
| Rhinitis allergic                  |                  |                  |
| subjects affected / exposed        | 2 / 403 (0.50%)  | 3 / 781 (0.38%)  |
| occurrences (all)                  | 2                | 4                |
| Rhinorrhoea                        |                  |                  |
| subjects affected / exposed        | 12 / 403 (2.98%) | 25 / 781 (3.20%) |
| occurrences (all)                  | 14               | 27               |
| Sneezing                           |                  |                  |
| subjects affected / exposed        | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                  | 0                | 1                |
| Snoring                            |                  |                  |
| subjects affected / exposed        | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)                  | 1                | 0                |
| Upper respiratory tract irritation |                  |                  |

|  |                           |                           |  |
|--|---------------------------|---------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                   | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Wheezing<br>subjects affected / exposed<br>occurrences (all)                       | 5 / 403 (1.24%)<br>5      | 6 / 781 (0.77%)<br>6      |  |
| Respiration abnormal<br>subjects affected / exposed<br>occurrences (all)           | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Psychiatric disorders  |                           |                           |  |
| Breath holding<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Dependent personality disorder<br>subjects affected / exposed<br>occurrences (all) | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Emotional distress<br>subjects affected / exposed<br>occurrences (all)             | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                       | 5 / 403 (1.24%)<br>5      | 4 / 781 (0.51%)<br>4      |  |
| Irritability<br>subjects affected / exposed<br>occurrences (all)                   | 330 / 403 (81.89%)<br>345 | 713 / 781 (91.29%)<br>738 |  |
| Middle insomnia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Selective eating disorder<br>subjects affected / exposed<br>occurrences (all)      | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Investigations   |                           |                           |  |
| Serum ferritin decreased   |                           |                           |  |

|  |                      |                      |
|--|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                     | 4 / 403 (0.99%)<br>4 | 1 / 781 (0.13%)<br>1 |
| Blood lead increased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |
| Body temperature decreased<br>subjects affected / exposed<br>occurrences (all)       | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |
| Body temperature increased<br>subjects affected / exposed<br>occurrences (all)       | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |
| Breath sounds abnormal<br>subjects affected / exposed<br>occurrences (all)           | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |
| Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 403 (0.50%)<br>2 | 2 / 781 (0.26%)<br>2 |
| Human rhinovirus test positive<br>subjects affected / exposed<br>occurrences (all)   | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |
| Occult blood positive<br>subjects affected / exposed<br>occurrences (all)            | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |
| Platelet count increased<br>subjects affected / exposed<br>occurrences (all)         | 1 / 403 (0.25%)<br>1 | 1 / 781 (0.13%)<br>1 |
| SARS-CoV-2 test positive<br>subjects affected / exposed<br>occurrences (all)         | 2 / 403 (0.50%)<br>2 | 2 / 781 (0.26%)<br>2 |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |
| Injury, poisoning and procedural   |                      |                      |

|                                |                 |                 |  |
|--------------------------------|-----------------|-----------------|--|
| complications                  |                 |                 |  |
| Accidental exposure to product |                 |                 |  |
| subjects affected / exposed    | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)              | 0               | 2               |  |
| Accident at home               |                 |                 |  |
| subjects affected / exposed    | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)              | 0               | 1               |  |
| Animal bite                    |                 |                 |  |
| subjects affected / exposed    | 1 / 403 (0.25%) | 1 / 781 (0.13%) |  |
| occurrences (all)              | 1               | 1               |  |
| Arthropod bite                 |                 |                 |  |
| subjects affected / exposed    | 2 / 403 (0.50%) | 2 / 781 (0.26%) |  |
| occurrences (all)              | 2               | 2               |  |
| Contusion                      |                 |                 |  |
| subjects affected / exposed    | 1 / 403 (0.25%) | 5 / 781 (0.64%) |  |
| occurrences (all)              | 1               | 5               |  |
| Corneal abrasion               |                 |                 |  |
| subjects affected / exposed    | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences (all)              | 1               | 0               |  |
| Craniocerebral injury          |                 |                 |  |
| subjects affected / exposed    | 1 / 403 (0.25%) | 3 / 781 (0.38%) |  |
| occurrences (all)              | 1               | 3               |  |
| Eyelid injury                  |                 |                 |  |
| subjects affected / exposed    | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences (all)              | 1               | 0               |  |
| Fall                           |                 |                 |  |
| subjects affected / exposed    | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)              | 0               | 1               |  |
| Foreign body ingestion         |                 |                 |  |
| subjects affected / exposed    | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)              | 0               | 1               |  |
| Head injury                    |                 |                 |  |
| subjects affected / exposed    | 1 / 403 (0.25%) | 4 / 781 (0.51%) |  |
| occurrences (all)              | 1               | 4               |  |
| Procedural pain                |                 |                 |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                              | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Road traffic accident<br>subjects affected / exposed<br>occurrences (all)     | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Scar<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Scrotal injury<br>subjects affected / exposed<br>occurrences (all)            | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Skin laceration<br>subjects affected / exposed<br>occurrences (all)           | 0 / 403 (0.00%)<br>0 | 4 / 781 (0.51%)<br>4 |  |
| Superficial injury of eye<br>subjects affected / exposed<br>occurrences (all) | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Thermal burn<br>subjects affected / exposed<br>occurrences (all)              | 1 / 403 (0.25%)<br>1 | 1 / 781 (0.13%)<br>1 |  |
| Animal scratch<br>subjects affected / exposed<br>occurrences (all)            | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Congenital, familial and genetic disorders                                    |                      |                      |  |
| Craniofacial deformity<br>subjects affected / exposed<br>occurrences (all)    | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Brachycephaly<br>subjects affected / exposed<br>occurrences (all)             | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Dacryostenosis congenital<br>subjects affected / exposed<br>occurrences (all) | 1 / 403 (0.25%)<br>1 | 1 / 781 (0.13%)<br>1 |  |
| Hydrocele   |                      |                      |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Kidney duplex<br>subjects affected / exposed<br>occurrences (all)               | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Macrocephaly<br>subjects affected / exposed<br>occurrences (all)                | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Plagiocephaly<br>subjects affected / exposed<br>occurrences (all)               | 3 / 403 (0.74%)<br>3 | 3 / 781 (0.38%)<br>3 |  |
| Strabismus congenital<br>subjects affected / exposed<br>occurrences (all)       | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Tethered oral tissue<br>subjects affected / exposed<br>occurrences (all)        | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Developmental hip dysplasia<br>subjects affected / exposed<br>occurrences (all) | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Nervous system disorders  |                      |                      |  |
| Nystagmus<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Drizzling<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Fine motor delay<br>subjects affected / exposed<br>occurrences (all)            | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Infant irritability<br>subjects affected / exposed<br>occurrences (all)         | 2 / 403 (0.50%)<br>2 | 2 / 781 (0.26%)<br>2 |  |
| Lethargy<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |

|   |                           |                           |  |
|---|---------------------------|---------------------------|--|
| Movement disorder<br>subjects affected / exposed<br>occurrences (all)             | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Myoclonus<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Petit mal epilepsy<br>subjects affected / exposed<br>occurrences (all)            | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Speech disorder developmental<br>subjects affected / exposed<br>occurrences (all) | 1 / 403 (0.25%)<br>1      | 1 / 781 (0.13%)<br>1      |  |
| Somnolence<br>subjects affected / exposed<br>occurrences (all)                    | 319 / 403 (79.16%)<br>322 | 681 / 781 (87.20%)<br>681 |  |
| <b>Blood and lymphatic system disorders</b>                                       |                           |                           |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                       | 4 / 403 (0.99%)<br>4      | 3 / 781 (0.38%)<br>3      |  |
| Iron deficiency anaemia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 403 (0.00%)<br>0      | 2 / 781 (0.26%)<br>2      |  |
| Thrombocytosis<br>subjects affected / exposed<br>occurrences (all)                | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)               | 20 / 403 (4.96%)<br>23    | 20 / 781 (2.56%)<br>21    |  |
| <b>Ear and labyrinth disorders</b>  |                           |                           |  |
| Cerumen impaction<br>subjects affected / exposed<br>occurrences (all)             | 2 / 403 (0.50%)<br>2      | 1 / 781 (0.13%)<br>1      |  |
| Conductive deafness<br>subjects affected / exposed<br>occurrences (all)           | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Ear disorder  |                           |                           |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                  | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                      | 5 / 403 (1.24%)<br>5 | 9 / 781 (1.15%)<br>9 |  |
| Eustachian tube dysfunction<br>subjects affected / exposed<br>occurrences (all)   | 1 / 403 (0.25%)<br>1 | 1 / 781 (0.13%)<br>1 |  |
| Middle ear effusion<br>subjects affected / exposed<br>occurrences (all)           | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Otorrhoea<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 403 (0.00%)<br>0 | 2 / 781 (0.26%)<br>2 |  |
| Tympanic membrane perforation<br>subjects affected / exposed<br>occurrences (all) | 0 / 403 (0.00%)<br>0 | 2 / 781 (0.26%)<br>2 |  |
| Eye disorders   |                      |                      |  |
| Eye movement disorder<br>subjects affected / exposed<br>occurrences (all)         | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Astigmatism<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 403 (0.25%)<br>1 | 1 / 781 (0.13%)<br>1 |  |
| Dacryostenosis acquired<br>subjects affected / exposed<br>occurrences (all)       | 1 / 403 (0.25%)<br>1 | 3 / 781 (0.38%)<br>3 |  |
| Eczema eyelids<br>subjects affected / exposed<br>occurrences (all)                | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Eye discharge<br>subjects affected / exposed<br>occurrences (all)                 | 3 / 403 (0.74%)<br>3 | 1 / 781 (0.13%)<br>1 |  |
| Eye swelling<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 403 (0.25%)<br>2 | 2 / 781 (0.26%)<br>2 |  |

|                                   |                 |                 |  |
|-----------------------------------|-----------------|-----------------|--|
| Eyelid rash                       |                 |                 |  |
| subjects affected / exposed       | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)                 | 0               | 1               |  |
| Ocular hyperaemia                 |                 |                 |  |
| subjects affected / exposed       | 1 / 403 (0.25%) | 1 / 781 (0.13%) |  |
| occurrences (all)                 | 1               | 1               |  |
| Pseudostrabismus                  |                 |                 |  |
| subjects affected / exposed       | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)                 | 0               | 1               |  |
| Scleral discolouration            |                 |                 |  |
| subjects affected / exposed       | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)                 | 0               | 1               |  |
| Swelling of eyelid                |                 |                 |  |
| subjects affected / exposed       | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)                 | 0               | 1               |  |
| Eyelid oedema                     |                 |                 |  |
| subjects affected / exposed       | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)                 | 0               | 1               |  |
| <b>Gastrointestinal disorders</b> |                 |                 |  |
| Mucous stools                     |                 |                 |  |
| subjects affected / exposed       | 0 / 403 (0.00%) | 2 / 781 (0.26%) |  |
| occurrences (all)                 | 0               | 2               |  |
| Abdominal distension              |                 |                 |  |
| subjects affected / exposed       | 1 / 403 (0.25%) | 0 / 781 (0.00%) |  |
| occurrences (all)                 | 1               | 0               |  |
| Abdominal pain                    |                 |                 |  |
| subjects affected / exposed       | 0 / 403 (0.00%) | 3 / 781 (0.38%) |  |
| occurrences (all)                 | 0               | 3               |  |
| Abnormal faeces                   |                 |                 |  |
| subjects affected / exposed       | 0 / 403 (0.00%) | 1 / 781 (0.13%) |  |
| occurrences (all)                 | 0               | 1               |  |
| Anal fissure                      |                 |                 |  |
| subjects affected / exposed       | 2 / 403 (0.50%) | 1 / 781 (0.13%) |  |
| occurrences (all)                 | 2               | 1               |  |
| Aphthous ulcer                    |                 |                 |  |

|   |                    |                    |
|---|--------------------|--------------------|
| subjects affected / exposed                 | 1 / 403 (0.25%)    | 0 / 781 (0.00%)    |
| occurrences (all)                           | 1                  | 0                  |
| Constipation                                |                    |                    |
| subjects affected / exposed                 | 12 / 403 (2.98%)   | 31 / 781 (3.97%)   |
| occurrences (all)                           | 13                 | 32                 |
| Diarrhoea                                   |                    |                    |
| subjects affected / exposed                 | 178 / 403 (44.17%) | 334 / 781 (42.77%) |
| occurrences (all)                           | 193                | 350                |
| Dysphagia                                   |                    |                    |
| subjects affected / exposed                 | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                           | 0                  | 1                  |
| Faeces discoloured                          |                    |                    |
| subjects affected / exposed                 | 1 / 403 (0.25%)    | 2 / 781 (0.26%)    |
| occurrences (all)                           | 1                  | 2                  |
| Faeces hard                                 |                    |                    |
| subjects affected / exposed                 | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                           | 0                  | 1                  |
| Flatulence                                  |                    |                    |
| subjects affected / exposed                 | 1 / 403 (0.25%)    | 4 / 781 (0.51%)    |
| occurrences (all)                           | 1                  | 4                  |
| Food protein-induced enterocolitis syndrome |                    |                    |
| subjects affected / exposed                 | 1 / 403 (0.25%)    | 0 / 781 (0.00%)    |
| occurrences (all)                           | 1                  | 0                  |
| Frequent bowel movements                    |                    |                    |
| subjects affected / exposed                 | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                           | 0                  | 1                  |
| Gastroesophageal reflux disease             |                    |                    |
| subjects affected / exposed                 | 9 / 403 (2.23%)    | 14 / 781 (1.79%)   |
| occurrences (all)                           | 9                  | 14                 |
| Gastroesophageal reflux in neonate          |                    |                    |
| subjects affected / exposed                 | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                           | 0                  | 1                  |
| Gingival cyst                               |                    |                    |
| subjects affected / exposed                 | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                           | 0                  | 1                  |

|                                  |                    |                    |
|----------------------------------|--------------------|--------------------|
| Gingival disorder                |                    |                    |
| subjects affected / exposed      | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                | 0                  | 1                  |
| Haematochezia                    |                    |                    |
| subjects affected / exposed      | 1 / 403 (0.25%)    | 5 / 781 (0.64%)    |
| occurrences (all)                | 1                  | 5                  |
| Infantile colic                  |                    |                    |
| subjects affected / exposed      | 2 / 403 (0.50%)    | 0 / 781 (0.00%)    |
| occurrences (all)                | 2                  | 0                  |
| Infantile spitting up            |                    |                    |
| subjects affected / exposed      | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                | 0                  | 1                  |
| Oral mucosal eruption            |                    |                    |
| subjects affected / exposed      | 1 / 403 (0.25%)    | 0 / 781 (0.00%)    |
| occurrences (all)                | 1                  | 0                  |
| Protein-losing gastroenteropathy |                    |                    |
| subjects affected / exposed      | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                | 0                  | 1                  |
| Regurgitation                    |                    |                    |
| subjects affected / exposed      | 1 / 403 (0.25%)    | 1 / 781 (0.13%)    |
| occurrences (all)                | 1                  | 1                  |
| Retching                         |                    |                    |
| subjects affected / exposed      | 1 / 403 (0.25%)    | 0 / 781 (0.00%)    |
| occurrences (all)                | 1                  | 0                  |
| Stomatitis                       |                    |                    |
| subjects affected / exposed      | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                | 0                  | 1                  |
| Teething                         |                    |                    |
| subjects affected / exposed      | 46 / 403 (11.41%)  | 75 / 781 (9.60%)   |
| occurrences (all)                | 55                 | 84                 |
| Toothache                        |                    |                    |
| subjects affected / exposed      | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |
| occurrences (all)                | 0                  | 1                  |
| Vomiting                         |                    |                    |
| subjects affected / exposed      | 159 / 403 (39.45%) | 317 / 781 (40.59%) |
| occurrences (all)                | 174                | 328                |

|  |                        |                        |  |
|--|------------------------|------------------------|--|
| Vomiting projectile<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 403 (0.25%)<br>1   | 1 / 781 (0.13%)<br>1   |  |
| Post-tussive vomiting<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 403 (0.25%)<br>1   | 1 / 781 (0.13%)<br>1   |  |
| <b>Skin and subcutaneous tissue disorders</b>  |                        |                        |  |
| Post inflammatory pigmentation<br>change<br>subjects affected / exposed<br>occurrences (all) | 0 / 403 (0.00%)<br>0   | 1 / 781 (0.13%)<br>1   |  |
| Acne<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 403 (0.25%)<br>1   | 0 / 781 (0.00%)<br>0   |  |
| Acne infantile<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 403 (0.00%)<br>0   | 2 / 781 (0.26%)<br>2   |  |
| Blood blister<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 403 (0.00%)<br>0   | 1 / 781 (0.13%)<br>1   |  |
| Dermatitis<br>subjects affected / exposed<br>occurrences (all)                               | 2 / 403 (0.50%)<br>2   | 9 / 781 (1.15%)<br>9   |  |
| Dermatitis atopic<br>subjects affected / exposed<br>occurrences (all)                        | 3 / 403 (0.74%)<br>3   | 8 / 781 (1.02%)<br>8   |  |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 403 (0.25%)<br>1   | 4 / 781 (0.51%)<br>4   |  |
| Dermatitis diaper<br>subjects affected / exposed<br>occurrences (all)                        | 22 / 403 (5.46%)<br>25 | 38 / 781 (4.87%)<br>41 |  |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                                 | 4 / 403 (0.99%)<br>4   | 4 / 781 (0.51%)<br>4   |  |
| Ecchymosis   |                        |                        |  |

|  |                  |                  |
|--|------------------|------------------|
| subjects affected / exposed                | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                          | 0                | 1                |
| Eczema                                     |                  |                  |
| subjects affected / exposed                | 10 / 403 (2.48%) | 16 / 781 (2.05%) |
| occurrences (all)                          | 10               | 16               |
| Eczema infantile                           |                  |                  |
| subjects affected / exposed                | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                          | 0                | 1                |
| Erythema                                   |                  |                  |
| subjects affected / exposed                | 1 / 403 (0.25%)  | 7 / 781 (0.90%)  |
| occurrences (all)                          | 1                | 7                |
| Ingrowing nail                             |                  |                  |
| subjects affected / exposed                | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)                          | 1                | 0                |
| Intertrigo                                 |                  |                  |
| subjects affected / exposed                | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                          | 0                | 1                |
| Miliaria                                   |                  |                  |
| subjects affected / exposed                | 3 / 403 (0.74%)  | 1 / 781 (0.13%)  |
| occurrences (all)                          | 3                | 1                |
| Palmar-plantar erythrodysesthesia syndrome |                  |                  |
| subjects affected / exposed                | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                          | 0                | 1                |
| Perioral dermatitis                        |                  |                  |
| subjects affected / exposed                | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                          | 0                | 1                |
| Pruritus                                   |                  |                  |
| subjects affected / exposed                | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                          | 0                | 1                |
| Rash erythematous                          |                  |                  |
| subjects affected / exposed                | 0 / 403 (0.00%)  | 2 / 781 (0.26%)  |
| occurrences (all)                          | 0                | 2                |
| Rash macular                               |                  |                  |
| subjects affected / exposed                | 1 / 403 (0.25%)  | 2 / 781 (0.26%)  |
| occurrences (all)                          | 1                | 2                |

|  |                           |                           |  |
|--|---------------------------|---------------------------|--|
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)    | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Rash papular<br>subjects affected / exposed<br>occurrences (all)           | 1 / 403 (0.25%)<br>1      | 0 / 781 (0.00%)<br>0      |  |
| Seborrhoea<br>subjects affected / exposed<br>occurrences (all)             | 1 / 403 (0.25%)<br>1      | 1 / 781 (0.13%)<br>1      |  |
| Seborrhoeic dermatitis<br>subjects affected / exposed<br>occurrences (all) | 4 / 403 (0.99%)<br>4      | 3 / 781 (0.38%)<br>3      |  |
| Skin discolouration<br>subjects affected / exposed<br>occurrences (all)    | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Skin exfoliation<br>subjects affected / exposed<br>occurrences (all)       | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Skin fissures<br>subjects affected / exposed<br>occurrences (all)          | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Skin irritation<br>subjects affected / exposed<br>occurrences (all)        | 0 / 403 (0.00%)<br>0      | 2 / 781 (0.26%)<br>2      |  |
| Umbilical erythema<br>subjects affected / exposed<br>occurrences (all)     | 0 / 403 (0.00%)<br>0      | 1 / 781 (0.13%)<br>1      |  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)              | 3 / 403 (0.74%)<br>4      | 5 / 781 (0.64%)<br>5      |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                   | 106 / 403 (26.30%)<br>117 | 216 / 781 (27.66%)<br>224 |  |
| Renal and urinary disorders<br>Renal hypertrophy                           |                           |                           |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                              | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Single functional kidney<br>subjects affected / exposed<br>occurrences (all)  | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Musculoskeletal and connective tissue disorders                               |                      |                      |  |
| Acquired plagiocephaly<br>subjects affected / exposed<br>occurrences (all)    | 1 / 403 (0.25%)<br>1 | 2 / 781 (0.26%)<br>2 |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 403 (0.00%)<br>0 | 2 / 781 (0.26%)<br>2 |  |
| Jaw clicking<br>subjects affected / exposed<br>occurrences (all)              | 0 / 403 (0.00%)<br>0 | 2 / 781 (0.26%)<br>2 |  |
| Joint noise<br>subjects affected / exposed<br>occurrences (all)               | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Muscle tightness<br>subjects affected / exposed<br>occurrences (all)          | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Muscular weakness<br>subjects affected / exposed<br>occurrences (all)         | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0 |  |
| Musculoskeletal stiffness<br>subjects affected / exposed<br>occurrences (all) | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1 |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)         | 0 / 403 (0.00%)<br>0 | 2 / 781 (0.26%)<br>3 |  |
| Torticollis<br>subjects affected / exposed<br>occurrences (all)               | 2 / 403 (0.50%)<br>2 | 3 / 781 (0.38%)<br>3 |  |
| Infections and infestations   |                      |                      |  |

|                             |                  |                  |
|-----------------------------|------------------|------------------|
| Acute sinusitis             |                  |                  |
| subjects affected / exposed | 1 / 403 (0.25%)  | 2 / 781 (0.26%)  |
| occurrences (all)           | 2                | 3                |
| Abscess limb                |                  |                  |
| subjects affected / exposed | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)           | 1                | 0                |
| Body tinea                  |                  |                  |
| subjects affected / exposed | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)           | 1                | 0                |
| Influenza                   |                  |                  |
| subjects affected / exposed | 3 / 403 (0.74%)  | 13 / 781 (1.66%) |
| occurrences (all)           | 3                | 13               |
| Bronchitis                  |                  |                  |
| subjects affected / exposed | 1 / 403 (0.25%)  | 3 / 781 (0.38%)  |
| occurrences (all)           | 1                | 3                |
| Bullous impetigo            |                  |                  |
| subjects affected / exposed | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)           | 1                | 0                |
| COVID-19                    |                  |                  |
| subjects affected / exposed | 5 / 403 (1.24%)  | 6 / 781 (0.77%)  |
| occurrences (all)           | 5                | 6                |
| Candida infection           |                  |                  |
| subjects affected / exposed | 0 / 403 (0.00%)  | 5 / 781 (0.64%)  |
| occurrences (all)           | 0                | 5                |
| Candida nappy rash          |                  |                  |
| subjects affected / exposed | 3 / 403 (0.74%)  | 10 / 781 (1.28%) |
| occurrences (all)           | 3                | 11               |
| Cellulitis                  |                  |                  |
| subjects affected / exposed | 2 / 403 (0.50%)  | 2 / 781 (0.26%)  |
| occurrences (all)           | 2                | 2                |
| Chronic sinusitis           |                  |                  |
| subjects affected / exposed | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)           | 1                | 0                |
| Conjunctivitis              |                  |                  |
| subjects affected / exposed | 15 / 403 (3.72%) | 17 / 781 (2.18%) |
| occurrences (all)           | 17               | 20               |

|   |                      |                        |
|---|----------------------|------------------------|
| Conjunctivitis bacterial<br>subjects affected / exposed<br>occurrences (all)  | 0 / 403 (0.00%)<br>0 | 4 / 781 (0.51%)<br>4   |
| Conjunctivitis viral<br>subjects affected / exposed<br>occurrences (all)      | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0   |
| Coxsackie viral infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 403 (0.25%)<br>1 | 2 / 781 (0.26%)<br>2   |
| Croup infectious<br>subjects affected / exposed<br>occurrences (all)          | 3 / 403 (0.74%)<br>4 | 24 / 781 (3.07%)<br>25 |
| Cystitis<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1   |
| Dacryocystitis<br>subjects affected / exposed<br>occurrences (all)            | 0 / 403 (0.00%)<br>0 | 1 / 781 (0.13%)<br>1   |
| Ear infection<br>subjects affected / exposed<br>occurrences (all)             | 0 / 403 (0.00%)<br>0 | 4 / 781 (0.51%)<br>4   |
| Erythema infectiosum<br>subjects affected / exposed<br>occurrences (all)      | 0 / 403 (0.00%)<br>0 | 2 / 781 (0.26%)<br>2   |
| Exanthema subitum<br>subjects affected / exposed<br>occurrences (all)         | 0 / 403 (0.00%)<br>0 | 2 / 781 (0.26%)<br>2   |
| Eye infection<br>subjects affected / exposed<br>occurrences (all)             | 1 / 403 (0.25%)<br>2 | 0 / 781 (0.00%)<br>0   |
| Folliculitis<br>subjects affected / exposed<br>occurrences (all)              | 1 / 403 (0.25%)<br>1 | 0 / 781 (0.00%)<br>0   |
| Fungal skin infection<br>subjects affected / exposed<br>occurrences (all)     | 0 / 403 (0.00%)<br>0 | 3 / 781 (0.38%)<br>3   |

|                                  |                  |                  |
|----------------------------------|------------------|------------------|
| Gastroenteritis                  |                  |                  |
| subjects affected / exposed      | 5 / 403 (1.24%)  | 8 / 781 (1.02%)  |
| occurrences (all)                | 5                | 8                |
| Gastroenteritis viral            |                  |                  |
| subjects affected / exposed      | 1 / 403 (0.25%)  | 9 / 781 (1.15%)  |
| occurrences (all)                | 1                | 9                |
| Gastrointestinal viral infection |                  |                  |
| subjects affected / exposed      | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                | 0                | 1                |
| Hand-foot-and-mouth disease      |                  |                  |
| subjects affected / exposed      | 3 / 403 (0.74%)  | 7 / 781 (0.90%)  |
| occurrences (all)                | 3                | 7                |
| Impetigo                         |                  |                  |
| subjects affected / exposed      | 3 / 403 (0.74%)  | 3 / 781 (0.38%)  |
| occurrences (all)                | 3                | 4                |
| Bronchiolitis                    |                  |                  |
| subjects affected / exposed      | 13 / 403 (3.23%) | 30 / 781 (3.84%) |
| occurrences (all)                | 16               | 31               |
| Injection site cellulitis        |                  |                  |
| subjects affected / exposed      | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                | 0                | 1                |
| Laryngotracheitis obstructive    |                  |                  |
| subjects affected / exposed      | 2 / 403 (0.50%)  | 2 / 781 (0.26%)  |
| occurrences (all)                | 2                | 2                |
| Nail infection                   |                  |                  |
| subjects affected / exposed      | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                | 0                | 1                |
| Nasopharyngitis                  |                  |                  |
| subjects affected / exposed      | 18 / 403 (4.47%) | 40 / 781 (5.12%) |
| occurrences (all)                | 20               | 46               |
| Onychomycosis                    |                  |                  |
| subjects affected / exposed      | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)                | 0                | 1                |
| Oral candidiasis                 |                  |                  |
| subjects affected / exposed      | 4 / 403 (0.99%)  | 5 / 781 (0.64%)  |
| occurrences (all)                | 4                | 5                |

|                                |                  |                  |
|--------------------------------|------------------|------------------|
| Oral viral infection           |                  |                  |
| subjects affected / exposed    | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)              | 0                | 1                |
| Otitis externa                 |                  |                  |
| subjects affected / exposed    | 1 / 403 (0.25%)  | 0 / 781 (0.00%)  |
| occurrences (all)              | 1                | 0                |
| Otitis media                   |                  |                  |
| subjects affected / exposed    | 29 / 403 (7.20%) | 47 / 781 (6.02%) |
| occurrences (all)              | 37               | 55               |
| Otitis media acute             |                  |                  |
| subjects affected / exposed    | 23 / 403 (5.71%) | 33 / 781 (4.23%) |
| occurrences (all)              | 28               | 42               |
| Otitis media chronic           |                  |                  |
| subjects affected / exposed    | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)              | 0                | 1                |
| Parainfluenzae virus infection |                  |                  |
| subjects affected / exposed    | 0 / 403 (0.00%)  | 2 / 781 (0.26%)  |
| occurrences (all)              | 0                | 2                |
| Paronychia                     |                  |                  |
| subjects affected / exposed    | 1 / 403 (0.25%)  | 1 / 781 (0.13%)  |
| occurrences (all)              | 1                | 1                |
| Parvovirus infection           |                  |                  |
| subjects affected / exposed    | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)              | 0                | 1                |
| Periorbital cellulitis         |                  |                  |
| subjects affected / exposed    | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)              | 0                | 1                |
| Pertussis                      |                  |                  |
| subjects affected / exposed    | 0 / 403 (0.00%)  | 1 / 781 (0.13%)  |
| occurrences (all)              | 0                | 1                |
| Pharyngitis                    |                  |                  |
| subjects affected / exposed    | 1 / 403 (0.25%)  | 5 / 781 (0.64%)  |
| occurrences (all)              | 1                | 5                |
| Pharyngitis streptococcal      |                  |                  |
| subjects affected / exposed    | 0 / 403 (0.00%)  | 3 / 781 (0.38%)  |
| occurrences (all)              | 0                | 3                |

|  |                 |                 |
|--|-----------------|-----------------|
| Pneumonia                                    |                 |                 |
| subjects affected / exposed                  | 1 / 403 (0.25%) | 2 / 781 (0.26%) |
| occurrences (all)                            | 1               | 2               |
| Pustule                                      |                 |                 |
| subjects affected / exposed                  | 0 / 403 (0.00%) | 1 / 781 (0.13%) |
| occurrences (all)                            | 0               | 1               |
| Respiratory syncytial virus<br>bronchiolitis |                 |                 |
| subjects affected / exposed                  | 3 / 403 (0.74%) | 3 / 781 (0.38%) |
| occurrences (all)                            | 3               | 3               |
| Respiratory syncytial virus infection        |                 |                 |
| subjects affected / exposed                  | 3 / 403 (0.74%) | 9 / 781 (1.15%) |
| occurrences (all)                            | 3               | 9               |
| Respiratory tract infection viral            |                 |                 |
| subjects affected / exposed                  | 1 / 403 (0.25%) | 2 / 781 (0.26%) |
| occurrences (all)                            | 1               | 2               |
| Rhinitis                                     |                 |                 |
| subjects affected / exposed                  | 0 / 403 (0.00%) | 5 / 781 (0.64%) |
| occurrences (all)                            | 0               | 5               |
| Roseola                                      |                 |                 |
| subjects affected / exposed                  | 1 / 403 (0.25%) | 2 / 781 (0.26%) |
| occurrences (all)                            | 1               | 2               |
| Rotavirus infection                          |                 |                 |
| subjects affected / exposed                  | 0 / 403 (0.00%) | 1 / 781 (0.13%) |
| occurrences (all)                            | 0               | 1               |
| Sinusitis                                    |                 |                 |
| subjects affected / exposed                  | 6 / 403 (1.49%) | 6 / 781 (0.77%) |
| occurrences (all)                            | 6               | 6               |
| Skin candida                                 |                 |                 |
| subjects affected / exposed                  | 3 / 403 (0.74%) | 5 / 781 (0.64%) |
| occurrences (all)                            | 3               | 5               |
| Skin infection                               |                 |                 |
| subjects affected / exposed                  | 0 / 403 (0.00%) | 1 / 781 (0.13%) |
| occurrences (all)                            | 0               | 1               |
| Suspected COVID-19                           |                 |                 |

|  |                         |                           |  |
|--|-------------------------|---------------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 1 / 403 (0.25%)<br>1    | 4 / 781 (0.51%)<br>4      |  |
| Tinea cruris<br>subjects affected / exposed<br>occurrences (all)   | 1 / 403 (0.25%)<br>1    | 1 / 781 (0.13%)<br>1      |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)  | 62 / 403 (15.38%)<br>79 | 125 / 781 (16.01%)<br>149 |  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)  | 2 / 403 (0.50%)<br>2    | 4 / 781 (0.51%)<br>4      |  |
| Viral infection<br>subjects affected / exposed<br>occurrences (all)  | 7 / 403 (1.74%)<br>7    | 13 / 781 (1.66%)<br>14    |  |
| Viral pharyngitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 403 (0.25%)<br>1    | 3 / 781 (0.38%)<br>3      |  |
| Viral rash<br>subjects affected / exposed<br>occurrences (all)   | 1 / 403 (0.25%)<br>1    | 3 / 781 (0.38%)<br>3      |  |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                                  | 12 / 403 (2.98%)<br>12  | 16 / 781 (2.05%)<br>17    |  |
| Wound infection<br>subjects affected / exposed<br>occurrences (all)  | 1 / 403 (0.25%)<br>1    | 0 / 781 (0.00%)<br>0      |  |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)  | 2 / 403 (0.50%)<br>2    | 1 / 781 (0.13%)<br>1      |  |
| Metabolism and nutrition disorders<br>Breast milk substitute intolerance<br>subjects affected / exposed<br>occurrences (all) | 1 / 403 (0.25%)<br>1    | 0 / 781 (0.00%)<br>0      |  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)   | 2 / 403 (0.50%)<br>2    | 4 / 781 (0.51%)<br>4      |  |

|                              |                    |                    |  |
|------------------------------|--------------------|--------------------|--|
| Feeding disorder             |                    |                    |  |
| subjects affected / exposed  | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |  |
| occurrences (all)            | 0                  | 1                  |  |
| Food intolerance             |                    |                    |  |
| subjects affected / exposed  | 0 / 403 (0.00%)    | 1 / 781 (0.13%)    |  |
| occurrences (all)            | 0                  | 1                  |  |
| Hypophagia                   |                    |                    |  |
| subjects affected / exposed  | 216 / 403 (53.60%) | 543 / 781 (69.53%) |  |
| occurrences (all)            | 217                | 544                |  |
| Iron deficiency              |                    |                    |  |
| subjects affected / exposed  | 1 / 403 (0.25%)    | 3 / 781 (0.38%)    |  |
| occurrences (all)            | 1                  | 3                  |  |
| Milk soy protein intolerance |                    |                    |  |
| subjects affected / exposed  | 1 / 403 (0.25%)    | 0 / 781 (0.00%)    |  |
| occurrences (all)            | 1                  | 0                  |  |
| Weight gain poor             |                    |                    |  |
| subjects affected / exposed  | 0 / 403 (0.00%)    | 3 / 781 (0.38%)    |  |
| occurrences (all)            | 0                  | 3                  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 02 November 2018 | The protocol was amended to revise the endpoints and success criteria based on using the strain M10713, for evaluating immune responses to the NHBA antigen.  |
| 10 April 2020    | The protocol was amended to outline measures that were applicable during special circumstances (e.g., COVID-19 pandemic). The purpose of the amendment was to protect subject's welfare, and ensure the potential benefit to the subject and promote data integrity.  |
| 09 December 2021 | The protocol was amended to update the criteria for the primary and key secondary immunogenicity objectives and the total number of enrolled subjects was revised to 1200.  |
| 24 October 2022  | The protocol was amended to shorten the safety follow-up period to 6 months in subjects who had not reached the 6-month safety follow-up after the last dose, at the time this amendment took effect.   |
| 19 December 2023 | The protocol was amended to align with the update of CDC's ACIP for the US NIP (National Immunization Program). According to this ACIP update, the 20-valent pneumococcal conjugate vaccine (PCV20) was listed as one of the recommended vaccines for the immunization of pneumococcal disease in children in U.S while PCV13 was no longer recommended for full series of pneumococcal vaccination. Children who received 3 PCV13 doses before 12 months but had not received their fourth booster dose, had the option to receive PCV20 or PCV13. Therefore, to incorporate the ACIP recommendations, subjects who had not reached their visit 5 at the time when this protocol amendment became effective had the option to receive either PCV13 or PCV20 based on the investigator judgment and/or parent's preference. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported