



## Clinical trial results:

### **A Phase 3b, Open-Label, Randomized, Multicenter Study to Assess the Safety and Immunogenicity of GlaxoSmithKline Biologicals Meningococcal group B Vaccine When Administered Concomitantly with GlaxoSmithKline Biologicals MenACWY Conjugate Vaccine to Healthy Infants**

#### **Summary**

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2016-005117-44  |
| Trial protocol           | Outside EU/EEA  |
| Global end of trial date | 14 October 2016 |

#### **Results information**

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v2 (current)     |
| This version publication date  | 07 February 2018 |
| First version publication date | 22 October 2017  |
| Version creation reason        |                  |

#### **Trial information**

##### **Trial identification**

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 205240 |
|-----------------------|--------|

##### **Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02106390 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### **Sponsors**

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline Biologicals   |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330  |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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                       | 11 August 2017  |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 14 October 2016 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 14 October 2016 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this trial was to assess the immunological non-inferiority of rMenB+OMV NZ and MenACWY when concomitantly administered compared to either alone in healthy infants at 3, 5, 7 and 13 months of age, as measured by the ratio of hSBA Geometric Mean Titers (GMTs) against each of the serogroup B indicator strains (for rMenB+OMV NZ) and serogroups A, C, W-135 and Y (for MenACWY) at one month after the fourth vaccination.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of vaccine(s), with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 05 June 2014 |
| 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 | Argentina: 163 |
| Country: Number of subjects enrolled | Mexico: 587    |
| Worldwide total number of subjects   | 750            |
| 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)  | 750 |
| 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:

750 healthy infants, aged 3 months were recruited from 3 sites in Argentina and 4 sites in Mexico.

### Pre-assignment

Screening details:

All enrolled subjects were included in the study.

### Period 1

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

Blinding implementation details:

This trial is designed as an open-trial; therefore, no blinding procedures were used.

### Arms

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

Arm description:

Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ / MenACWY vaccines, concomitantly administered at 3, 5, 7 and 13 months of age.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | GlaxoSmithKline Biologicals Meningococcal group B Vaccine |
| Investigational medicinal product code |   |
| Other name                             | rMENB+OMVNZ; Bexsero                                      |
| Pharmaceutical forms                   | Suspension for injection                                  |
| Routes of administration               | Intramuscular use   |

Dosage and administration details:

1 mL Pre-filled syringe. The volume delivered in a single dose was 0.5 mL.

|  |  |
|--|--|
| Investigational medicinal product name | GlaxoSmithKline Biologicals Meningococcal ACWY Conjugate Vaccine |
| Investigational medicinal product code |  |
| Other name                             | MenACWY; Menveo  |
| Pharmaceutical forms                   | Powder and solution for solution for injection                   |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

Powder (vial)+ Solution (syringe or vial). The volume delivered after reconstitution was 0.5 mL.

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | rMenB Group |
|------------------|-------------|

Arm description:

Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ administered at 3, 5, 7 and 13 months of age.

|  |   |
|--|---|
| Arm type                               | Active comparator   |
| Investigational medicinal product name | GlaxoSmithKline Biologicals Meningococcal group B Vaccine |
| Investigational medicinal product code |   |
| Other name                             | rMENB+OMVNZ; Bexsero                                      |
| Pharmaceutical forms                   | Suspension for injection                                  |
| Routes of administration               | Intramuscular use   |

Dosage and administration details:

1 mL Pre-filled syringe. The volume delivered in a single dose was 0.5 mL.

|   |  |
|---|--|
| <b>Arm title</b>  | MenACWY Group  |
| Arm description:<br>Approximately 250 healthy infants aged 3 months who received 4 doses of MenACWY administered at 3, 5, 7 and 13 months of age. |  |
| Arm type  | Active comparator  |
| Investigational medicinal product name  | GlaxoSmithKline Biologicals Meningococcal ACWY Conjugate Vaccine |
| Investigational medicinal product code  |  |
| Other name  | MenACWY; Menveo  |
| Pharmaceutical forms  | Powder and solution for solution for injection                   |
| Routes of administration  | Intramuscular use  |

Dosage and administration details:

Powder (vial)+ Solution (syringe or vial). The volume delivered after reconstitution was 0.5 mL.

| <b>Number of subjects in period 1</b> | rMenB+ACWY Group | rMenB Group | MenACWY Group |
|---------------------------------------|------------------|-------------|---------------|
| Started                               | 252              | 250         | 248           |
| Completed                             | 203              | 202         | 205           |
| Not completed                         | 49               | 48          | 43            |
| Consent withdrawn by subject          | 15               | 16          | 15            |
| Adverse event, non-fatal              | -                | 2           | 1             |
| Other: Administrative Reason          | 8                | 5           | 12            |
| Other: Unspecified                    | 1                | 4           | 2             |
| Lost to follow-up                     | 25               | 20          | 13            |
| Protocol deviation                    | -                | 1           | -             |

## Baseline characteristics

### Reporting groups

|  |                  |
|--|------------------|
| Reporting group title  | rMenB+ACWY Group |
| Reporting group description:<br>Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ / MenACWY vaccines, concomitantly administered at 3, 5, 7 and 13 months of age. |                  |
| Reporting group title  | rMenB Group      |
| Reporting group description:<br>Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ administered at 3, 5, 7 and 13 months of age.                                   |                  |
| Reporting group title  | MenACWY Group    |
| Reporting group description:<br>Approximately 250 healthy infants aged 3 months who received 4 doses of MenACWY administered at 3, 5, 7 and 13 months of age.  |                  |

| Reporting group values                           | rMenB+ACWY Group | rMenB Group | MenACWY Group |
|--|------------------|-------------|---------------|
| Number of subjects                               | 252              | 250         | 248           |
| Age categorical<br>Units: Subjects               |                  |             |               |
| In utero   | 0                | 0           | 0             |
| Preterm newborn infants (gestation age<37 weeks) | 0                | 0           | 0             |
| Newborns (0-27 days)                             | 0                | 0           | 0             |
| Infants and toddlers (28 days-23 months)         | 252              | 250         | 248           |
| Children (2-11 years)                            | 0                | 0           | 0             |
| Adolescents (12-17 years)                        | 0                | 0           | 0             |
| Adults (18-64 years)                             | 0                | 0           | 0             |
| From 65-84 years                                 | 0                | 0           | 0             |
| 85 years and over                                | 0                | 0           | 0             |
| Age continuous<br>Units: days                    |                  |             |               |
| arithmetic mean                                  | 104.0            | 101.4       | 102.7         |
| standard deviation                               | ± 10.72          | ± 10.57     | ± 10.9        |
| Gender categorical<br>Units: Subjects            |                  |             |               |
| Female   | 120              | 118         | 139           |
| Male   | 132              | 132         | 109           |
| Race/Ethnicity, Customized<br>Units: Subjects    |                  |             |               |
| White  | 17               | 20          | 17            |
| Other  | 235              | 230         | 231           |

| Reporting group values             | Total |  |  |
|------------------------------------|-------|--|--|
| Number of subjects                 | 750   |  |  |
| Age categorical<br>Units: Subjects |       |  |  |
| In utero                           | 0     |  |  |

|  |     |  |  |
|--|-----|--|--|
| Preterm newborn infants (gestation age<37 weeks) | 0   |  |  |
| Newborns (0-27 days)                             | 0   |  |  |
| Infants and toddlers (28 days-23 months)         | 750 |  |  |
| Children (2-11 years)                            | 0   |  |  |
| Adolescents (12-17 years)                        | 0   |  |  |
| Adults (18-64 years)                             | 0   |  |  |
| From 65-84 years                                 | 0   |  |  |
| 85 years and over                                | 0   |  |  |
| Age continuous                                   |     |  |  |
| Units: days                                      |     |  |  |
| arithmetic mean                                  |     |  |  |
| standard deviation                               | -   |  |  |
| Gender categorical                               |     |  |  |
| Units: Subjects                                  |     |  |  |
| Female   | 377 |  |  |
| Male   | 373 |  |  |
| Race/Ethnicity, Customized                       |     |  |  |
| Units: Subjects                                  |     |  |  |
| White  | 54  |  |  |
| Other  | 696 |  |  |

## End points

### End points reporting groups

|  |                  |
|--|------------------|
| Reporting group title  | rMenB+ACWY Group |
| Reporting group description:<br>Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ / MenACWY vaccines, concomitantly administered at 3, 5, 7 and 13 months of age. |                  |
| Reporting group title  | rMenB Group      |
| Reporting group description:<br>Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ administered at 3, 5, 7 and 13 months of age.                                   |                  |
| Reporting group title  | MenACWY Group    |
| Reporting group description:<br>Approximately 250 healthy infants aged 3 months who received 4 doses of MenACWY administered at 3, 5, 7 and 13 months of age.  |                  |

### Primary: Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers (GMTs) against each of the serogroup B indicator strains

|   |  |
|---|--|
| End point title   | Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers (GMTs) against each of the serogroup B indicator strains <sup>[1]</sup> |
| End point description:<br>Human serum bactericidal activity (hSBA) titers against each of the serogroup B indicator strains- H44/76,5/99,NZ98/254 & M10713 after receiving 4 doses of rMenB+OMV NZ / MenACWY vaccines, concomitantly administered, versus corresponding response in subjects who received rMenB+OMV NZ administered alone, were presented in terms of vaccine group specific geometric mean titers (GMTs). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. |  |
| End point type  | Primary  |
| End point timeframe:<br>At Day 331 (one month after the fourth vaccination)   |  |
| Notes:  |  |

[1] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group    | rMenB Group         |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 148                 | 158                 |  |  |
| Units: Titers                            |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| H44/76                                   | 92 (67 to 128)      | 104 (77 to 141)     |  |  |
| 5/99                                     | 1850 (1122 to 3050) | 1790 (1128 to 2842) |  |  |
| NZ98/254                                 | 39 (29 to 53)       | 38 (28 to 52)       |  |  |
| M10713                                   | 13 (7.82 to 21)     | 12 (7.72 to 20)     |  |  |



## Statistical analyses

|   |                                |
|---|--------------------------------|
| <b>Statistical analysis title</b>   | Statistical analysis 1         |
| Statistical analysis description:<br>H44/76- The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) was performed for the H44/76 serogroup B indicator strain,at one month after the fourth vaccination." |                                |
| Comparison groups   | rMenB+ACWY Group v rMenB Group |
| Number of subjects included in analysis   | 306                            |
| Analysis specification  | Pre-specified                  |
| Analysis type   | non-inferiority <sup>[2]</sup> |
| Method  | ANOVA                          |
| Parameter estimate  | GMT ratio                      |
| Point estimate  | 0.89                           |
| Confidence interval   |                                |
| level   | 95 %                           |
| sides   | 2-sided                        |
| lower limit   | 0.71                           |
| upper limit   | 1.1                            |

Notes:

[2] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) is > 0.5 for all serogroup B indicator strains.

|   |                                |
|---|--------------------------------|
| <b>Statistical analysis title</b>   | Statistical analysis 2         |
| Statistical analysis description:<br>5/99-The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) was performed for the 5/99 serogroup B indicator strain,at one month after the fourth vaccination. |                                |
| Comparison groups   | rMenB+ACWY Group v rMenB Group |
| Number of subjects included in analysis   | 306                            |
| Analysis specification  | Pre-specified                  |
| Analysis type   | non-inferiority <sup>[3]</sup> |
| Method  | ANOVA                          |
| Parameter estimate  | GMT ratio                      |
| Point estimate  | 1.03                           |
| Confidence interval   |                                |
| level   | 95 %                           |
| sides   | 2-sided                        |
| lower limit   | 0.74                           |
| upper limit   | 1.45                           |

Notes:

[3] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) is > 0.5 for all serogroup B indicator strains.

|  |                        |
|--|------------------------|
| <b>Statistical analysis title</b>  | Statistical analysis 3 |
| Statistical analysis description:<br>NZ98/254-The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) was performed for the NZ98/254 serogroup B indicator strain,at one month after the fourth |                        |

vaccination.

|   |                                |
|---|--------------------------------|
| Comparison groups                       | rMenB+ACWY Group v rMenB Group |
| Number of subjects included in analysis | 306                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[4]</sup> |
| Method                                  | ANOVA                          |
| Parameter estimate                      | GMT ratio                      |
| Point estimate                          | 1.01                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 0.82                           |
| upper limit                             | 1.25                           |

Notes:

[4] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ is > 0.5 for all serogroup B indicator strains.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

M10713-The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) was performed for the M10713 serogroup B indicator strain, at one month after the fourth vaccination.

|   |                                |
|---|--------------------------------|
| Comparison groups                       | rMenB+ACWY Group v rMenB Group |
| Number of subjects included in analysis | 306                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[5]</sup> |
| Method                                  | ANOVA                          |
| Parameter estimate                      | GMT ratio                      |
| Point estimate                          | 1.03                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 0.77                           |
| upper limit                             | 1.4                            |

Notes:

[5] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ is > 0.5 for all serogroup B indicator strains.

### **Primary: hSBA Geometric Mean Titers (GMTs) against each of the serogroups A, C, W-135 and Y**

|                 |   |
|-----------------|---|
| End point title | hSBA Geometric Mean Titers (GMTs) against each of the serogroups A, C, W-135 and Y <sup>[6]</sup> |
|-----------------|---|

End point description:

hSBA titers against N. meningitidis serogroups A, C, W-135 and Y after receiving four doses of either rMenB+OMV NZ / MenACWY concomitantly administered versus corresponding response in subjects who received MenACWY administered alone were presented in terms of vaccine group specific GMTs. This outcome measure applies to only rMenB+ACWY and MenACWY groups as the serogroups A,C,W-135 & Y were assessed only for these two groups.

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

End point timeframe:

At Day 331 (one month after the fourth vaccination)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group  | MenACWY Group    |  |  |
|--|-------------------|------------------|--|--|
| Subject group type                       | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed              | 161               | 156              |  |  |
| Units: Titers                            |                   |                  |  |  |
| geometric mean (confidence interval 95%) |                   |                  |  |  |
| Serogroup A                              | 409 (300 to 556)  | 165 (122 to 224) |  |  |
| Serogroup C                              | 452 (312 to 655)  | 421 (294 to 602) |  |  |
| Serogroup W                              | 721 (493 to 1053) | 536 (370 to 776) |  |  |
| Serogroup Y                              | 410 (293 to 575)  | 391 (280 to 546) |  |  |

## Statistical analyses

| Statistical analysis title  | Statistical analysis 1           |
|---|----------------------------------|
| Statistical analysis description:   |                                  |
| Serogroup A-The comparison of adjusted GMTs ratio (rMenB+OMV NZ + Men ACWY versus MenACWY) was performed for serogroup A at one month after the fourth vaccination. |                                  |
| Comparison groups   | MenACWY Group v rMenB+ACWY Group |
| Number of subjects included in analysis   | 317                              |
| Analysis specification  | Pre-specified                    |
| Analysis type   | non-inferiority <sup>[7]</sup>   |
| Method  | ANOVA                            |
| Parameter estimate  | GMT ratio                        |
| Point estimate  | 2.48                             |
| Confidence interval   |                                  |
| level   | 95 %                             |
| sides   | 2-sided                          |
| lower limit   | 1.97                             |
| upper limit   | 3.11                             |

Notes:

[7] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMVNZ + MenACWY versus MenACWY) was > 0.5 for all serogroups A, C, W-135 and Y.

| Statistical analysis title  | Statistical analysis 2           |
|---|----------------------------------|
| Statistical analysis description:   |                                  |
| Serogroup C-The comparison of adjusted GMTs ratio (rMenB+OMV NZ + Men ACWY versus MenACWY) was performed for the serogroup C at one month after the fourth vaccination. |                                  |
| Comparison groups   | MenACWY Group v rMenB+ACWY Group |

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 317                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[8]</sup> |
| Method                                  | ANOVA                          |
| Parameter estimate                      | GMT ratio                      |
| Point estimate                          | 1.07                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 0.83                           |
| upper limit                             | 1.38                           |

Notes:

[8] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMVNZ + MenACWY versus MenACWY) was > 0.5 for all serogroups A, C, W-135 and Y.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Serogroup W-The comparison of adjusted GMTs ratio (rMenB+OMV NZ + Men ACWY versus MenACWY) was performed for the serogroup W-135 at one month after the fourth vaccination.

|   |                                  |
|---|----------------------------------|
| Comparison groups                       | MenACWY Group v rMenB+ACWY Group |
| Number of subjects included in analysis | 317                              |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | non-inferiority <sup>[9]</sup>   |
| Method                                  | ANOVA                            |
| Parameter estimate                      | GMT ratio                        |
| Point estimate                          | 1.34                             |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | 1.04                             |
| upper limit                             | 1.74                             |

Notes:

[9] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMVNZ + MenACWY versus MenACWY) was > 0.5 for all serogroups A, C, W-135 and Y.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Serogroup Y-The comparison of adjusted GMTs ratio (rMenB+OMV NZ + Men ACWY versus MenACWY) was performed for the serogroup Y at one month after the fourth vaccination.

|   |                                  |
|---|----------------------------------|
| Comparison groups                       | MenACWY Group v rMenB+ACWY Group |
| Number of subjects included in analysis | 317                              |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | non-inferiority <sup>[10]</sup>  |
| Method                                  | ANOVA                            |
| Parameter estimate                      | GMT ratio                        |
| Point estimate                          | 1.05                             |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | 0.82                             |
| upper limit                             | 1.35                             |

Notes:

[10] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMVNZ + MenACWY versus MenACWY) was > 0.5 for all serogroups A, C, W-135 and Y.

### Secondary: hSBA Geometric Mean Titers against each of the serogroup B indicator strains.

|                 |   |
|-----------------|---|
| End point title | hSBA Geometric Mean Titers against each of the serogroup B indicator strains. <sup>[11]</sup> |
|-----------------|---|

End point description:

hSBA GMTs against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 at baseline (Day 1). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups.

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

End point timeframe:

At Day 1

Notes:

[11] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group    | rMenB Group         |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 191                 | 206                 |  |  |
| Units: Titers                            |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| H44/76                                   | 1.03 (0.99 to 1.08) | 1.02 (0.98 to 1.07) |  |  |
| 5/99                                     | 1.09 (0.99 to 1.21) | 1.07 (0.97 to 1.17) |  |  |
| NZ98/254                                 | 1.06 (1.01 to 1.12) | 1.07 (1.02 to 1.12) |  |  |
| M10713                                   | 1.88 (1.51 to 2.34) | 1.59 (1.29 to 1.96) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: hSBA Geometric Mean Titers against each of the serogroup B indicator strains.

|                 |   |
|-----------------|---|
| End point title | hSBA Geometric Mean Titers against each of the serogroup B indicator strains. <sup>[12]</sup> |
|-----------------|---|

End point description:

hSBA GMTs against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 at one month after the third vaccination (Day 151). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups.

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

End point timeframe:

At Day 151 (one month after the third vaccination)

Notes:

[12] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group  | rMenB Group       |  |  |
|--|-------------------|-------------------|--|--|
| Subject group type                       | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed              | 181               | 206               |  |  |
| Units: Titers                            |                   |                   |  |  |
| geometric mean (confidence interval 95%) |                   |                   |  |  |
| H44/76                                   | 116 (100 to 135)  | 129 (113 to 147)  |  |  |
| 5/99                                     | 891 (752 to 1055) | 935 (803 to 1088) |  |  |
| NZ98/254                                 | 32 (26 to 39)     | 33 (27 to 40)     |  |  |
| M10713                                   | 9.09 (6.57 to 13) | 10 (7.50 to 14)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: hSBA Geometric Mean Titers against each of the serogroup B indicator strains.

|                 |   |
|-----------------|---|
| End point title | hSBA Geometric Mean Titers against each of the serogroup B indicator strains. <sup>[13]</sup> |
|-----------------|---|

End point description:

hSBA GMTs against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 before the fourth vaccination (Day 301). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups.

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

End point timeframe:

At Day 301 (before the fourth vaccination)

Notes:

[13] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group    | rMenB Group       |  |  |
|--|---------------------|-------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group   |  |  |
| Number of subjects analysed              | 173                 | 204               |  |  |
| Units: Titers                            |                     |                   |  |  |
| geometric mean (confidence interval 95%) |                     |                   |  |  |
| H44/76                                   | 7.68 (5.91 to 9.99) | 8.31 (6.54 to 11) |  |  |

|          |                     |                     |  |  |
|----------|---------------------|---------------------|--|--|
| 5/99     | 131 (107 to 161)    | 109 (90 to 132)     |  |  |
| NZ98/254 | 3.21 (2.44 to 4.21) | 2.93 (2.25 to 3.81) |  |  |
| M10713   | 2.48 (1.89 to 3.27) | 2.40 (1.85 to 3.10) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: hSBA Geometric Mean Titers against each of the serogroup B indicator strains.

|                 |   |
|-----------------|---|
| End point title | hSBA Geometric Mean Titers against each of the serogroup B indicator strains. <sup>[14]</sup> |
|-----------------|---|

End point description:

hSBA GMTs against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 at one month after the fourth vaccination (Day 331). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups.

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

End point timeframe:

At Day 331 (one month after the fourth vaccination)

Notes:

[14] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group    | rMenB Group        |  |  |
|--|---------------------|--------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed              | 181                 | 196                |  |  |
| Units: Titers                            |                     |                    |  |  |
| geometric mean (confidence interval 95%) |                     |                    |  |  |
| H44/76                                   | 122 (98 to 151)     | 126 (104 to 154)   |  |  |
| 5/99                                     | 1404 (1016 to 1939) | 1262 (934 to 1706) |  |  |
| NZ98/254                                 | 37 (30 to 45)       | 36 (30 to 44)      |  |  |
| M10713                                   | 18 (14 to 24)       | 17 (13 to 22)      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: hSBA Geometric Mean Titers against each of the serogroups A,C,W-135 & Y.

|                 |  |
|-----------------|--|
| End point title | hSBA Geometric Mean Titers against each of the serogroups A,C,W-135 & Y. <sup>[15]</sup> |
|-----------------|--|

End point description:

hSBA GMTs against each of the N. meningitidis serogroups A, C, W-135, Y at baseline (Day 1). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups A,C,W-135 & Y were assessed only for these two groups.

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

End point timeframe:

At Day 1

Notes:

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

Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group    | MenACWY Group       |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 213                 | 210                 |  |  |
| Units: Titers                            |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| Serogroup A                              | 2.05 (1.97 to 2.15) | 2.08 (1.99 to 2.17) |  |  |
| Serogroup C                              | 2.16 (1.98 to 2.35) | 2.09 (1.92 to 2.27) |  |  |
| Serogroup W                              | 2.33 (2.13 to 2.55) | 2.31 (2.11 to 2.52) |  |  |
| Serogroup Y                              | 2.06 (1.95 to 2.17) | 2.16 (2.05 to 2.28) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y

|                 |   |
|-----------------|---|
| End point title | hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y <sup>[16]</sup> |
|-----------------|---|

End point description:

hSBA GMTs against each of the N. meningitidis serogroups A, C, W-135, Y at one month after the third vaccination (Day 151). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups A,C,W-135 & Y were assessed only for these two groups.

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

End point timeframe:

At Day 151 (one month after the third vaccination)

Notes:

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

Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.



| End point values                         | rMenB+ACWY Group | MenACWY Group    |  |  |
|--|------------------|------------------|--|--|
| Subject group type                       | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed              | 215              | 214              |  |  |
| Units: Titers                            |                  |                  |  |  |
| geometric mean (confidence interval 95%) |                  |                  |  |  |
| Serogroup A                              | 303 (242 to 379) | 136 (108 to 169) |  |  |
| Serogroup C                              | 388 (320 to 469) | 416 (345 to 502) |  |  |
| Serogroup W                              | 347 (282 to 427) | 298 (244 to 364) |  |  |
| Serogroup Y                              | 226 (182 to 282) | 283 (228 to 351) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: hSBA Geometric Mean Titers against each of the serogroups A,C,W-135 & Y.

|                 |  |
|-----------------|--|
| End point title | hSBA Geometric Mean Titers against each of the serogroups A,C,W-135 & Y. <sup>[17]</sup> |
|-----------------|--|

End point description:

hSBA GMTs against each of the N. meningitidis serogroups A, C, W-135, Y before the fourth vaccination (Day 301). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups A,C,W-135 & Y were assessed only for these two groups.

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

End point timeframe:

At Day 301 (before the fourth vaccination)

Notes:

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

Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group | MenACWY Group   |  |  |
|--|------------------|-----------------|--|--|
| Subject group type                       | Reporting group  | Reporting group |  |  |
| Number of subjects analysed              | 203              | 204             |  |  |
| Units: Titers                            |                  |                 |  |  |
| geometric mean (confidence interval 95%) |                  |                 |  |  |
| Serogroup A                              | 20 (15 to 28)    | 15 (11 to 21)   |  |  |
| Serogroup C                              | 31 (23 to 41)    | 43 (32 to 58)   |  |  |
| Serogroup W                              | 48 (37 to 63)    | 47 (36 to 62)   |  |  |
| Serogroup Y                              | 38 (30 to 49)    | 43 (33 to 55)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: hSBA Geometric Mean Titers against each of the serogroups A,C,W-135 & Y.

|                 |  |
|-----------------|--|
| End point title | hSBA Geometric Mean Titers against each of the serogroups A,C,W-135 & Y. <sup>[18]</sup> |
|-----------------|--|

End point description:

hSBA GMTs against each of the N.meningitidis serogroups A, C, W-135, Y at one month after the fourth vaccination (Day 331). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups A,C,W-135 & Y were assessed only for these two groups.

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

End point timeframe:

At Day 331 (one month after the fourth vaccination)

Notes:

[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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group | MenACWY Group    |  |  |
|--|------------------|------------------|--|--|
| Subject group type                       | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed              | 199              | 204              |  |  |
| Units: Titers                            |                  |                  |  |  |
| geometric mean (confidence interval 95%) |                  |                  |  |  |
| Serogroup A                              | 329 (269 to 403) | 132 (108 to 161) |  |  |
| Serogroup C                              | 331 (268 to 409) | 311 (252 to 384) |  |  |
| Serogroup W                              | 576 (458 to 723) | 428 (342 to 537) |  |  |
| Serogroup Y                              | 377 (304 to 466) | 363 (294 to 448) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with hSBA titers $\geq 1:5$ against each of the serogroup B indicator strains

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with hSBA titers $\geq 1:5$ against each of the serogroup B indicator strains <sup>[19]</sup> |
|-----------------|--|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:5$  against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 before the first vaccination (Day 1). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups.

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

End point timeframe:

At Day 1

Notes:

[19] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group  | rMenB Group      |  |  |
|----------------------------------|-------------------|------------------|--|--|
| Subject group type               | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed      | 191               | 206              |  |  |
| Units: Percentage of subjects    |                   |                  |  |  |
| number (confidence interval 95%) |                   |                  |  |  |
| H44/76                           | 0 (0.0 to 2.3)    | 1 (0.01 to 2.8)  |  |  |
| 5/99                             | 1 (0.15 to 4.5)   | 1 (0.13 to 3.7)  |  |  |
| NZ98/254                         | 1 (0.01 to 2.9)   | 1 (0.01 to 2.7)  |  |  |
| M10713                           | 16 (11.4 to 22.7) | 11 (6.9 to 15.9) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with hSBA titers $\geq 1:5$ against each of the serogroup B indicator strains

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with hSBA titers $\geq 1:5$ against each of the serogroup B indicator strains <sup>[20]</sup> |
|-----------------|--|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:5$  against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 one month after the third vaccination (Day 151). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups.

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

End point timeframe:

At Day 151 (one month after the third vaccination)

Notes:

[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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | rMenB Group         |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 181                 | 206                 |  |  |
| Units: Percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) |                     |                     |  |  |
| H44/76                           | 100 (97.6 to 100.0) | 100 (98.2 to 100.0) |  |  |
| 5/99                             | 100 (97.3 to 100.0) | 100 (98.1 to 100.0) |  |  |

|          |                   |                   |  |  |
|----------|-------------------|-------------------|--|--|
| NZ98/254 | 96 (92.2 to 98.4) | 97 (93.7 to 98.9) |  |  |
| M10713   | 70 (62.7 to 77.0) | 68 (61.1 to 74.3) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with hSBA titers $\geq 1:5$ against each of the serogroup B strains.

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq 1:5$ against each of the serogroup B strains. <sup>[21]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:5$  against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 before the fourth vaccination (Day 301). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups.

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

End point timeframe:

At Day 301 (before the fourth vaccination)

Notes:

[21] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | rMenB Group       |  |  |
|----------------------------------|---------------------|-------------------|--|--|
| Subject group type               | Reporting group     | Reporting group   |  |  |
| Number of subjects analysed      | 173                 | 204               |  |  |
| Units: Percentage of subjects    |                     |                   |  |  |
| number (confidence interval 95%) |                     |                   |  |  |
| H44/76                           | 74 (65.4 to 81.2)   | 75 (67.9 to 80.7) |  |  |
| 5/99                             | 100 (97.4 to 100.0) | 97 (93.9 to 99.1) |  |  |
| NZ98/254                         | 42 (34.2 to 49.3)   | 36 (29.7 to 43.3) |  |  |
| M10713                           | 33 (25.7 to 41.2)   | 31 (24.5 to 37.7) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with hSBA titers $\geq 1:5$ against each of the serogroup B strains.

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq 1:5$ against each of the serogroup B strains. <sup>[22]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:5$  against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 after the fourth vaccination (Day 331). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups.

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

End point timeframe:

At Day 331 (One month after the fourth vaccination)

Notes:

[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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | rMenB Group        |  |  |
|----------------------------------|---------------------|--------------------|--|--|
| Subject group type               | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed      | 181                 | 196                |  |  |
| Units: Percentage of subjects    |                     |                    |  |  |
| number (confidence interval 95%) |                     |                    |  |  |
| H44/76                           | 100 (97.4 to 100.0) | 99 (97.1 to 99.99) |  |  |
| 5/99                             | 99 (95.0 to 99.83)  | 97 (93.0 to 98.8)  |  |  |
| NZ98/254                         | 100 (98.0 to 100.0) | 98 (94.9 to 99.4)  |  |  |
| M10713                           | 87 (80.8 to 91.7)   | 87 (81.6 to 91.5)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with hSBA titers $\geq 1:8$ against each of the serogroup B indicator strains

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with hSBA titers $\geq 1:8$ against each of the serogroup B indicator strains <sup>[23]</sup> |
|-----------------|--|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:8$  against each of the N. meningitidis serogroup B indicator strains at baseline (Day 1). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups.

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

End point timeframe:

At Day 1

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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group | rMenB Group     |  |  |
|----------------------------------|------------------|-----------------|--|--|
| Subject group type               | Reporting group  | Reporting group |  |  |
| Number of subjects analysed      | 191              | 206             |  |  |
| Units: Percentage of subjects    |                  |                 |  |  |
| number (confidence interval 95%) |                  |                 |  |  |
| H44/76                           | 0 (0.0 to 2.3)   | 0 (0.0 to 1.8)  |  |  |
| 5/99                             | 1 (0.02 to 3.5)  | 1 (0.01 to 2.9) |  |  |
| NZ98/254                         | 1 (0.01 to 2.9)  | 1 (0.01 to 2.7) |  |  |
| M10713                           | 12 (7.3 to 17.1) | 8 (4.6 to 12.5) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with hSBA titers $\geq 1:8$ against each of the serogroup B indicator strains

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with hSBA titers $\geq 1:8$ against each of the serogroup B indicator strains <sup>[24]</sup> |
|-----------------|--|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:8$  against each of the N. meningitidis serogroup B indicator strains at one month after third vaccination (Day 151). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups.

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

End point timeframe:

At Day 151 (one month after the 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | rMenB Group         |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 181                 | 206                 |  |  |
| Units: Percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) |                     |                     |  |  |
| H44/76                           | 100 (97.6 to 100.0) | 100 (98.2 to 100.0) |  |  |
| 5/99                             | 100 (97.3 to 100.0) | 100 (98.1 to 100.0) |  |  |
| NZ98/254                         | 92 (87.4 to 95.7)   | 92 (87.6 to 95.5)   |  |  |
| M10713                           | 65 (57.2 to 72.1)   | 59 (52.2 to 66.0)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with hSBA titers $\geq 1:8$ against each of the serogroup B indicator strains

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with hSBA titers $\geq 1:8$ against each of the serogroup B indicator strains <sup>[25]</sup> |
|-----------------|--|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:8$  against each of the N. meningitidis serogroup B indicator strains before the fourth vaccination (Day 301). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups.

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

End point timeframe:

At Day 301 (before 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | rMenB Group       |  |  |
|----------------------------------|---------------------|-------------------|--|--|
| Subject group type               | Reporting group     | Reporting group   |  |  |
| Number of subjects analysed      | 173                 | 204               |  |  |
| Units: Percentage of subjects    |                     |                   |  |  |
| number (confidence interval 95%) |                     |                   |  |  |
| H44/76                           | 58 (49.5 to 67.0)   | 56 (48.9 to 63.5) |  |  |
| 5/99                             | 100 (97.4 to 100.0) | 97 (93.2 to 98.8) |  |  |
| NZ98/254                         | 26 (19.6 to 33.2)   | 26 (20.6 to 33.1) |  |  |
| M10713                           | 21 (14.4 to 27.9)   | 23 (17.5 to 29.7) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with hSBA titers $\geq 1:8$ against each of the serogroup B indicator strains

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with hSBA titers $\geq 1:8$ against each of the serogroup B indicator strains <sup>[26]</sup> |
|-----------------|--|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:8$  against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 at one month after the fourth vaccination (Day 331). This outcome measure applies to only rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups.

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

End point timeframe:

At Day 331 (one 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | rMenB Group        |  |  |
|----------------------------------|---------------------|--------------------|--|--|
| Subject group type               | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed      | 181                 | 196                |  |  |
| Units: Percentage of subjects    |                     |                    |  |  |
| number (confidence interval 95%) |                     |                    |  |  |
| H44/76                           | 100 (97.4 to 100.0) | 99 (97.1 to 99.99) |  |  |
| 5/99                             | 99 (95.0 to 99.83)  | 97 (93.0 to 98.8)  |  |  |
| NZ98/254                         | 98 (94.4 to 99.4)   | 94 (90.2 to 97.2)  |  |  |
| M10713                           | 83 (76.5 to 88.6)   | 82 (76.4 to 87.5)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with hSBA titers $\geq 1:4$ against each of the serogroups A, C, W-135 and Y

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq 1:4$ against each of the serogroups A, C, W-135 and Y <sup>[27]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:4$  against each of the N. meningitidis serogroups A, C, W-135 and Y before the first vaccination (Day 1). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups were assessed only for these two groups.

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

End point timeframe:

At Day 1

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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group | MenACWY Group   |  |  |
|----------------------------------|------------------|-----------------|--|--|
| Subject group type               | Reporting group  | Reporting group |  |  |
| Number of subjects analysed      | 213              | 210             |  |  |
| Units: Percentage of subjects    |                  |                 |  |  |
| number (confidence interval 95%) |                  |                 |  |  |
| Serogroup A                      | 1 (0.11 to 3.4)  | 1 (0.12 to 3.5) |  |  |
| Serogroup C                      | 4 (1.7 to 7.5)   | 3 (1.4 to 6.9)  |  |  |
| Serogroup W                      | 4 (1.8 to 8.0)   | 4 (1.4 to 7.2)  |  |  |



|             |                |                |  |  |
|-------------|----------------|----------------|--|--|
| Serogroup Y | 2 (0.5 to 4.7) | 5 (2.3 to 8.6) |  |  |
|-------------|----------------|----------------|--|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with hSBA titers $\geq$ 1:4 against each of the serogroups A, C, W-135 and Y

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq$ 1:4 against each of the serogroups A, C, W-135 and Y <sup>[28]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers $\geq$  1:4 against each of the N. meningitidis serogroups A, C, W-135 and Y at one month after the third vaccination (Day 151). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups were assessed only for these two groups.

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

End point timeframe:

At Day 151 (one month after the third 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | MenACWY Group       |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 215                 | 214                 |  |  |
| Units: Percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) |                     |                     |  |  |
| Serogroup A                      | 99 (97.4 to 99.99)  | 96 (92.0 to 98.0)   |  |  |
| Serogroup C                      | 100 (98.2 to 100.0) | 100 (98.2 to 100.0) |  |  |
| Serogroup W                      | 100 (97.9 to 100.0) | 100 (98.1 to 100.0) |  |  |
| Serogroup Y                      | 99 (96.0 to 99.71)  | 100 (98.3 to 100.0) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with hSBA titers $\geq$ 1:4 against each of the serogroups A, C, W-135 and Y

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq$ 1:4 against each of the serogroups A, C, W-135 and Y <sup>[29]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:4$  against each of the N. meningitidis serogroups A, C, W-135 and Y before the fourth vaccination (Day 301). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups were assessed only for these two groups.

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

End point timeframe:

At Day 301 (before the 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group  | MenACWY Group     |  |  |
|----------------------------------|-------------------|-------------------|--|--|
| Subject group type               | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed      | 203               | 204               |  |  |
| Units: Percentage of subjects    |                   |                   |  |  |
| number (confidence interval 95%) |                   |                   |  |  |
| Serogroup A                      | 68 (60.5 to 73.9) | 63 (55.4 to 69.2) |  |  |
| Serogroup C                      | 88 (82.3 to 92.0) | 89 (84.1 to 93.4) |  |  |
| Serogroup W                      | 93 (88.7 to 96.7) | 96 (91.3 to 98.0) |  |  |
| Serogroup Y                      | 91 (85.8 to 94.3) | 95 (90.6 to 97.3) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with hSBA titers $\geq 1:4$ against each of the serogroups A, C, W-135 and Y

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq 1:4$ against each of the serogroups A, C, W-135 and Y <sup>[30]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers  $\geq 1:4$  against each of the N. meningitidis serogroups A, C, W-135 and Y at one month after the fourth vaccination (Day 331). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups were assessed only for these two groups.

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

End point timeframe:

At Day 331 (one month after the fourth vaccination)

Notes:

[30] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | MenACWY Group       |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 199                 | 204                 |  |  |
| Units: Percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) |                     |                     |  |  |
| Serogroup A                      | 100 (98.1 to 100.0) | 98 (94.3 to 99.2)   |  |  |
| Serogroup C                      | 100 (98.1 to 100.0) | 100 (98.1 to 100.0) |  |  |
| Serogroup W                      | 100 (98.0 to 100.0) | 100 (98.0 to 100.0) |  |  |
| Serogroup Y                      | 100 (98.2 to 100.0) | 99 (97.3 to 99.99)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Within-subject Geometric Mean Ratios (GMRs) against each of the serogroup B indicator strains

|                 |   |
|-----------------|---|
| End point title | Within-subject Geometric Mean Ratios (GMRs) against each of the serogroup B indicator strains <sup>[31]</sup> |
|-----------------|---|

End point description:

Geometric Mean Ratios(GMRs) of GMTs against each of the serogroup B indicator strains- H44/76, 5/99, N98/254 & M10713 were calculated at one month after the fourth vaccination (Day 331) versus pre fourth vaccination(Day 301).

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

End point timeframe:

At Day 331 (one month after fourth vaccination)

Notes:

[31] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group    | rMenB Group         |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 155                 | 195                 |  |  |
| Units: Ratio                             |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| H44/76                                   | 17 (13 to 22)       | 16 (12 to 20)       |  |  |
| 5/99                                     | 9.60 (6.99 to 13)   | 12 (8.86 to 16)     |  |  |
| NZ98/254                                 | 11 (8.35 to 15)     | 12 (9.39 to 16)     |  |  |
| M10713                                   | 5.99 (4.20 to 8.54) | 6.75 (4.90 to 9.29) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Within-subject Geometric Mean Ratios (GMRs) against each of serogroups A, C, W-135 and Y

|                 |  |
|-----------------|--|
| End point title | Within-subject Geometric Mean Ratios (GMRs) against each of serogroups A, C, W-135 and Y <sup>[32]</sup> |
|-----------------|--|

End point description:

Geometric Mean Ratios(GMRs) of GMTs against each of the serogroups A,C,W-135 & Y were calculated at one month after the fourth vaccination (Day 331) versus pre fourth vaccination (Day 301).

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

End point timeframe:

At Day 331 (one month after the fourth vaccination)

Notes:

[32] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | rMenB+ACWY Group  | MenACWY Group       |  |  |
|--|-------------------|---------------------|--|--|
| Subject group type                       | Reporting group   | Reporting group     |  |  |
| Number of subjects analysed              | 197               | 201                 |  |  |
| Units: Ratio                             |                   |                     |  |  |
| geometric mean (confidence interval 95%) |                   |                     |  |  |
| Serogroup A                              | 16 (13 to 21)     | 8.75 (6.69 to 11)   |  |  |
| Serogroup C                              | 11 (8.86 to 14)   | 7.79 (6.25 to 9.71) |  |  |
| Serogroup W                              | 13 (10 to 16)     | 9.44 (7.52 to 12)   |  |  |
| Serogroup Y                              | 9.75 (8.00 to 12) | 8.97 (7.36 to 11)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with four-fold increases in hSBA titers against each of the serogroup B indicator strains

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with four-fold increases in hSBA titers against each of the serogroup B indicator strains <sup>[33]</sup> |
|-----------------|--|

End point description:

Percentage of subjects with four-fold increase in hSBA titers against each of the N. meningitidis serogroup B indicator strains-H44/76,5/99,NZ98/254 & M10713 at one month after the fourth vaccination (Day 331) over pre-fourth vaccination (Day 301). This outcome measure applies to only groups rMenB+ACWY and rMenB as the serogroup B indicator strains were assessed only for these two groups.

For serogroup B strains, 4-fold increase in titers was defined as post 4th vaccination titer  $\geq 8$  (if pre 4th vaccination titer was  $< 2$ ) or post 4th vaccination titer  $\geq 4 \times$  pre 4th vaccination titer (if pre 4th vaccination titer was  $\geq 2$ ).

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

End point timeframe:

At Day 331 (one month after the fourth vaccination)

Notes:

[33] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group  | rMenB Group       |  |  |
|----------------------------------|-------------------|-------------------|--|--|
| Subject group type               | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed      | 155               | 195               |  |  |
| Units: Percentage of subjects    |                   |                   |  |  |
| number (confidence interval 95%) |                   |                   |  |  |
| H44/76                           | 93 (86.0 to 96.8) | 92 (87.2 to 95.6) |  |  |
| 5/99                             | 94 (88.2 to 97.6) | 95 (90.9 to 97.9) |  |  |
| NZ98/254                         | 81 (73.5 to 86.5) | 79 (73.1 to 84.9) |  |  |
| M10713                           | 58 (48.7 to 66.3) | 60 (52.5 to 67.0) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with four-fold increases in hSBA titers against each of the serogroups A, C, W-135 and Y

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with four-fold increases in hSBA titers against each of the serogroups A, C, W-135 and Y <sup>[34]</sup> |
|-----------------|---|

End point description:

Percentages of subjects with four-fold increases in hSBA against each of the N. meningitidis serogroups A,C,W & Y at one month after the fourth vaccination (Day 331) over pre-fourth vaccination(Day 301). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups were assessed only for these two groups.

For serogroups A, C, W and Y, 4-fold increase in titers was defined as post 4th vaccination titer  $\geq 16$  (if pre 4th vaccination titer was  $< 4$ ) or post 4th vaccination titer  $\geq 4 \times$  pre 4th vaccination titer (if pre 4th vaccination titer was  $\geq 4$ ).

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

End point timeframe:

At Day 331 (one month after the fourth vaccination)

Notes:

[34] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group  | MenACWY Group     |  |  |
|----------------------------------|-------------------|-------------------|--|--|
| Subject group type               | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed      | 197               | 201               |  |  |
| Units: Percentage of subjects    |                   |                   |  |  |
| number (confidence interval 95%) |                   |                   |  |  |
| Serogroup A                      | 90 (84.4 to 93.5) | 71 (64.6 to 77.6) |  |  |
| Serogroup C                      | 88 (81.9 to 92.0) | 77 (70.1 to 82.9) |  |  |
| Serogroup W                      | 89 (83.0 to 93.5) | 84 (77.9 to 89.7) |  |  |
| Serogroup Y                      | 82 (75.6 to 86.9) | 81 (74.4 to 85.8) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with hSBA titers $\geq$ 1:8 against each of the serogroups A, C, W-135 and Y

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq$ 1:8 against each of the serogroups A, C, W-135 and Y <sup>[35]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers $\geq$  1:8 against each of the N. meningitidis serogroups A, C, W-135 and Y at baseline (Day 1). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups were assessed only for these two groups.

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

End point timeframe:

At Day 1

Notes:

[35] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group | MenACWY Group   |  |  |
|----------------------------------|------------------|-----------------|--|--|
| Subject group type               | Reporting group  | Reporting group |  |  |
| Number of subjects analysed      | 213              | 210             |  |  |
| Units: Percentage of subjects    |                  |                 |  |  |
| number (confidence interval 95%) |                  |                 |  |  |
| Serogroup A                      | 1 (0.01 to 2.6)  | 1 (0.01 to 2.7) |  |  |
| Serogroup C                      | 2 (0.8 to 5.6)   | 2 (0.5 to 4.9)  |  |  |
| Serogroup W                      | 4 (1.5 to 7.3)   | 3 (0.8 to 5.9)  |  |  |
| Serogroup Y                      | 0 (0.0 to 1.7)   | 2 (0.5 to 4.8)  |  |  |

## Statistical analyses

**Secondary: Percentage of subjects with hSBA titers $\geq$ 1:8 against each of the serogroups A, C, W-135 and Y**

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq$ 1:8 against each of the serogroups A, C, W-135 and Y <sup>[36]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers $\geq$  1:8 against each of the N. meningitidis serogroups A, C, W-135 & Y at one month after the third vaccination (Day 151). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups were assessed only for these two groups.

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

End point timeframe:

At Day 151 (one month before the third vaccination)

Notes:

[36] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | MenACWY Group       |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 215                 | 214                 |  |  |
| Units: Percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) |                     |                     |  |  |
| Serogroup A                      | 99 (97.4 to 99.99)  | 96 (92.0 to 98.0)   |  |  |
| Serogroup C                      | 100 (98.2 to 100.0) | 100 (98.2 to 100.0) |  |  |
| Serogroup W                      | 100 (97.9 to 100.0) | 99 (97.1 to 99.99)  |  |  |
| Serogroup Y                      | 98 (95.3 to 99.5)   | 99 (97.4 to 99.99)  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of subjects with hSBA titers $\geq$ 1:8 against each of the serogroups A, C, W-135 and Y**

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq$ 1:8 against each of the serogroups A, C, W-135 and Y <sup>[37]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers $\geq$  1:8 against each of the N. meningitidis serogroups A, C, W-135 & Y before the fourth vaccination (Day 301). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups were assessed only for these two groups.

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

End point timeframe:

At Day 301 (before the fourth vaccination)

Notes:

[37] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group  | MenACWY Group     |  |  |
|----------------------------------|-------------------|-------------------|--|--|
| Subject group type               | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed      | 203               | 204               |  |  |
| Units: Percentage of subjects    |                   |                   |  |  |
| number (confidence interval 95%) |                   |                   |  |  |
| Serogroup A                      | 65 (58.0 to 71.6) | 58 (50.8 to 64.9) |  |  |
| Serogroup C                      | 77 (70.5 to 82.7) | 85 (79.3 to 89.9) |  |  |
| Serogroup W                      | 92 (86.5 to 95.4) | 91 (85.8 to 94.8) |  |  |
| Serogroup Y                      | 86 (80.1 to 90.2) | 91 (85.8 to 94.3) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with hSBA titers $\geq$ 1:8 against each of the serogroups A, C, W-135 and Y

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with hSBA titers $\geq$ 1:8 against each of the serogroups A, C, W-135 and Y <sup>[38]</sup> |
|-----------------|---|

End point description:

Percentage of subjects with hSBA titers $\geq$  1:8 against each of the N. meningitidis serogroups A, C, W-135 & Y at one month after the fourth vaccination (Day 331). This outcome measure applies to only rMenB+ACWY and MENACWY groups as the serogroups were assessed only for these two groups.

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

End point timeframe:

At Day 331 (one month after the fourth vaccination)

Notes:

[38] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | rMenB+ACWY Group    | MenACWY Group       |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 199                 | 204                 |  |  |
| Units: Percentage of subjects    |                     |                     |  |  |
| number (confidence interval 95%) |                     |                     |  |  |
| Serogroup A                      | 100 (98.1 to 100.0) | 96 (92.4 to 98.3)   |  |  |
| Serogroup C                      | 99 (97.1 to 99.99)  | 100 (98.1 to 100.0) |  |  |



|             |                     |                     |  |  |
|-------------|---------------------|---------------------|--|--|
| Serogroup W | 100 (98.0 to 100.0) | 100 (98.0 to 100.0) |  |  |
| Serogroup Y | 98 (95.7 to 99.69)  | 99 (97.3 to 99.99)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with solicited local and systemic Adverse Events (AEs)

|                 |   |
|-----------------|---|
| End point title | Number of subjects with solicited local and systemic Adverse Events (AEs) |
|-----------------|---|

End point description:

Number of subjects with solicited local and systemic AEs during the 7 days (including the day of vaccination) after any vaccination

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

End point timeframe:

From Day 1 (6 hours) to Day 7 after each vaccination (Days 1, 61, 121 and 301)

| End point values                        | rMenB+ACWY Group | rMenB Group     | MenACWY Group   |  |
|---|------------------|-----------------|-----------------|--|
| Subject group type                      | Reporting group  | Reporting group | Reporting group |  |
| Number of subjects analysed             | 240              | 232             | 237             |  |
| Units: Participants                     |                  |                 |                 |  |
| Any                                     | 235              | 226             | 194             |  |
| Any local                               | 220              | 214             | 157             |  |
| Any Systemic                            | 217              | 217             | 178             |  |
| Erythema (vaccination 1)                | 101              | 102             | 44              |  |
| Induration (vaccination 1)              | 111              | 102             | 22              |  |
| Swelling (vaccination 1)                | 82               | 86              | 22              |  |
| Tenderness (vaccination 1)              | 162              | 159             | 73              |  |
| Change in Eating Habits (vaccination 1) | 53               | 47              | 34              |  |
| Diarrhea (vaccination 1)                | 46               | 41              | 42              |  |
| Irritability (vaccination 1)            | 111              | 121             | 87              |  |
| Persistent Crying (vaccination 1)       | 124              | 132             | 85              |  |
| Rash (vaccination 1)                    | 19               | 28              | 18              |  |
| Sleepiness (vaccination 1)              | 69               | 78              | 54              |  |
| Vomiting (vaccination 1)                | 14               | 28              | 23              |  |
| Fever (vaccination 1)                   | 49               | 54              | 10              |  |
| Treatment of Pain/Fever (vaccination 1) | 82               | 98              | 25              |  |
| Erythema (vaccination 2)                | 97               | 102             | 47              |  |
| Induration (vaccination 2)              | 99               | 110             | 32              |  |
| Swelling (vaccination 2)                | 78               | 83              | 24              |  |
| Tenderness (vaccination 2)              | 142              | 138             | 66              |  |
| Change in Eating Habits (vaccination 2) | 46               | 44              | 31              |  |
| Diarrhea (vaccination 2)                | 37               | 36              | 24              |  |
| Irritability (vaccination 2)            | 99               | 95              | 70              |  |

|   |     |     |    |  |
|---|-----|-----|----|--|
| Persistent Crying (vaccination 2)       | 104 | 108 | 66 |  |
| Rash (vaccination 2)                    | 16  | 21  | 13 |  |
| Sleepiness (vaccination 2)              | 51  | 55  | 45 |  |
| Vomiting (vaccination 2)                | 10  | 21  | 17 |  |
| Fever (vaccination 2)                   | 48  | 54  | 15 |  |
| Treatment of Pain/Fever (vaccination 2) | 74  | 91  | 29 |  |
| Erythema (vaccination 3)                | 86  | 96  | 35 |  |
| Induration (vaccination 3)              | 92  | 103 | 30 |  |
| Swelling (vaccination 3)                | 73  | 82  | 19 |  |
| Tenderness (vaccination 3)              | 139 | 128 | 59 |  |
| Change in Eating Habits (vaccination 3) | 42  | 45  | 33 |  |
| Diarrhea (vaccination 3)                | 24  | 40  | 25 |  |
| Irritability (vaccination 3)            | 83  | 84  | 61 |  |
| Persistent Crying (vaccination 3)       | 90  | 92  | 60 |  |
| Rash (vaccination 3)                    | 10  | 11  | 11 |  |
| Sleepiness (vaccination 3)              | 39  | 46  | 39 |  |
| Vomiting (vaccination 3)                | 7   | 27  | 14 |  |
| Fever (vaccination 3)                   | 37  | 38  | 25 |  |
| Treatment of Pain/Fever (vaccination 3) | 57  | 69  | 31 |  |
| Erythema (vaccination 4)                | 73  | 88  | 37 |  |
| Induration (vaccination 4)              | 84  | 93  | 29 |  |
| Swelling (vaccination 4)                | 75  | 74  | 21 |  |
| Tenderness (vaccination 4)              | 126 | 129 | 64 |  |
| Change in Eating Habits (vaccination 4) | 59  | 45  | 40 |  |
| Diarrhea (vaccination 4)                | 29  | 28  | 23 |  |
| Irritability (vaccination 4)            | 81  | 74  | 57 |  |
| Persistent Crying (vaccination 4)       | 84  | 89  | 56 |  |
| Rash (vaccination 4)                    | 11  | 13  | 6  |  |
| Sleepiness (vaccination 4)              | 50  | 37  | 33 |  |
| Vomiting (vaccination 4)                | 15  | 14  | 11 |  |
| Fever (vaccination 4)                   | 53  | 46  | 19 |  |
| Treatment of Pain/Fever (vaccination 4) | 71  | 67  | 31 |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with unsolicited adverse events

|                 |  |
|-----------------|--|
| End point title | Number of subjects with unsolicited adverse events |
|-----------------|--|

End point description:

An unsolicited adverse event (AE) is defined as any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product at any dose that does not necessarily have to have a causal relationship with this treatment.

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

End point timeframe:

From Day 1 to Day 7 after each vaccination (Days 1, 61, 121 and 301)

| End point values                    | rMenB+ACWY Group | rMenB Group     | MenACWY Group   |  |
|-------------------------------------|------------------|-----------------|-----------------|--|
| Subject group type                  | Reporting group  | Reporting group | Reporting group |  |
| Number of subjects analysed         | 249              | 249             | 246             |  |
| Units: Participants                 |                  |                 |                 |  |
| Any                                 | 103              | 116             | 70              |  |
| Any unsolicited AEs( vaccination 1) | 63               | 62              | 20              |  |
| Any unsolicited AEs( vaccination 2) | 60               | 69              | 29              |  |
| Any unsolicited AEs( vaccination 3) | 57               | 63              | 23              |  |
| Any unsolicited AEs( vaccination 4) | 44               | 58              | 13              |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with SAEs, AEs leading to withdrawal and medically attended AEs (MAEs)

|                 |   |
|-----------------|---|
| End point title | Number of subjects with SAEs, AEs leading to withdrawal and medically attended AEs (MAEs) |
|-----------------|---|

End point description:

A serious adverse event is any untoward medical occurrence that at any dose results in death/ is life threatening/requires prolonged hospitalization/Persistent or significant disability/incapacity/congenital anomaly/or birth defect.

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

End point timeframe:

Throughout the whole study period (from Day 1 upto Day 331)

| End point values                        | rMenB+ACWY Group | rMenB Group     | MenACWY Group   |  |
|---|------------------|-----------------|-----------------|--|
| Subject group type                      | Reporting group  | Reporting group | Reporting group |  |
| Number of subjects analysed             | 249              | 249             | 246             |  |
| Units: Participants                     |                  |                 |                 |  |
| Any SAEs                                | 6                | 13              | 11              |  |
| Any Medically Attended AEs              | 177              | 188             | 183             |  |
| Any AEs leading to premature withdrawal | 0                | 2               | 1               |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local and systemic AEs were collected from day 1 (6 hours) upto day 7 after each vaccination. Unsolicited AEs were collected from day 1 to day 7.

Adverse event reporting additional description:

Serious Adverse Events (SAEs) were collected throughout the whole study period (from day 1 to day 331). All the unsolicited AEs were reported by non-systematic assessment and the solicited AEs were reported by systematic assessment

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | rMenB+ACWY Group |
|-----------------------|------------------|

Reporting group description:

Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ / MenACWY vaccines, concomitantly administered at 3, 5, 7 and 13 months of age.

|                       |             |
|-----------------------|-------------|
| Reporting group title | rMenB Group |
|-----------------------|-------------|

Reporting group description:

Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ administered at 3, 5, 7 and 13 months of age

|                       |               |
|-----------------------|---------------|
| Reporting group title | MenACWY Group |
|-----------------------|---------------|

Reporting group description:

Approximately 250 healthy infants aged 3 months who received 4 doses of MenACWY administered at 3, 5, 7 and 13 months of age.

| Serious adverse events                            | rMenB+ACWY Group | rMenB Group      | MenACWY Group    |
|---|------------------|------------------|------------------|
| Total subjects affected by serious adverse events |                  |                  |                  |
| subjects affected / exposed                       | 6 / 249 (2.41%)  | 13 / 249 (5.22%) | 11 / 246 (4.47%) |
| number of deaths (all causes)                     | 0                | 0                | 0                |
| number of deaths resulting from adverse events    |                  |                  |                  |
| Injury, poisoning and procedural complications    |                  |                  |                  |
| Limb injury                                       |                  |                  |                  |
| subjects affected / exposed                       | 0 / 249 (0.00%)  | 1 / 249 (0.40%)  | 0 / 246 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            | 0 / 0            |
| Multiple injuries                                 |                  |                  |                  |
| subjects affected / exposed                       | 0 / 249 (0.00%)  | 1 / 249 (0.40%)  | 0 / 246 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            | 0 / 0            |
| Skull fracture                                    |                  |                  |                  |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 249 (0.00%) | 0 / 249 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vascular disorders                              |                 |                 |                 |
| Kawasaki's disease                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 249 (0.40%) | 0 / 249 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Febrile convulsion                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 249 (0.00%) | 0 / 249 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Blood and lymphatic system disorders            |                 |                 |                 |
| Anaemia   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 249 (0.00%) | 1 / 249 (0.40%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Immune system disorders                         |                 |                 |                 |
| Milk allergy                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 249 (0.00%) | 0 / 249 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Atelectasis                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 249 (0.00%) | 1 / 249 (0.40%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Bronchospasm                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 249 (0.00%) | 0 / 249 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|  |                                   |                                   |                                   |
|--|-----------------------------------|-----------------------------------|-----------------------------------|
| Infections and infestations<br>Bronchiolitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                     | 1 / 249 (0.40%)<br>0 / 1<br>0 / 0 | 3 / 249 (1.20%)<br>0 / 3<br>0 / 0 | 4 / 246 (1.63%)<br>0 / 5<br>0 / 0 |
| Bronchitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 249 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 249 (0.40%)<br>0 / 1<br>0 / 0 | 0 / 246 (0.00%)<br>0 / 0<br>0 / 0 |
| Exanthema subitum<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 1 / 249 (0.40%)<br>0 / 1<br>0 / 0 | 0 / 249 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 246 (0.00%)<br>0 / 0<br>0 / 0 |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 1 / 249 (0.40%)<br>0 / 1<br>0 / 0 | 2 / 249 (0.80%)<br>0 / 2<br>0 / 0 | 0 / 246 (0.00%)<br>0 / 0<br>0 / 0 |
| Gastroenteritis viral<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 0 / 249 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 249 (0.40%)<br>0 / 1<br>0 / 0 | 0 / 246 (0.00%)<br>0 / 0<br>0 / 0 |
| Pertussis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 0 / 249 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 249 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 246 (0.41%)<br>0 / 1<br>0 / 0 |
| Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 0 / 249 (0.00%)<br>0 / 0<br>0 / 0 | 2 / 249 (0.80%)<br>0 / 2<br>0 / 0 | 1 / 246 (0.41%)<br>0 / 1<br>0 / 0 |
| Pneumonia bacterial<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 1 / 249 (0.40%)<br>0 / 1<br>0 / 0 | 3 / 249 (1.20%)<br>0 / 3<br>0 / 0 | 1 / 246 (0.41%)<br>0 / 1<br>0 / 0 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Pneumonia viral                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 249 (0.00%) | 1 / 249 (0.40%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pyelonephritis                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 249 (0.40%) | 0 / 249 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Urinary tract infection                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 249 (0.40%) | 0 / 249 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Urosepsis                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 249 (0.40%) | 0 / 249 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

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

| <b>Non-serious adverse events</b>                     | <b>rMenB+ACWY Group</b> | <b>rMenB Group</b> | <b>MenACWY Group</b> |
|---|-------------------------|--------------------|----------------------|
| Total subjects affected by non-serious adverse events |                         |                    |                      |
| subjects affected / exposed                           | 240 / 249 (96.39%)      | 232 / 249 (93.17%) | 221 / 246 (89.84%)   |
| Nervous system disorders                              |                         |                    |                      |
| Somnolence  |                         |                    |                      |
| subjects affected / exposed                           | 106 / 249 (42.57%)      | 115 / 249 (46.18%) | 87 / 246 (35.37%)    |
| occurrences (all)                                     | 226                     | 236                | 189                  |
| General disorders and administration site conditions  |                         |                    |                      |
| Injection site pain                                   |                         |                    |                      |
| subjects affected / exposed                           | 212 / 249 (85.14%)      | 207 / 249 (83.13%) | 131 / 246 (53.25%)   |
| occurrences (all)                                     | 593                     | 583                | 267                  |
| Crying  |                         |                    |                      |
| subjects affected / exposed                           | 176 / 249 (70.68%)      | 184 / 249 (73.90%) | 129 / 246 (52.44%)   |
| occurrences (all)                                     | 434                     | 463                | 301                  |
| Injection site erythema                               |                         |                    |                      |

|   |                           |                           |                           |
|---|---------------------------|---------------------------|---------------------------|
| subjects affected / exposed<br>occurrences (all)  | 147 / 249 (59.04%)<br>424 | 162 / 249 (65.06%)<br>480 | 104 / 246 (42.28%)<br>211 |
| Injection site induration<br>subjects affected / exposed<br>occurrences (all)   | 144 / 249 (57.83%)<br>575 | 152 / 249 (61.04%)<br>609 | 57 / 246 (23.17%)<br>116  |
| Injection site swelling<br>subjects affected / exposed<br>occurrences (all)   | 130 / 249 (52.21%)<br>380 | 138 / 249 (55.42%)<br>403 | 56 / 246 (22.76%)<br>88   |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 125 / 249 (50.20%)<br>201 | 121 / 249 (48.59%)<br>210 | 60 / 246 (24.39%)<br>79   |
| Gastrointestinal disorders<br>Diarrhoea<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                                      | 108 / 249 (43.37%)<br>181 | 98 / 249 (39.36%)<br>196  | 89 / 246 (36.18%)<br>163  |
| Vomiting<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)   | 36 / 249 (14.46%)<br>51   | 64 / 249 (25.70%)<br>105  | 49 / 246 (19.92%)<br>82   |
| Respiratory, thoracic and mediastinal disorders<br>Bronchial hyperreactivity<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 17 / 249 (6.83%)<br>25    | 12 / 249 (4.82%)<br>16    | 15 / 246 (6.10%)<br>26    |
| Bronchospasm<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)   | 9 / 249 (3.61%)<br>13     | 12 / 249 (4.82%)<br>16    | 13 / 246 (5.28%)<br>23    |
| Skin and subcutaneous tissue disorders<br>Rash<br>subjects affected / exposed<br>occurrences (all)  | 46 / 249 (18.47%)<br>62   | 57 / 249 (22.89%)<br>81   | 42 / 246 (17.07%)<br>62   |
| Dermatitis diaper   |                           |                           |                           |



|   |                    |                    |                    |
|---|--------------------|--------------------|--------------------|
| subjects affected / exposed                 | 12 / 249 (4.82%)   | 16 / 249 (6.43%)   | 14 / 246 (5.69%)   |
| occurrences (all)                           | 16                 | 16                 | 15                 |
| Dermatitis atopic                           |                    |                    |                    |
| subjects affected / exposed                 | 6 / 249 (2.41%)    | 11 / 249 (4.42%)   | 17 / 246 (6.91%)   |
| occurrences (all)                           | 6                  | 12                 | 20                 |
| Psychiatric disorders                       |                    |                    |                    |
| Irritability                                |                    |                    |                    |
| alternative assessment type: Non-systematic |                    |                    |                    |
| subjects affected / exposed                 | 155 / 249 (62.25%) | 170 / 249 (68.27%) | 125 / 246 (50.81%) |
| occurrences (all)                           | 409                | 418                | 320                |
| Eating disorder                             |                    |                    |                    |
| alternative assessment type: Non-systematic |                    |                    |                    |
| subjects affected / exposed                 | 110 / 249 (44.18%) | 100 / 249 (40.16%) | 85 / 246 (34.55%)  |
| occurrences (all)                           | 214                | 194                | 162                |
| Infections and infestations                 |                    |                    |                    |
| Nasopharyngitis                             |                    |                    |                    |
| subjects affected / exposed                 | 81 / 249 (32.53%)  | 87 / 249 (34.94%)  | 78 / 246 (31.71%)  |
| occurrences (all)                           | 161                | 164                | 135                |
| Viral upper respiratory tract infection     |                    |                    |                    |
| subjects affected / exposed                 | 72 / 249 (28.92%)  | 82 / 249 (32.93%)  | 86 / 246 (34.96%)  |
| occurrences (all)                           | 104                | 127                | 123                |
| Pharyngitis                                 |                    |                    |                    |
| subjects affected / exposed                 | 50 / 249 (20.08%)  | 50 / 249 (20.08%)  | 50 / 246 (20.33%)  |
| occurrences (all)                           | 57                 | 59                 | 60                 |
| Bronchiolitis                               |                    |                    |                    |
| subjects affected / exposed                 | 34 / 249 (13.65%)  | 34 / 249 (13.65%)  | 37 / 246 (15.04%)  |
| occurrences (all)                           | 40                 | 37                 | 37                 |
| Gastroenteritis                             |                    |                    |                    |
| subjects affected / exposed                 | 31 / 249 (12.45%)  | 40 / 249 (16.06%)  | 38 / 246 (15.45%)  |
| occurrences (all)                           | 37                 | 44                 | 43                 |
| Conjunctivitis                              |                    |                    |                    |
| subjects affected / exposed                 | 20 / 249 (8.03%)   | 18 / 249 (7.23%)   | 24 / 246 (9.76%)   |
| occurrences (all)                           | 23                 | 18                 | 25                 |
| Candida nappy rash                          |                    |                    |                    |
| subjects affected / exposed                 | 15 / 249 (6.02%)   | 12 / 249 (4.82%)   | 6 / 246 (2.44%)    |
| occurrences (all)                           | 16                 | 14                 | 6                  |

|                             |                  |                  |                  |
|-----------------------------|------------------|------------------|------------------|
| Rhinitis                    |                  |                  |                  |
| subjects affected / exposed | 14 / 249 (5.62%) | 13 / 249 (5.22%) | 19 / 246 (7.72%) |
| occurrences (all)           | 17               | 16               | 21               |
| Viral rash                  |                  |                  |                  |
| subjects affected / exposed | 13 / 249 (5.22%) | 14 / 249 (5.62%) | 13 / 246 (5.28%) |
| occurrences (all)           | 13               | 14               | 13               |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported